Pathology of the lower female genital tract

Vulva

**The moist, hair-bearing skin & delicate membrane of the vulva are vulnerable to many nonspecific microbe-induced inflammations & dermatologic disorders.

Intense itching (pruritus**) & subsequent scratching often exacerbate the primary condition.

The 5 most important specific forms of vulvar infection related to **Sexually Transmitted Diseases in North America are:

(1)human papillomavirus (**HPV**), producing condylomataacuminata& vulvar intraepithelial neoplasia;

(2)herpes genitalis{herpes simplex virus [**HSV**1 or 2]} causing a vesicular eruption;

(3) **gonococcal**suppurativeinfection of the vulvovaginal glands;

(4) **syphilis**, with its primary chancre at the site of inoculation;

(5) **candida** vulvitis.

Vulvar Diseases		Cause /RF		Grossly	Histology	Note
non-neoplastic cannot transform to cancer	Contact Dermatitis	is a reactive inflammation to exogenous stimulus, whether (I) **Irritant contact dermatitis** to an irritant e.g., urine, soaps, detergents, antiseptics, deodorants, or alcohol; or (II) **Allergic contact dermatitis** to an allergen e.g., allergy to perfumes & other additives in creams, lotions, & soaps, chemical treatments on clothing & other antigens.		, Both irritant & allergic contact dermatitis may present as well-defined erythematous weeping & crusting papules & plaque	either as an (1) **acute** spongiotic dermatitis (fluid sacs) or as (2) **subacute** dermatitis with epithelial hyperplasia.	One of the most common causes of vulvar pruritus
	•Lichen sclerosus	uncertain, (?)autoimmune •postmenopausal women.		Both may coexist in different areas in the same female & both may appear grossly as depigmented white patches (leukoplakia). •smooth, white plaques; **thinned** out skin	thinning of epidermis, disappearance of rete pegs, hydropic degeneration of basal cells	•Although the lesion in lichen sclerosis is **not pre-malignant** by itself, women with symptomatic lichen sclerosis have 15% chance of developing SCCa in their lifetime.
	•Lichen Simplex Chronicus	•End result of many inflammatory conditions.			hyperkeratosis + hypergranulosis + acanthosis(thickening epidermis) + epithelium shows no atypia with pronounced leukocytic infiltration of the dermis	•**no increased predisposition to cancer**, however, maybe present at margins of adjacent cancer.
	•Condyloma into 2 distinctive biologic forms:	I)Condyloma talata not commonly seen today	secondary syphilis	moist, flat or minimally elevated, highly infectious ‹syphilitic lesions,	.	•**HPV types isolated from cancers differ from those found in condylomas.** •**Condylomais not precancerous by itself**
		condylomata acuminate more common	• **Anogenital warts (HPV type 6 and HPV type11)**	They occur anywhere on the anogenital surface, usually single, but more .often multiple On the vulva, • they range from a few mm to many cm in Ø& are red-pink to pink-brown	papillary & distinctly elevated or flat & rugose • **Hallmark= koilocytosis (perinuclear cytoplasmic vacuolization + nuclear pleomorphism).**	

Vulvar diseases		Cause		Grossly	Histology	Note
Neoplastic vulvar diseases	**Vulvar Intraepithelial Neoplasia(VIN)** •high grade VIN= VIN II or VIN III. •VIN III = carcinoma in situ.	**•genetic, immunologic, or environmental influences (e.g., cigarette smoking or super infection with new strains of HPV) determine the course.**		**•may be multiple foci, or it may coexist with an invasive lesion.**		**•VIN may be present for many years before progression to cancer.**
	Invasive Carcinoma of Vulva Squamous Cell Carcinoma (most common); Others adenocarcinomas, melanomas, or basal cell carcinomas .	**basaloid or poorly differentiated SCC**	*most common (75% to 90%) *HPV-related (types 16 & 18) *relatively younger	HPV lesions also in vagina and cervix.	Poorly differentiated cells	•3% of all genital tract cancers in women. • > 60 years. • 90% squamous cell carcinomas;
		well-differentiated SCC	*Less common ***Not** HPV-related *older women (60-70s).	Maybe found adjacent to lichen simplex or sclerosus	well to moderately differentiated The overlying epithelium **lacks** the typical cytologic changes of VIN &T tend to be well differentiated SCC	
	Extramammary Paget Disease	**like that of the breast, is essentially a form of intraepithelial carcinoma**		red, scaly, crusted plaque or as an inflammatory dermatosis.	Showlarge malignant epithelioid cells infiltrate the epidermis, singly & in groups, with abundant granular cytoplasm & occasional cytoplasmic vacuoles **containing mucin that stains <u>positive</u> for PAS.** When the Paget cells are confined to the epidermis, the lesion may persist for years or decades without evidence of invasion.	Unlike the breast, where Paget disease is always associated with an underlying ca, the majority of cases of vulvar Paget disease have no demonstrable underlying ca.

VAGINA

VAGINITIS

*Vaginitis is a relatively common transient clinical problem produces a **vaginal discharge (leukorrhea).**

*A large variety of organisms have been implicated, including bacteria, fungi, & parasites and …..

*Many represent **normal commensals (normal flora)** that become pathogenic in conditions such as

(1) DM,

(2) systemic antibiotic therapy that disrupts the normal microbial flora,
(3) after abortion or pregnancy, or

(4) in elderly persons with compromised immune function, &

(5) in patients with AIDS.

****Candidal(monilial) vaginitis** produces **a curdy white discharge.**

*This organism is present in about 5% of normal adults, & so the appearance of symptomatic infection almost always involves predisposing influences or sexual transmission of a new, more aggressive strain.

****T. vaginalis** produces a **watery copious gray-green discharge** in which parasites can be identified microscopically.

****Nonspecific atrophic vaginitis** may be encountered in **postmenopausal** women with preexisting mucosal atrophy (lack of estrogen)

**Vaginal Neoplastic Diseases:

vaginal clear cell adenocarcinoma	Sarcoma botryoides(embryonal rhabdomyosarcoma)
•Are usually encountered in young women in their late teens to early 20s whose mothers took **diethylstilbestrol during pregnancy**. •Sometimes these cancers do not appear until the 3rd or 4th decade of life. •The **risk for ca is less than 1 per 1000** of those exposed in utero. •In about one-third of instances these **clear cell adenocarcinoma** arise in the **cervix**.	•Rare sarcoma of **skeletal** muscle type •infants and **children**<5 years. •soft polypoid masses (botryoides= grape-like). •Primitive cells (**rhabdomyoblasts**)

cervix

The cervix serves as a **barrier** to the entrance of air & the microflora of the normal vagina, yet **it must permit** the escape of menstrual flow & be capable of dilating to accommodate childbirth.

CERVICITIS

*clinically : Cervicitis are extremely common & are associated with a mucopurulent (pus + mucous) to purulent **vaginal discharge**.

*histology : Cytologic examination of the discharge reveals WBC & inflammatory atypia of shed epithelial cells, as well as possible microorganisms.

***Grossly**, nonspecific cervicitis may be either:

acute nonspecific form	**chronic nonspecific cervicitis.**
relatively uncommon	common
limited to **postpartum (after delivery or abortion)** women& is usually caused by staphylococci or streptococci	nearly ubiquitous entity

Frequently, overgrowth of the regenerating squamous epithelium blocks the orifices of endocervical glands in the transformation zone to produce small **Nabothian cysts lined by columnar mucus-secreting epithelium

Cervical Intraepithelial Neoplasia (CIN)

Intraepithelial :

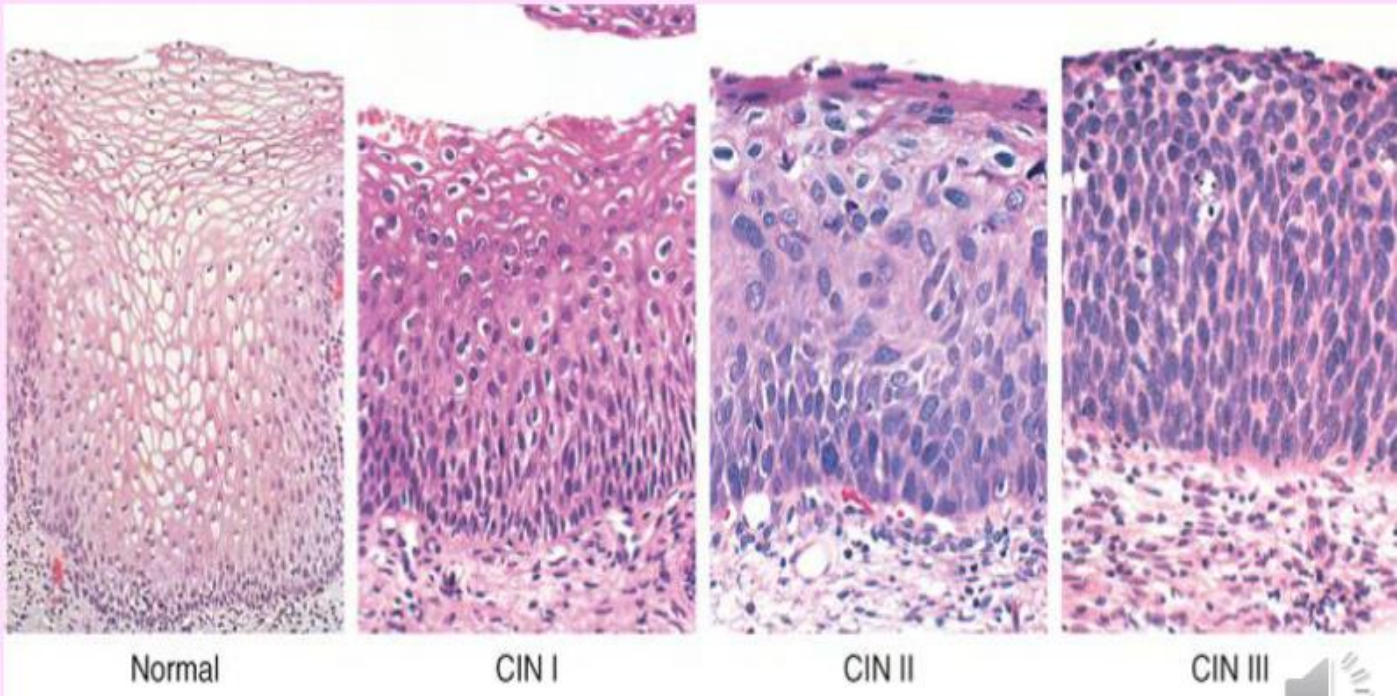
يعني ما تعدت BM

**Dysplasia graded depending on the extent of epithelial involvement:

طبعا قصدنا عن squ epithelium وتعتمد تقسيمة على كم هو ماخد من كل epithelium كل ما تقدم مرحلة كانت بصير اصعب انه يرجع لنورمال وتزيد ال possibility انه يتحول لكانسر لحد ما يوصل المرحلة ٣ بصير اصلا كانسر بمحله وما برجع

كل ما زادت مرحلة بتزيد dysplasia ويقل differentiation و maturation

Spectrum of CIN: Normal cervical squamous epithelium for comparison. CIN I with koilocytotic atypia; CIN II with progressive atypia in all epithelial layers CIN III (ca in situ) with full thickness diffuse atypia & loss of maturation.



	*CIN I:	*CIN II	CIN III	(IV)
The extent	Mild dysplasia (<third of full epithelial thickness)	Moderate dysplasia (up to 2/3 of full epithelial thickness)	Severe dysplasia in full epithelial thickness (carcinoma in situ	**the alterations are confined to the epithelial layer & its glands.** n
Morphology	begin with **mild dysplasia**, **characterized** by **Koilocytosis{**produced by cytopathic effect of HPV} seen mostly in the superficial layers of the epithelium, **composed** of **nuclear hyperchromasia& angulation with perinuclear vacuolization**	**dysplasia is more severe**, (1) maturation of keratinocytes delayed into the middle third of the epithelium, (2) cell & nuclear size pleomorphism, heterogeneity of nuclear chromatin & (3) **mitoses** above the basal layer, extending in to the middle third of the epithelium. The superficial layer of cells shows some differentiation.	**greater pleomorphismin cell & nuclear size, marked hyperchromasia, &, disorderly orientation of the cells,** & normal or abnormal mitoses; **these changes affect virtually all layers of the epithelium & are characterized by loss of maturation (F19-7& 19-8);** i.e., the differentiation of surface cells & koilocytotic changes have usually disappeared	**In time, dysplastic changes become more atypical & may extend into the end cervical glands, but** **Thesechanges constitute carcinoma in situ.** **The next stage, if it is to appear, is invasive ca, however, as emphasized, there is no inevitability to this progression**

*It is important to emphasize here that: nearly all invasive cervical SCC arise from precursor CIN.

*However, Not all cases of CIN progress to invasive ca& indeed many persist without change or even regress!

يعني كل كانسر اصله CIN بس مو كل كل CIN بضرورة بتبعه كانسر

**CIN-Epidemiology and Pathogenesis

*peak age of CIN is 30 years, whereas invasive cancer is about 45 years.

**RISK FACTORS :

*HPV

-high-risk HPV types (16, 18, 45, and 31), account for majority of cervical ca

-HPV 16 and 18 usually integrate into the host genome and express large amounts of **E6 and E7 proteins, which block or inactivate tumor suppressor genes p53and RB, respectively**.

-Recently introduced **HPV vaccine** used in USA and Europe is effective in preventing HPV infections and hence cervical cancers.

كان زمان هاد الكانسر شائع بسمن لما صاروا يعملوا PAP smear قلت نسبة حدوثه كتير غير هيك عملوله مطعوم

-HPV can be detected by molecular methods in nearly all precancerous lesions and invasive neoplasms.

شو اهمية هاي العبارة ؟؟؟ لانه مثلا لو عملنا خزعة عشان نشوف هاد الفيروس ما رح يميزلنا بين الحالات يلي ما قبل الكانسر والحالات يلي وصلت للكانسر لانه موجود فيهم كلهم عشان هيك ب PAP SMEAAR بشوفه التغيرات يلي بتحصل على الخلي مو الفيروس

-**Cytological examination** can detect CIN long before any abnormality can be seen grossly.

اصلا عبيل ما يبين الكانسر GROSSLY بده وقت كبيييير

طب بعد الفحص مين رح نضل نتابع ؟؟

-**The follow-up of such women has revealed that:**

(I) Precancerous CIN may precede the development of an overt ca by many years, or in some cases even decades.

Overt صريح واضح

However, **a fraction of cases of CIN progress to invasive ca.**

-**The precancerous CIN may begin as:**

(I) low-grade & progress to higher CIN grade, or

ممكن تبدأ ب low وبعدها تتطور الى high

(II) high-grade CIN arise de novo, depending on:

ممكن من اولها تكون high

•the **location of the HPV infection** in the transformation zone.

•**type of HPV** infection(high or low risk)

•other contributing host factors

*Important risk factors for the development of CIN & invasive cervical ca are:

(1**) Early age** at first intercourse.

(2) **Multiple** sexual partners.

(3) A **male partner with multiple** previous sexual partners.

(4)**Persistent infection** by "high-risk" **HPV** papilloma viruses.

*Many other risk factors can be related to these 4, including the

1-higher incidence in lower socioeconomic groups

2-the association with multiple pregnancies,& rarity among virgins,.

*They point to the likelihood of sexual transmission of a causative agent, in this case > **HPV**.

Cervical cancer

*most common are **SCC (75%),** followed by adenocarcinomas and adenosquamous carcinomas (20%), and neuroendocrine carcinomas (<5%).

*SCC now has peak incidence at 45 years, almost **10 to 15 years after detection of their precursors: cervical intraepithelial neoplasia(CIN).**

*The only reliable way to monitor the course of the disease is with careful follow-up & repeat biopsies.

****Grossly**

*invasive cervical ca develop in the region of the **transformation zone** & range from **invisible** microscopic foci of early stromal invasion to grossly **visible exophytic** cancers encircling the os Ca encircling the cervix & penetrating into the underlying stroma produce a "barrel cervix," which can be identified by direct palpation.

**spread :

*Extension into the **parametrial** soft tissues can fix the uterus to the pelvic structures.

*Spread to **pelvic LNs** is determined by

(1) T depth (ranging from < 1% for T < 3 mm in depth to more than 10% once invasion is more than 5 mm), &

(2) the presence of capillary-lymphatic invasion,

****Clinical Aspects Of Cervical Cancers**

Stage 0	**stage 1**	**stage 2**	**stage 3**	**stage 4**
The vast majorities of cervical T are diagnosed in the preinvasive phase & appear as white areas on colposcopy examination after application of dilute acetic acid	*With the advent of the Pap smear, an increase proportion of cervical ca are diagnosed early in their course	**More advanced** cervical ca are invariably seen in:- •(1) women who either have never had a Pap smear, or •(2) have waited many years since the prior smear. •Such T may cause unexpected **vaginal bleeding, leukorrhea, painful coitus (dyspareunia), & dysuria**.		
•CIN: treatment by **laser or cone biopsy**	•Invasive cancer: surgical excision			
Prognosis: the 5-year survival: **100%**	**90%**	**82%**	**35%**	**10%.**

****Prevention:**

HPV vaccine can prevent the occurrence of cervical ca.

Detection of precursors by cytologic examination & their eradication by **laser vaporization** or **cone biopsy** is the most effective method of cancer prevention.

Endocervical Polyp

Is **inflammatory lesion which may protrude as polypoid mass through the exocervix.

**grossly :

It can be large (few cm), soft & smooth with glistening surface & underlying cystically dilated spaces filled with mucinous secretion.

A rounded, soft, sessile gelatinous polyp fills the endocervical canal

they have **no malignant potential.

Uterine Pathology

ENDOMETRITIS

•Inflammation of the endometrium.

•Causes:

1-pelvic inflammatory disease **(PID)**

2-miscarriage or delivery

3-intrauterine device **(IUCD)**.

زي اللولب

•Clinically:

Fever (infection) , abdominal pain, menstrual abnormalities, infertility and ectopic pregnancy due to damage to the fallopian tubes.

لانه ممكن خلال ال infection of uterus يتضرر معه fallopian tube

•Rx: removal of cause, antibiotics, D&C.

**types :

Acute	Chronic	Occasionally **TB endometritis**
due to N. gonorrhoeae or C. trachomatis	frequently due to chlamydial & Mycoplasma	may present, frequently with TB salpingitis & peritonitis
with predominant neutrophilic cell respond	with predominant lymphoplasma cytic cell response	
	the diagnosis of which requires the presence of plasma cells in the endometrium.. لانه ال lymphocytes اصلا موجودةبالتالي لازم اعتمد بالتشخيص على plasma cells	

ADENOMYOSIS

•Is the growth of the basal layer of the endometrium down into the myometrium.

Adeno معناها glands

Myosis معناها SMC

يعني glands+ stroma جوا العضلة رح تنزف بالعضلة ما رح يطلع برا ورح تنتفخ وتضغط على الاعصاب بزيادة ويعمل الم

طب شو سبب تبعه ؟؟ ما بعرفوا بس يعتقد انه صار proliferation of basal layer عنيف قامت ال gland غطست لجوا العضلة هي وال stroma تبعتها

•Endometrial stroma, glands, or both embedded in myometrium.

•Grossly

• Thick uterine wall, enlarged uterus.

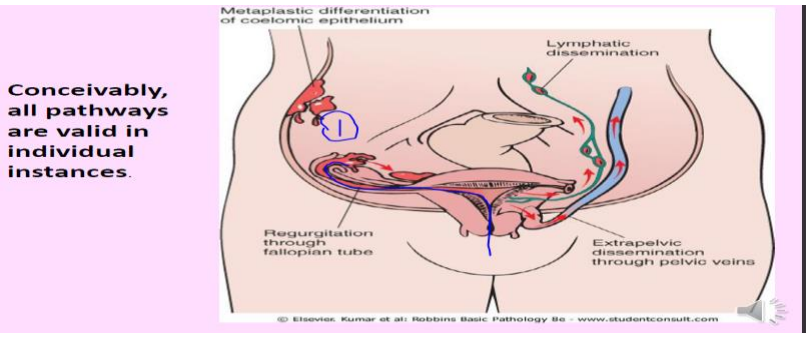
اكيد لانه صار growth

•Clinically :

• Derived from **stratum basalis** **<u>no cyclical bleeding.</u>**

•Marked adenomyosis may produce **premenstrual menorrhagia, dysmenorrhea (painful menses),** (due to enlarged uterus, uterine contractions are exaggerated)& pelvic pain

ENDOMETRIOSIS

Def.	• Is the presence of endometrial glands and stroma outside the uterus. • It occurs in 10% of women in their reproductive years & in 50% of women with infertility	
	•Multifocal, **multiple tissues in pelvis** (ovaries, pouch of Douglas, uterine ligaments, tubes, and rectovaginal septum). طب الالم بهاي الحالة وين رح يكون ؟؟ حسب المكان يلي رح تروح عليه البطانة المهاجرة عشان هيك حكينا بالكلينيكال سكلز انه مكان الالم variable	•Sometimes **distant** sites e.g. **umbilicus, lymph nodes, lungs**, etc
•ENDOMETRIOSIS-Pathogenesis Three theories:	1-***regurgitation theory. (***most accepted). Menstrual backflow through tubes and implantation. Accidental implantation of endometrial tissue during previous **caesarean section** in the abdominal wound caused the formation of a raised greyish-white mass of endometriotic tissue mass in the umbilicus within which there are several small blood-filled cysts. المفروض الدم يطلع من الرحم لحتى يطلع برا الجسم هون بهاي الحالة بصيرله backflow على fallopian tubes وممكن بهاي الحالة ال endometrial tissue يصر عليه implementation وبالتالي يحصل ectopic pregnancy وهاي ال glands and stroma بتكون functional و viable وبصير عليها كل phases الا انه مكانها مو مزبوط هلا النظرية بتفسرانه ازا راحت على مناطق قريبة من uterus طب ازا راحت على مناطق بعيدة ؟؟؟ يعني extrapelvic زي مثلا القلب او LN او skeletal muscles عجزت عن تفسيرها  2-***metaplastic theory***. Endometrial differentiation of coelomic epithelium. لانه ال origin تبع peritoneum هو نفسه endometrial tissue يعني انه اجا من epithelium بس هذا لا يفسر وجوده بمناطق غير epi زي المناطق يلي فيها CT مثلا ligaments 3-***vascular* or *lymphatic dissemination theory. May*** explain extrapelvic or intranodalim plants.	
•Grossly:	**in contrast to adenomyosis, **endometriosis** almost always contains **functioning endometrium ,**which undergoes **cyclic bleeding.** **Because blood collects in these abnormal foci, they usually appear grossly as **red-blue (new) to yellow-brown (old) nodules or implants**. contains **functional is endometrium ,**sounder goes **cyclic bleeding** **In the affected ovaries, **large blood-filled cysts** may form **chocolate cysts** as the blood ages **.**Seepage & organization of the blood leads to widespread fibrosis. هلا ال ovaries هي عبارة عن كرة مغلقة رح يضل ينتج دم بدون ما يطلع ويضل يتجمع ويتراكم يتغير لونه رح يبطل احمر رح يصير متل لون التشوكلت	

<table>
<tr><td></td><td>*Consequences: fibrosis, sealing of tubal fimbriated ends, and distortion of the ovaries. >> sterility</td></tr>
<tr><td>•Histology</td><td>*In all sites, the histologic diagnosis of endometriosis depends on finding 2 of the following 3 features within the lesions:
لازم نلاقي شغلتين من تلاتة
(1)endometrial gland,
(2) endometrial stroma (Positive CD10 immuno-stain) or
(3) hemosiderin pigment</td></tr>
<tr><td>•Clinical manifestations of endometriosis depend on its site:</td><td>►Endometriosis is a common cause of dysmenorrhea (painful menses) & pelvic pain; both of which are present in almost all cases of endometriosis as a result of intrapelvic bleeding & periuterine adhesions.
<table>
<tr><td>►Extensive scarring of the oviducts & ovaries</td><td>►rectal wall involvement,</td><td>►involvement of the uterine</td><td>►bladder serosa</td><td>►Ovarian endometriosis</td></tr>
<tr><td>produces lower abdominal discomfort & eventually causes sterility.</td><td>Pain on defecation</td><td>Dyspareunia (painful intercourse) &</td><td>dysuria</td><td>may present as a pelvic mass (chocolate cyst</td></tr>
</table></td></tr>
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DYSFUNCTIONAL UTERINE BLEEDING & ENDOMETRIAL HYPERPLASIA

**The most common problem for which women seek medical attention is some disturbance in menstrual function:

(1)Menorrhagia=profuse or prolonged menstrual bleeding

(2)Metrorrhagia = irregular bleeding between the periods,

(3)Ovulatory(intermenstrual) bleeding or

هدول تنين اتوقع انهم نفس الاشي

(4)Postmenopausal bleeding.

**Common causes include endometrial polyps, hyperplasia, ca, leiomyomas, & endometritis.

Vaginal bleeding may also be due to cervical & vagina lesions, such as polyps, cervicitis, or ca.

Dysfunctional Uterine Bleeding.

-Is the abnormal uterine bleeding **in the absence of a well-defined organic lesion in the uterus.**

-The 4 causes of dysfunctional bleeding are :

(I) Failure of ovulation . An ovulatory cycles are very common at both ends of reproductive life.

•with any dysfunction of the hypothalamic-pituitary axis.

• adrenal,

• thyroid;

• with a functioning ovarian lesion producing an excess of estrogen;

• with malnutrition

• debilitating disease •obesity •severe physical or emotional stress.

Whatever the cause…

****failure of ovulation** leads to >>>

an **excess of estrogen** relative to progesterone,>>>

with the endometrium (E) going through a proliferative phase that is **not followed by the normal secretory phase. >>>**

The E shows relatively **scant stroma**, which **requires progesterone for its support. >>>**

The **poorly supported** E partially **collapses,** >>>

rupturing the spiral arteries, causes the **bleeding.**

(II) Inadequate luteal phase.

The **corpus luteum may fail to mature** normally or may regress prematurely, leading to a **relative lack of progesterone**.

(III) Contraceptive-induced bleeding

Older oral contraceptives containing **synthetic estrogens** & progestin induced a variety of E responses e.g**., inactive, non secretory glands with decidual-like stroma**. The pills in current use have corrected these abnormalities.

(IV) Endo myometrial disorders ,including **E** polyps, chronic endometritis & submucosal leiomyomas.

Endometrial Hyperplasia

•prolonged or marked excess of **estrogen** relative to progestin >exaggerated proliferation > may progress to cancer

شو اشهر سبب بعمل نزيف بالبنات بغير اوقات البيريود intermenstrual ؟؟ هو زيادة الاستروجين طب ليش ؟

لانه ال endometrium المفروض فيه layer طبيعية بقدر ال BV الموجودة ولو الاستروجين زاد يحدث تضاعف رهيب للخلايا تبعت endometrium ،، hyperplasia ،،،، اسرع من تكاثرتبع BV وبالتالي كمية glands اكتر من BV بالتالي الدم ما رح يكفيهم ورح يموتوا قبل معادهم بقوم واقعين ونازل دم

طب السؤال الذييطرح نفسه شو سبب زيادة الاستروجين ؟؟؟

هو اصلا من وين بطلع ؟؟ من ال granulosa cells طب متى بتوقف افراز الاستروجين لما يحصل ovulation لانه رح تتحول لحالة اسمها corpus lutuem يلي بفرز البروجستيرون

اول سبب ؟؟؟ هو انه ما يصير ovulation

****Causes : any estrogen excess** may lead to **EH,** Including

***Endogenous:**

(1)failure of ovulation, such as is seen **around the menopause**;

(2)**estrogen-producing ovarian lesions** such as:

*polycystic ovaries (including Stein-Leventhal syndrome);

*cortical stromal hyperplasia; (from suprarenal gland)

*granulosa-theca cell tumors of the ovary.

common risk factor is **obesity, because adipose tissue processes steroid precursors into estrogens.

مين يلي فيها استروجين اكتر الست الرفيعة ولا تخينة ؟؟ تخينة

***Exogenous:** prolonged **administration** of estrogenic steroids without counterbalancing progestin

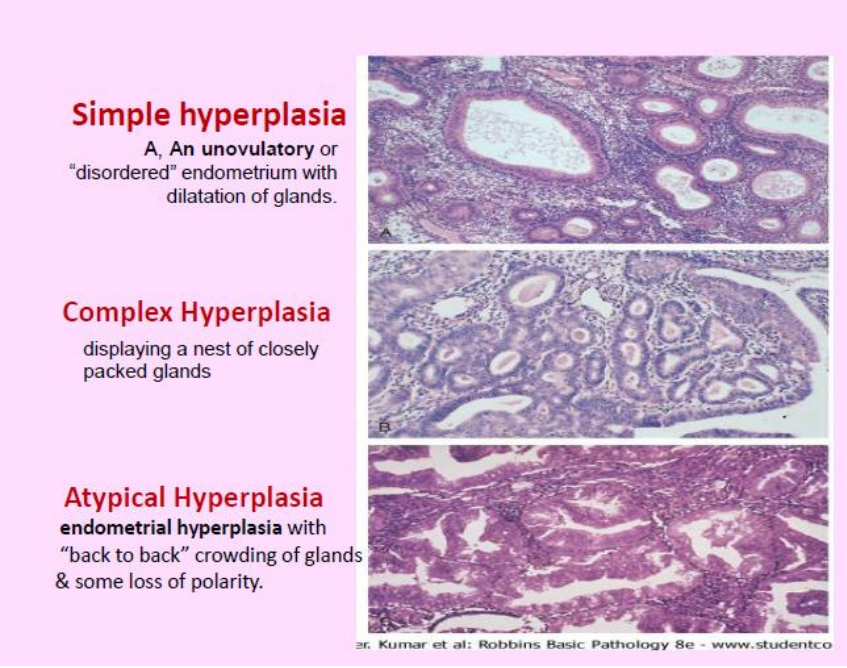
طب ليه اصلا بتوخد استروجين ؟؟ دكتور العظام كتبلها اياه بعدين بتروح تراجع على دكتور نسائية بروح بوقف عنها الاستروجين ودائرة ما رح توقف

• severity is based on architectural crowding and cytological atypia, ranging from:

1-Simple hyperplasia

2-Complex hyperplasia

3-Atypical hyperplasia (20% risk of cancer).



*simple :

بصير proliferation +dilation

يعني بتصير ال glands منفخة وال epi لساته columnar وفي dense stroma

* complex :

زادوا عدد الغدد بشكلكبير وضغطوا على بعض packed glands

*typical :

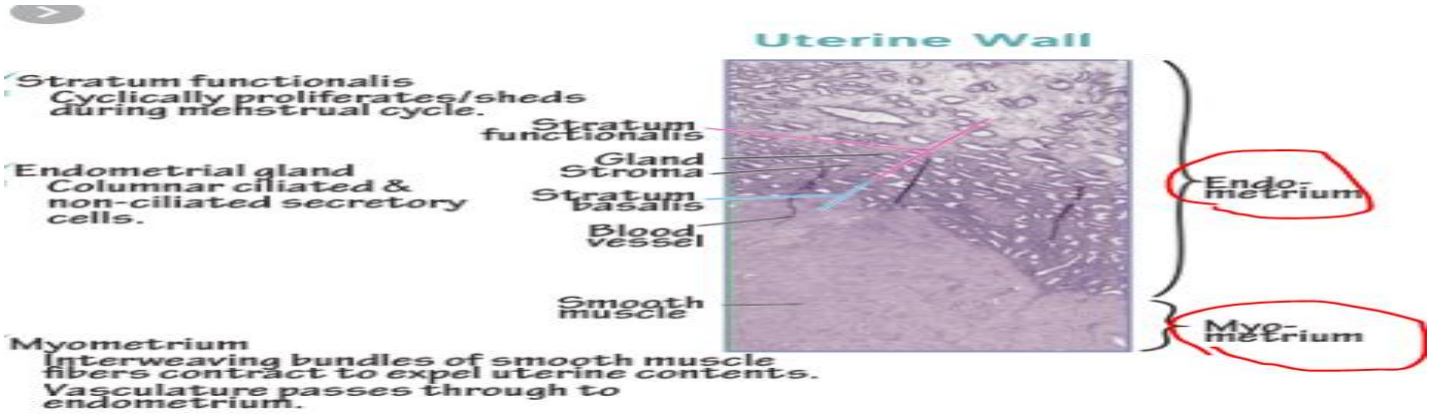
صار شكل الخلايا مختلف وزاد اللون الازرق

وهاي المرحلة يلي بتعمل وبتقلب ل cancer وكل المراحل بتعمل bleeding

•The 3 types represent a continuum based on the level & duration of the estrogen excess.

•Not surprisingly, in time, the **EH** may become autonomous proliferation, no longer needing estrogenic influence, eventually giving rise to **carcinoma**.

Uterine tumors



TUMORS OF THE ENDOMETRIUM

Benign Endometrial Polyps

- Sessile or pedunculated.
- Cystically dilated Endometrial glands, with small muscular arteries and Fibrotic stroma.
- in most E polyps, the stromal cells are monoclonal& have a cytogenetic rearrangement at 6p21, making it clear that they are the neoplastic component of the polyp.
- no risk of endometrial cancer

Endometrial Carcinoma

- It is **The most common cancer in female genital tract.**
- **Common in 50s and 60s** and is **distinctly uncommon** in women younger than 40 years of age
- Arise in one of two clinical settings:

1)**Perimenopausal women with estrogen excess**

2)***older women with endometrial atrophy.***

•These scenarios are correlated with differences in histology:

•**1-endometrioid**

•2-***serous carcinoma***, respectively

•Termed because similar to normal endometrium.

	Endometrioid carcinoma:	**Papillary Serous carcinoma**
****Risk factors**	point to **increase estrogen stimulation** include: endometrial hyperplasia رح نلاقي انهم بشبهوا تبعون 1-**Obesity;** (mostly an association and not a true risk factor) 2- **Infertility**(nulliparous, often with nonovulatory cycles)**;** **3- Prolonged estrogen replacement therapy; Estrogen-secreting ovarian tumors**. 4- Other risk factors **Diabetes and Hypertension** • **Precancerous** lesion is atypical endometrial hyperplasia. •**Breast ca occurs in women with E ca (& vice versa) more frequently than by chance alone**	***No relation with endometrial hyperplasia.** ***Not hormone-dependent.**
****Patho genesis**	Endometrial ca is the 2nd most common cancer associated with **hereditary nonpolyposis colon cancer syndrome** (lynch syndrome) ,an inherited genetic defect in a DNA mismatch repair gene, resulting in (microsatellite instability). *Mutations in DNA **mismatch repair genes** and **PTEN.** ***Both mismatch repair gene &** PTEN **mutations** are **early events** in endometrial carcinogenesis, occurring in the progression from abnormal proliferation to atypical hyperplasia.	(1) it typically arises in a background of **atrophy**, sometimes in the setting of an **endometrial polyp** (2) Mutations in DNA mismatch repair genes & PTEN are **rare** in serous ca; however, (3) **all cases have mutations in the p53 tumor suppressor gene.**
Grossly	**fungatingor infiltrative**, infiltrating the myometrium.	
H	T **closely resemble normal E,** ranging from **mucinous** to **tubal (ciliated)** to **squamous** or **adenosquamous** differentiation. من اسمه endometriod يعني بشبه ال endometrium الطبيعي يعني رح تفرز Mucin وتكون squ. Epi	**forms small papillae** (rather than the glands seen in endometrioid ca) & has much greater cytological atypia.

<table>
<tr><th></th><th>Endometrioid carcinoma:</th><th>Papillary Serous carcinoma</th></tr>
<tr><td>Prognosis</td><td>*depends on stage
the grading (grades I-III) & the staging closely parallel outcome:
<table><tr><td>stage I</td><td>confined to the corpus</td><td>5-year survival</td></tr><tr><td>stage II</td><td>involvement of the cervix</td><td>90%</td></tr><tr><td>stage III</td><td>beyond the uterus but within the true pelvis</td><td>20%</td></tr><tr><td>stage IV</td><td>distant metastases or involvement of other viscera.</td><td></td></tr></table>.</td><td>They behave as poorly differentiated cancers are not graded, & are particularly aggressive.
مين احسن الاصل ولا تقليد ؟ الاصل بالتالي هاد التقليد هو الاخطر
*prognosis is strongly dependent on the extent of tumor, as determined by operative staging with peritoneal cytology; since even very small or superficial serous T may spread via the fallopian tube to the peritoneal cavity.</td></tr>
<tr><td>Clinically,</td><td colspan="2">**irregular bleeding is the first clinical indication of all E ca, caused by erosion & ulceration of the T surface
**With progression, the uterus may be palpably enlarged, &in time, extension of the E ca beyond the uterus fixed it to surrounding structures.
**Fortunately, E ca is usually late-metastasizing cancer, but dissemination eventually occurs, with involvement of ovary ,LN & distant sites.</td></tr>
</table>

Tumors of the myometrium

Lieomyoma= fibroids Benign tumor of smooth muscle cells بسموها الستات الياف الرحم	**Lieomyosarcoma** • Malignant counterpart of leiomyoma.
****Most common benign tumor in females (30% -50% in reproductive life).** ****Estrogen-dependent; shrink after menopause.** ****Grossly,** •site : (intramural) في النص في الجدار (submucosal) بارز لجوا ومشوه البطانة (subserosal). بارز لبرا • Size : rang from **small (1 gram)** to **massive** T. • shape : **are firm, white,** ***not encapsulated, sharply circumscribed masses**, sharply و unencapsulated وبنفس الوقت شكله زابط طب هون السؤال كيف circumscribed ??? كأنه الجملة متناقضة ؟؟ لا هي مو متناقضة هو بضغط على انسجة الرحم يلي حواليه فبعمل atrophy فيها ويبان لونها مختلف وكأنها كابسول يعني زي ما الدكتورة كاتبة بالصور >>the well-developed **false capsule** of compressed muscle & fibrous tissue around the it. •cut section : with a characteristic **firm gray-white** masses with **whorled cut surface.** smooth muscle لونه مش احمر لانه عبارة عن whorls وفي بكون زي الدواماااات •**Tumor** may be **single**, but **most** often they are **multiple.** •**Pedunculated** submucosal leiomyoma, arising from the fundus & protruding through the cervical os. **Torsion** of the pedicle results in impairment of the tumor blood supply with its subsequent necrosis & gangrene. هاي مكتوبة بالصور : معناها انه بس يكبر الورم رح يدلدل pedicle ولما يوقع رح يلمس ال organs التانيين ويوخد دم منهم •2ry Changes include May develop areas of hemorrhage**& cystic softening**,& after menopause, they may become **densely collagenous**& **calcified**. cystic changes وتركت مكانها فاضي ca خلايا من الورم ماتتترسب عليها ****Clinically**: 1) asymptomatic or 2)symptomatic; *Menorrhagia submucosa فممكن توقع ،،،، لما توقع ممكن submucosa لانه الورم ضاغط على ال bleeding يصير *a dragging sensation *anemia, etc... • **Larger L** may develop **ischemic necrosis** (if extensive, called **Red degeneration**, causing **severe pain,** which requires it's removal) هاي بتصير during pregnancy بدنا نتخيل انه هاي كرة والبيبي وهو بلعب فيها عمل compression on veins فبصير الورم congested يعني يحتقن وجزءمن الورم ممكن abortion يموت والطفل ممكن يصيرله **Leiomyomas **almost never (rare)** transform into sarcomas, and the presence of multiple lesions does not increase the risk of malignancy.	•Typically **arise de novo** from the mesenchymal cells of the myometrium, **not from preexisting leiomyomas**. •Almost always solitary tumors, in contrast to the frequently multiple benign leiomyomas. ****Grossly,**leiomyosarcomas may develop as: (a)bulky masses **infiltrating** the uterine wall. (b)**polypoid** lesions. •They are frequently Soft ,Hemorrhagic, **necrotic, infiltrative** borders. • Diagnosis: coagulative necrosis, cytological atypia, and mitotic