* The Female Genital System
* Outline:
* Diseases of the vagina.
* Diseases of the cervix.
* Diseases of the endo-myometrium.
* Diseases of the ovaries.
* Diseases of fallopian tubes.
* **Vaginal pathologic diseases**
* **Vaginitis** is a common transient clinical problem produces a vaginal discharge (leukorrhea).
* Many organisms cause it, including bacteria, fungi, and parasites. Many represent normal commensals that become pathogenic in conditions such as
* **diabetes.**
* **systemic antibiotic therapy that kills normal microbial flora.**
* **pregnancy.**
* **elderly persons with compromised immune function.**
* **in patients with the acquired immunodeficiency syndrome.**
* **Cervical pathology**

**Cervical carcinoma**

* Since the introduction of the Papanicolaou (Pap) smear 50 years ago, the incidence of cervical cancer has dropped.
* The Pap smear remains the most successful cancer screening test ever developed. In populations that are screened regularly, cervical cancer mortality is reduced by as much as 99%.
* **Detection of precursor lesions by the Pap smear at an early stage, permits discovery of these lesions when curative treatment is possible**.
* On the basis of histology, precancerous changes are graded as follows (**depending on the extent of involvement):**
* \***CIN I:** Mild dysplasia (<third of full epithelial thickness)
* \***CIN II**: Moderate dysplasia (up to 2/3 of full epithelial thickness)
* \***CIN III**: Severe dysplasia in full epithelial thickness (carcinoma in situ)
* **Dysplasia means increased N/C ratio, nuclear enlargement,   
  hyperchromasia, and abnormal nuclear membranes**
* ***Epidemiology and Pathogenesis***
* The peak age incidence of CIN is about 30 years, whereas that of invasive carcinoma is about 45 years.
* Precancerous changes usually take many years, perhaps decades, to evolve into overt carcinomas.
* **Important risk factors for the development of CIN and invasive carcinoma are:**

-**Early age at first intercourse**

**-Multiple sexual partners**

**-A male partner with multiple previous sexual partners**

**-Persistent infection by "high-risk" papillomaviruses.**

Those risk factors point to **sexual transmission of a causative agent, in this case HPV.**

* HPV can be detected by molecular methods in **nearly all precancerous lesions and invasive neoplasms.**
* More specifically, certain high-risk HPV types, including **16, 18,** account for the majority of cervical carcinomas.
* The recently introduced HPV vaccine used in USA and Europe is very effective in preventing HPV infections and hence cervical cancers
* **Cervical cancer**
* The most common cervical carcinomas are **squamous cell carcinomas (75%),** followed by adenocarcinomas and adenosquamous carcinomas.
* with a peak incidence at about 45 years.
* **Mortality is most strongly related to tumor extent (stage)**
* **Detection of precursors by cytologic examination(pap smear) and their eradication is the most effective method of cancer prevention.**
* Endometrial pathology
* **Endometrial Hyperplasia**
* An excess of estrogen relative to progestin, will induce exaggerated endometrial proliferation (hyperplasia), **which can be pre-neoplastic**
* The severity of hyperplasia is classified based on architectural crowding and cytologic atypia, ranging from:

**1- Simple hyperplasia to**

**2- Complex hyperplasia, and finally**

**3- Atypical hyperplasia.**

* These three categories **represent a continuum** based on the level and duration of the estrogen excess.
* In time the hyperplasia may become autonomously proliferating, no longer needing estrogenic influence, **eventually giving rise to carcinoma**.
* **Simple hyperplasia carries a negligible risk, while a person with atypical hyperplasia has a 20% risk of developing endometrial carcinoma**.
* **Causes of estrogen excess**: unovulatory cycles, prolonged use of estrogen without counterbalancing progestin; estrogen-producing ovarian lesions and tumors; obesity (because adipose tissue processes steroid precursors into estrogens).
* **Endometrial Carcinoma**
* is the most frequent cancer in the female genital tract.
* **Endometrial cancer appears most frequently in 50s and 60s and is distinctly uncommon in women younger than 40 years of age.**
* ***endometrial carcinoma frequently arises on a background of endometrial hyperplasia.***
* **Endometrioid carcinoma**

**Risk factors for endometrioid carcinoma**:

* **Obesity: increased synthesis of estrogens in fat depots and from adrenal and ovarian precursors;**
* **Diabetes and Hypertension (mostly an association and not a true risk factor)**
* **Infertility: women tend to be nulliparous, often with nonovulatory cycles.**
* **Prolonged estrogen replacement therapy**
* **Estrogen-secreting ovarian tumors.**
* **Tumors of the myometrium:   
    
  Lieomyoma:**
* Benign tumors that arise **from the smooth muscle cells in the myometrium**, referred to as *fibroids.*
* They are **the most common benign tumor in females and are found in 30% to 50% of women during reproductive life**.
* Estrogens and possibly oral contraceptives stimulate their growth; conversely, they shrink post-menopausally.
* May be single, but most often multiple firm tumors within the uterus .
* range in size from small to massive neoplasms.
* most commonly are embedded within the myometrium (intramural), whereas others may lie directly beneath the endometrium (submucosal) or directly beneath the serosa (subserosal )
* ***Leiomyomas of the uterus may be entirely asymptomatic and be discovered only on routine pelvic or post mortem examination.***
* **The most frequent manifestation is menorrhagia**. Large masses in the pelvic region may become palpable to the woman or may produce a dragging sensation.
* **Benign leiomyomas almost never transform into sarcomas**, and the presence of multiple lesions does not increase the risk of harboring a malignancy.
* **Lieomyosarcoma**
* Typically arise de novo from the smooth muscle cells of the myometrium, not from preexisting leiomyomas.
* They are **almost always solitary** tumors, in contrast to the frequently multiple leiomyomas.
* They are frequently **soft, hemorrhagic, and necrotic.**
* The diagnostic features of leiomyosarcoma include tumor coagulative necrosis, cytologic atypia, and mitotic activity.

* Leiomyoma
* Leiomyosarcoma
* **POLYCYSTIC OVARIES**
* **Oligomenorrhea, hirsutism, infertility, and sometimes obesity** may appear in young women (usually in girls after menarche) secondary to excessive production of estrogens **and androgens (mostly the latter**) by multiple cystic follicles in the ovaries.
* The ovaries are **usually twice normal in size, are gray-white with a smooth outer cortex, and are studded with subcortical cysts 0.5 to 1.5 cm** in diameter. There is a conspicuous absence of corpora lutea.
* **Ovarian tumors**
* Ovarian tumors can be categorized into

**1- surface epithelial tumors (65-70%) .**

**2- germ cell tumors(15-20%).**

**3- sex cord stromal tumors (5-10%).**

**4- metastasis (5%).**

* The malignant forms of epithelial tumors also account for almost 90% of ovarian cancers.
* 1- Serous (most common) .
* 2- Mucinous.
* 3- Endometrioid.
* Each can be benign , malignant or border line
* Several risk factors for epithelial ovarian cancers have been recognized. Two of the most important are nulliparity and family history.
* Only 5% to 10% of ovarian cancers are familial. A majority of hereditary ovarian cancers seem to be caused by mutations in the *BRCA* genes, *BRCA1* and *BRCA2*
* **Pathology of the Fallopian tubes**
* *Inflammation (****Salpingitis****)*
* almost always bacterial in origin.
* ***Chlamydia****,* ***Mycoplasma*** *,* **coliforms**, (postpartum) **strept.** and **staph.** are now the major offenders.
* fever, lower abdominal or pelvic pain, and pelvic masses when the tubes become distended with either exudate or secretions.
* *Complications:*
* Adherence of tube to ovary 🡪 *tubo-ovarian* ***abscess***.
* more serious🡪 **adhesions** of the tubal plicae, and increasing the risk of **tubal ectopic pregnancy**.
* Damage or **obstruction** of the tubal lumina may produce permanent **sterility**
* **Ectopic pregnancy**
* is implantation of the fertilized ovum in any site other than the normal uterine location.
* Incidence: 1% of pregnancies.
* In 90% of these cases 🡪in fallopian tubes
* other sites: ovaries, abdominal cavity
* Predisposing factors: tubal obstruction (50% either due to chronic inflammatory changes in the oviduct; tumors; and endometriosis); **IUCD**..
* In 50% of tubal pregnancies, no anatomic cause can be demonstrated.
* Early: normal early development of the embryo, with the formation of placental tissue, the amniotic sac, and decidual changes
* Later: the placenta eventually burrows through the wall, causing **intratubal hematoma (hematosalpinx), intraperitoneal hemorrhage.**
* Rupture of an ectopic pregnancy may be catastrophic, with the sudden onset of intense **abdominal pain** and signs of an **acute abdomen**, often followed by **shock**.
* **Prompt surgical intervention is necessary.**