

*Diseases of Female
Genital Tract and Breast*

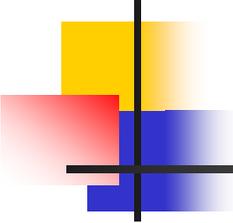
女性生殖系統及乳房疾病

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醫學系病理學科

分機:3130

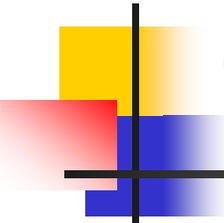
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學習目標

- 能說明女性生殖系統常見的疾病
- 能說明乳房常見的疾病
- 能說明子宮頸癌、子宮內膜癌、卵巢癌及乳癌的危險因子、組織分類及臨床表現

參考資料: Pathology for the Health-Related Professions,
Ivan Damjanov, Saunders, Co. 3rd. ed. 2006, Chap 15, 16

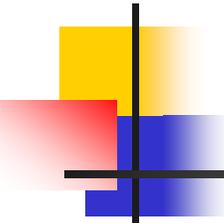


Overview of Major Diseases

- **Infections:**
 - Direct contact with the external world
 - Many infections are venereal in nature
 - Infections are an important cause of infertility
- **Hormonal disorders:** abnormal secretion of estrogen and progesterone
- **Benign or malignant tumors**
 - Related to sexually transmitted diseases or hormonal influence
 - Screening reduced the mortality of cervical ca.
- **Disorders related to pregnancy**

Inflammatory Diseases

- **Anatomic classification**
 - Vulvitis, Vaginitis, Cervicitis, Endometritis, Salpingitis, Oophoritis
 - **Pelvic Inflammatory Disease (PID):** inflammation of entire female genital tract
- **Pathogenetic classification:** ascending, hematogenous
- **Chronologic classification:** acute, chronic or recurrent
- **Etiologic classification**
 - **Bacteria:** Neisseria gonorrhoeae (gonorrhoea) Treponema pallidum (syphilis)
 - **Virus:** HPV: Condyloma acuminatum HSV
 - **Chlamydia**
 - **Fungus:** Candida albicans (DM, pregnancy)
 - **Protozoal:** Trichomonas vaginalis

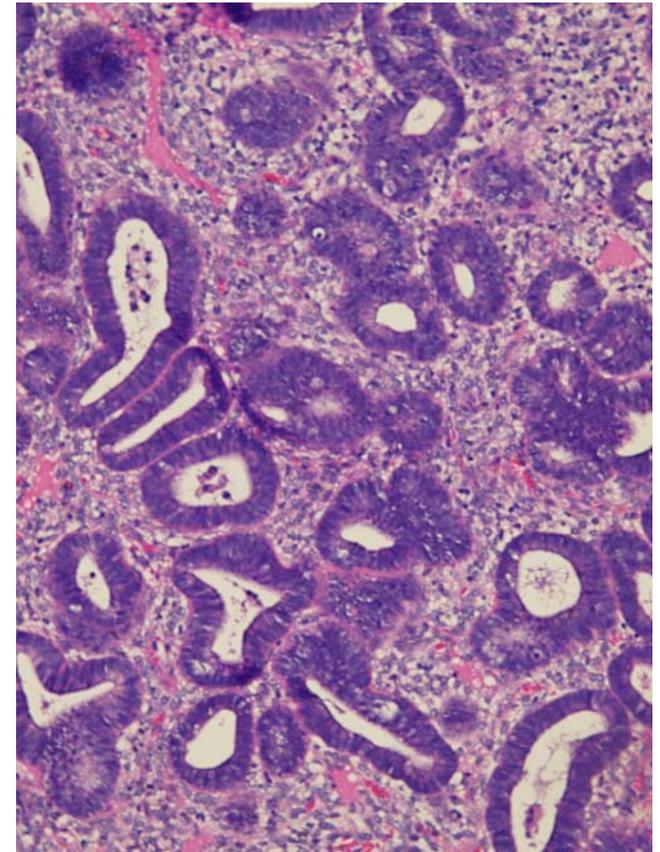


Pelvic Inflammatory Disease

- Salpingo-oophoritis
- Tuboovarian abscess
- Pyosalpinx
- Hydrosalpinx
- **Complications:** peritonitis, bacteremia, infertility

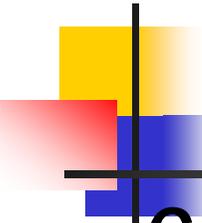
Hormonally Induced Lesions

- **Endometrial hyperplasia**
 - abnormal vaginal bleeding
 - 長期estrogen刺激:無排卵週期,停經,肥胖,長期服用
 - 分類:
 - Simple hyperplasia (cystic, mild hyperplasia)
 - Complex hyperplasia (adenomatous hyperplasia)
 - Atypical hyperplasia

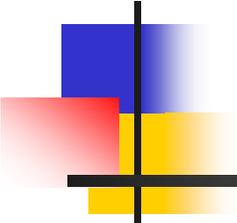


Simple hyperplasia with no atypia

Neoplasia and related disorders

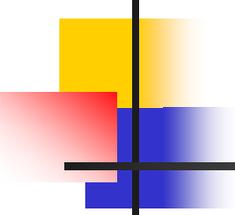


- Carcinoma of the Cervix
- Carcinoma of the Vulva
- Carcinoma of the Vagina
- Tumors of the Uterus
 - Endometrial Carcinoma
 - Leiomyoma
- Endometriosis
- Tumors and tumorlike conditions of the ovary
 - Ovary cysts
 - Ovarian Neoplasms

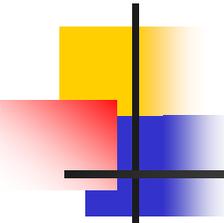


Cervix

Risk Factors of Cervical Carcinoma



- ♣ **Early age at first intercourse**
- ♣ **Multiple sexual partners**
- ♣ **Presence of cancer associated HPV**
- ♣ **Persistent detection of high risk HPV**
- **HPV**
 - **low-risk: 6, 11, 42, 44**
 - **high-risk: 16, 18, 31, 33**



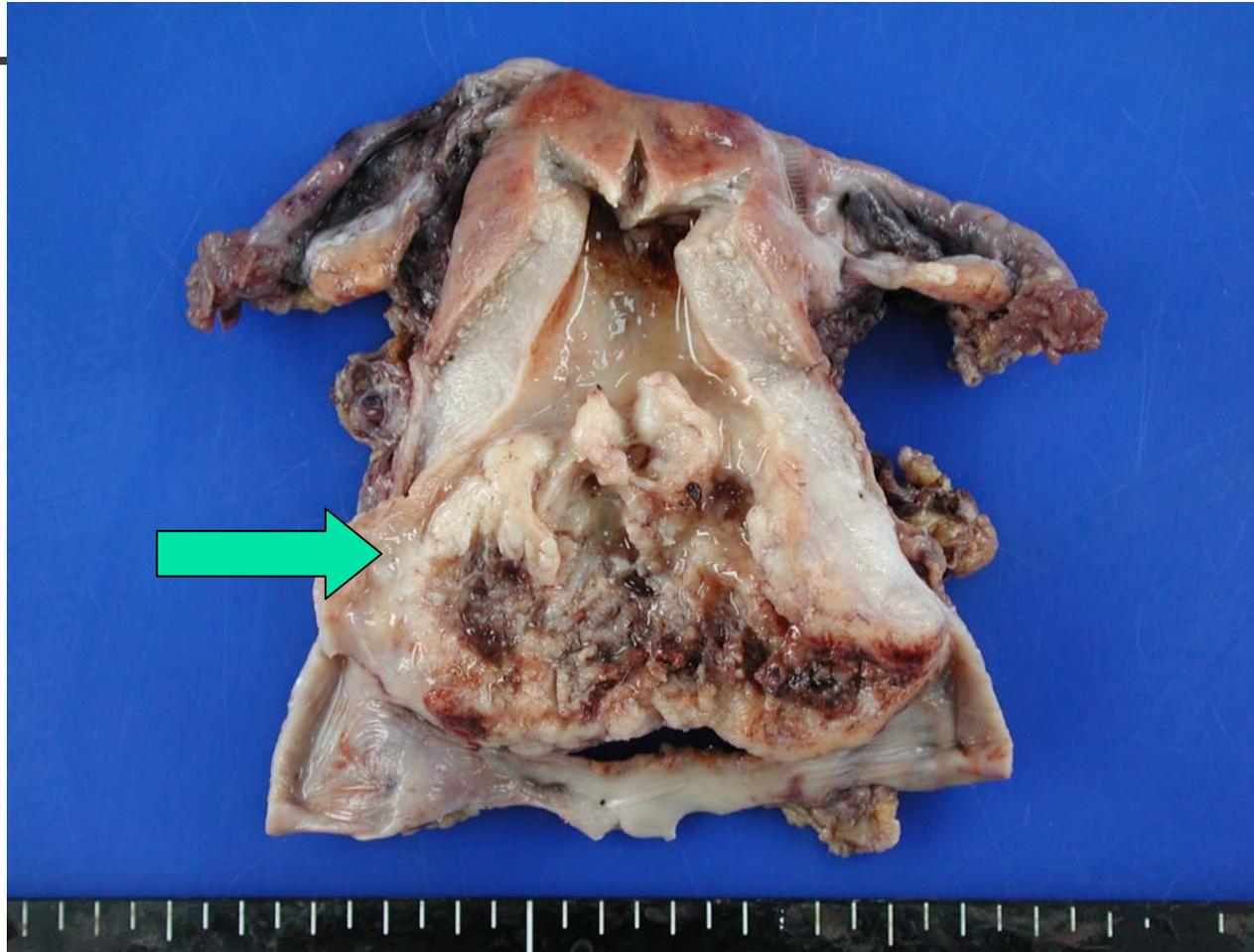
Intraepithelial Squamous Neoplasia of the Cervix

■ **Classification**

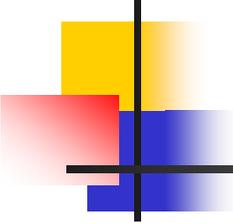
- **Dysplasia/CIS system:** mild, moderate, severe dysplasia, carcinoma in situ
- **CIN system:** CIN I, CIN II, CIN III
- **Bethesda system (NCI, 1988):** squamous intraepithelial lesion (SIL)
 - low-grade SIL: condyloma, CIN I
 - high-grade SIL: CIN II, CIN III

Squamous Cell Carcinoma of the Cervix

40~50 y/o



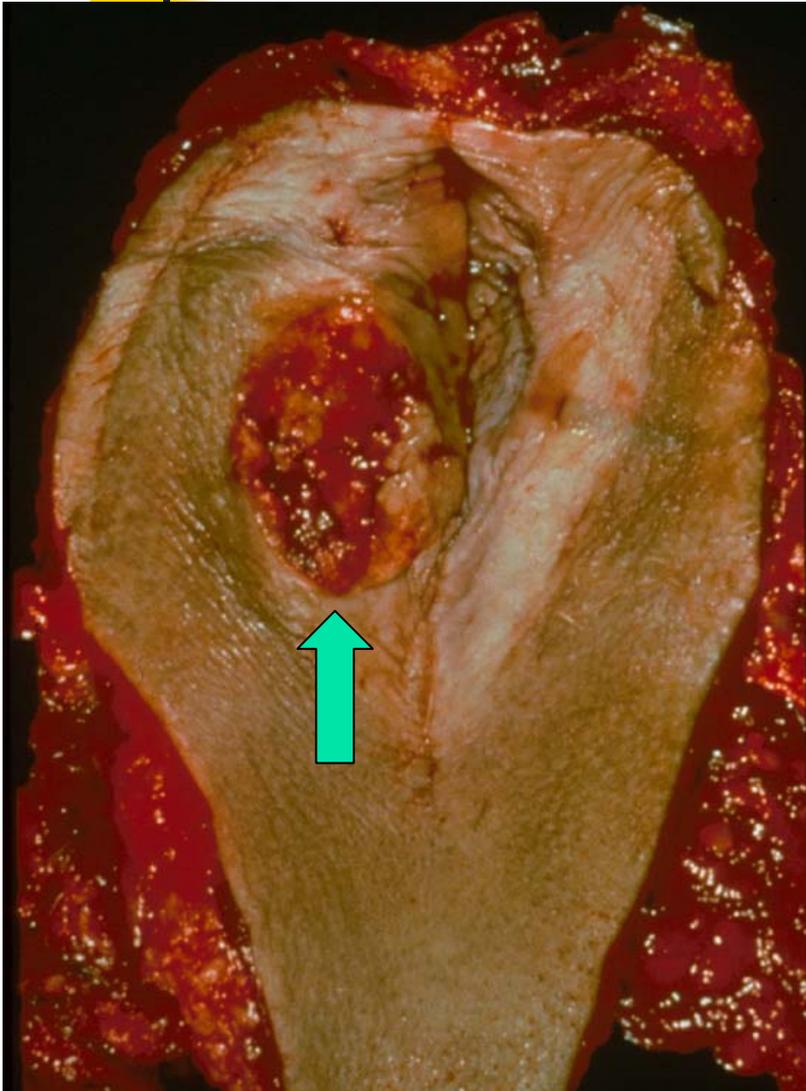
Adenocarcinoma: 10~15%; HPV-16,18; 可與CIN並存



Staging of Cervical Cancer

- **Stage 0: CIS**
- **Stage I: Confined to uterus**
- **Stage II: Extend beyond the uterus but not onto pelvic wall. Carcinoma involves the vagina but not lower 1/3.**
- **Stage III: Extend onto pelvic wall or lower 1/3 of vagina**
- **Stage IV: Extend beyond true pelvis or involved mucosa of bladder or rectum**

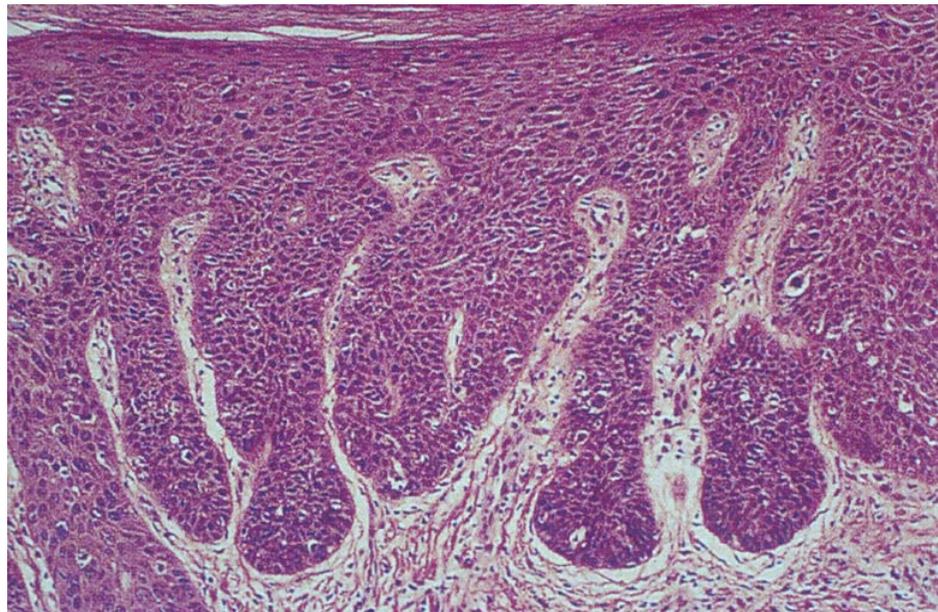
Carcinoma of the Vulva



- Older women
- 85% squamous cell carcinoma
- 15% adenocarcinoma
- Preceded by carcinoma in situ and by preneoplastic lesion (vulvar intraepithelial neoplasia, VIN)

Carcinoma of the Vagina

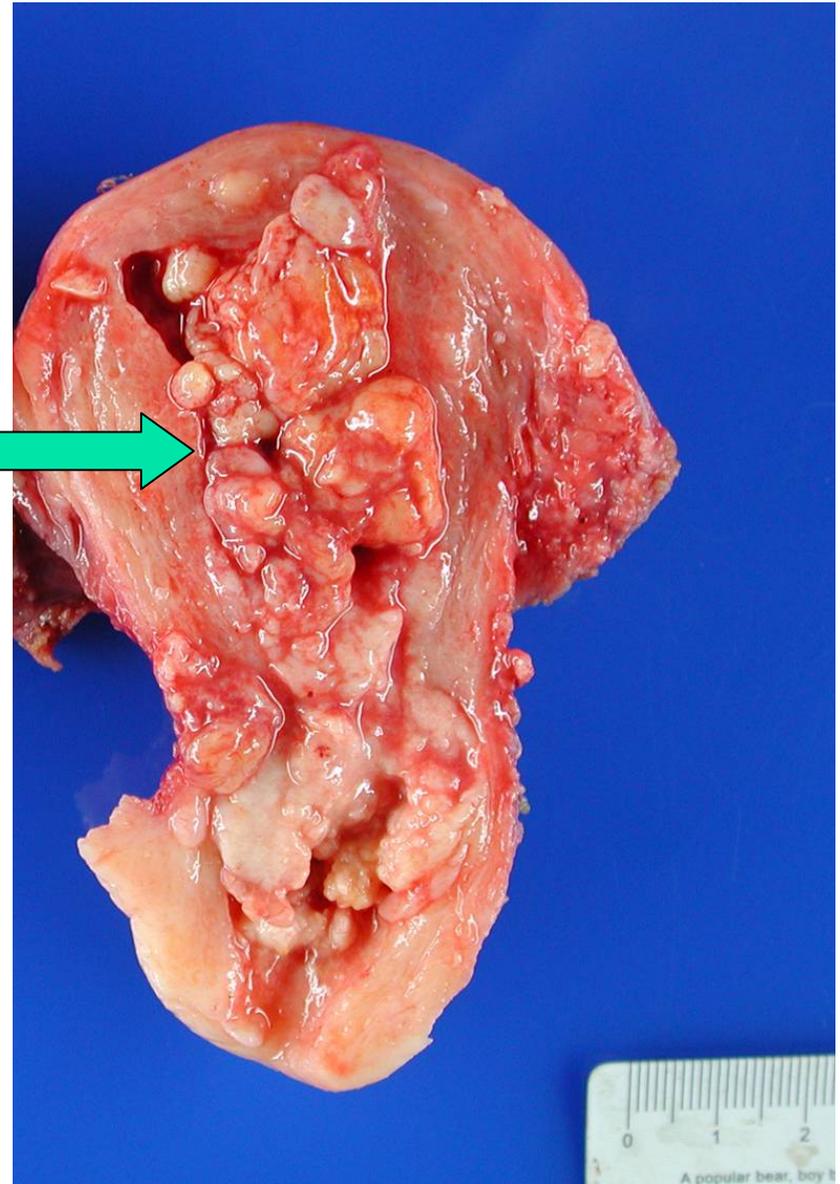
- Older women
- Squamous Cell Carcinoma, preceded by vaginal intraepithelial neoplasia (VAIN)

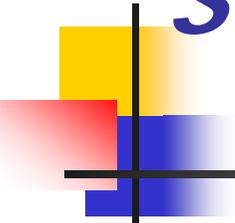


Tumors of the Uterus

Endometrial Carcinoma

- 55~65 y/o
- 危險因子: 肥胖, 糖尿病, 不孕, 高血壓
- **Symptom:** vaginal bleeding
- **Diagnosis:** Endometrial biopsy, diagnostic D & C
- 組織分類:
 - endometrioid carcinoma: > 75%
 - serous, clear cell, squamous, mixed carcinoma





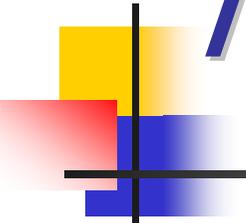
Staging of Endometrial Carcinoma

I: confined to the corpus

II: involved in the corpus & the cervix

III: extend outside the uterus

IV: extend outside true pelvis or involved mucosa of bladder or rectum



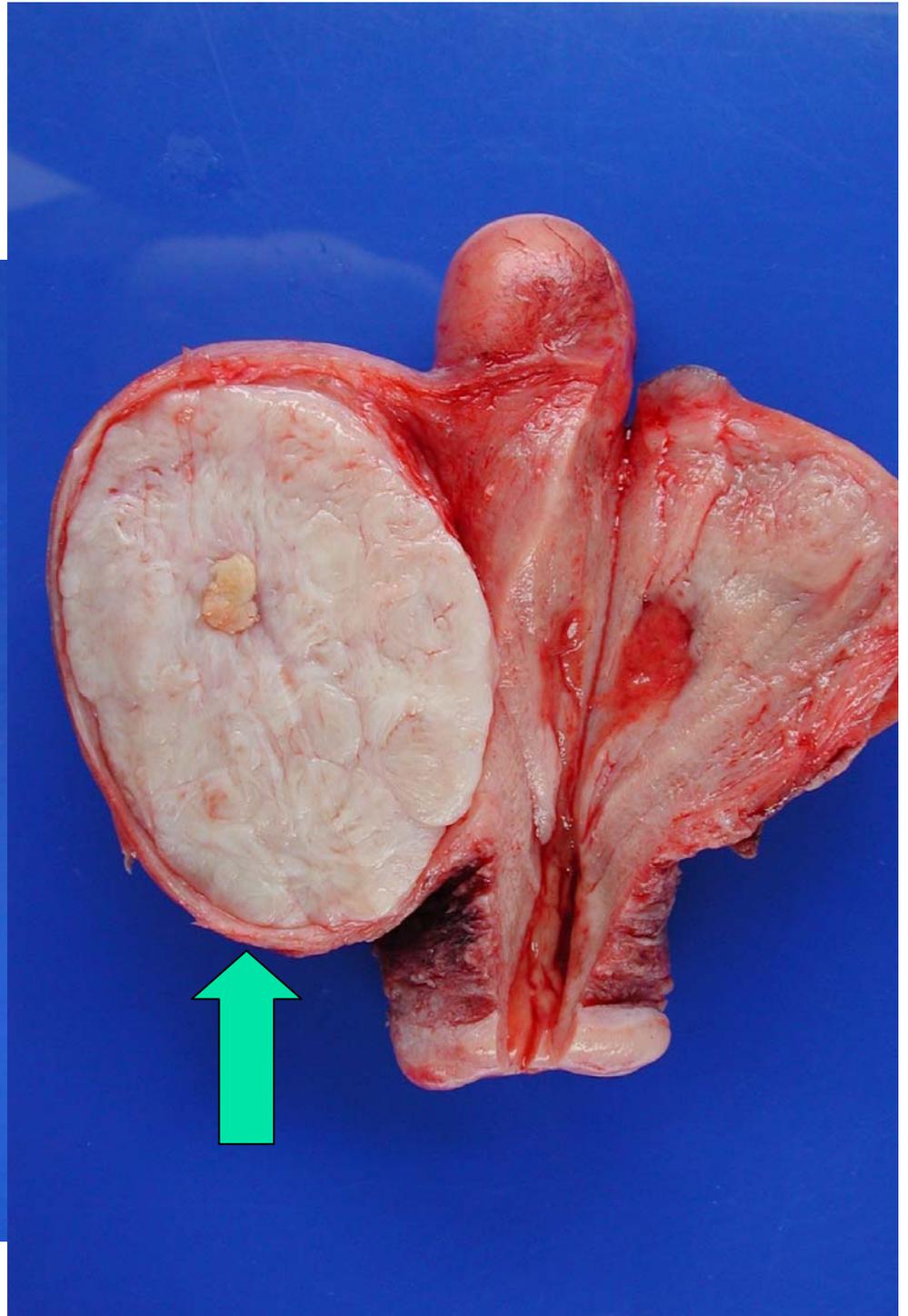
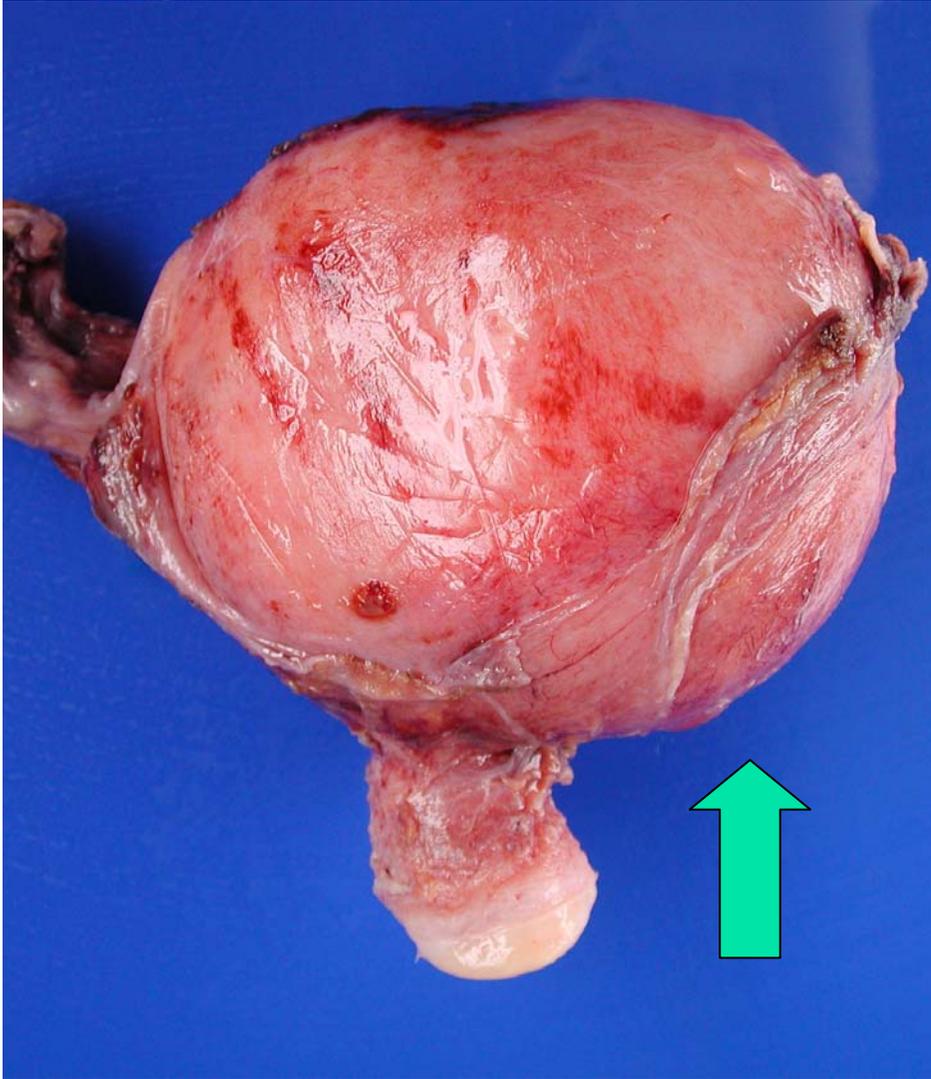
Tumors of the Myometrium

- **Leiomyoma**

- 25%，生育期婦女
- 最常見良性腫瘤
- 成因未明
- 分類：**Intramural**、**Submucosal**、**Subserosal**

**Symptom: depend on size and location,
'mass effect', bleeding**

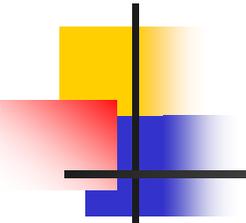
Leiomyoma



Endometriosis

- **Definition:** presence of **endometrial glands** or **stroma** in locations outside the uterus
- **Locations:**
ovary (chocolate cyst),
uterine ligament,
pelvic peritoneum,
op scar, umbilicus, etc.
- **S/S:** dysmenorrhea,
pelvic pain
infertility(30 ~ 40%)





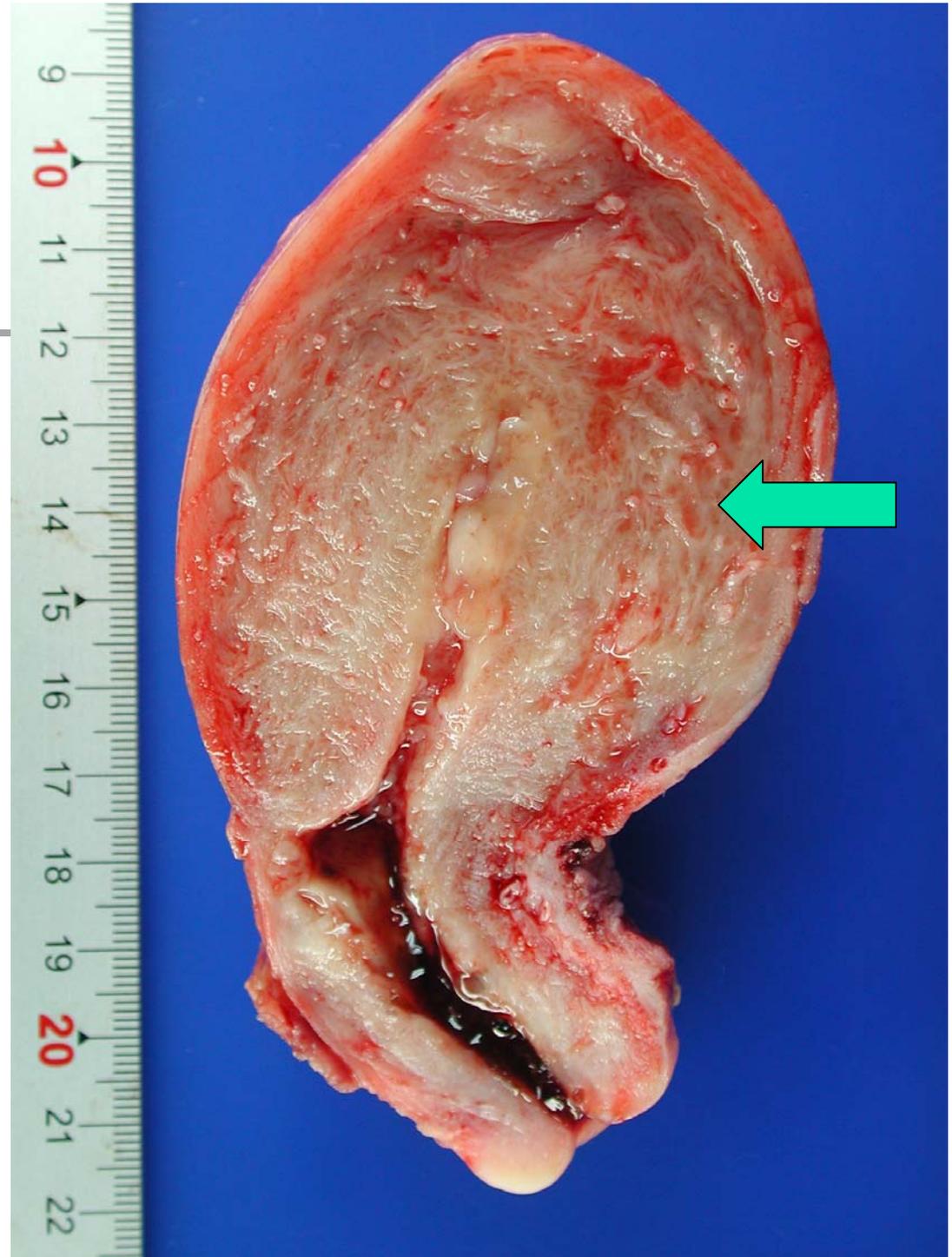
Potential Origins of Endometriosis

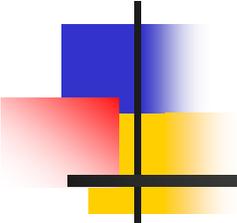
- **Regurgitation**
- **Metaplastic**
- **Vascular or lymphatic dissemination**
- **Intraoperative implantation**

Adenomyosis

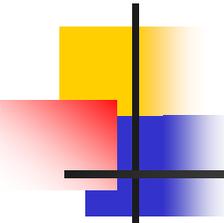
肌層腺體症

Presence of
endometrial glands
or stroma in
myometrium



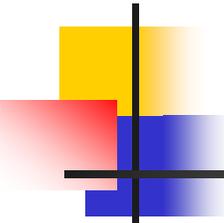


Ovary



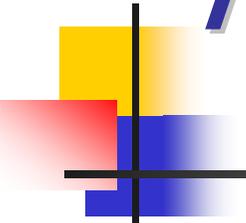
Ovary cysts

- **Follicular cyst and luteal cyst**
- **Polycystic Ovarian Disease
(Stein-Leventhal Syndrome)**
 - 年輕女性，肥胖 (40%)
 - 多毛症 (50%)，無排卵週期，不孕



Tumors of Ovary

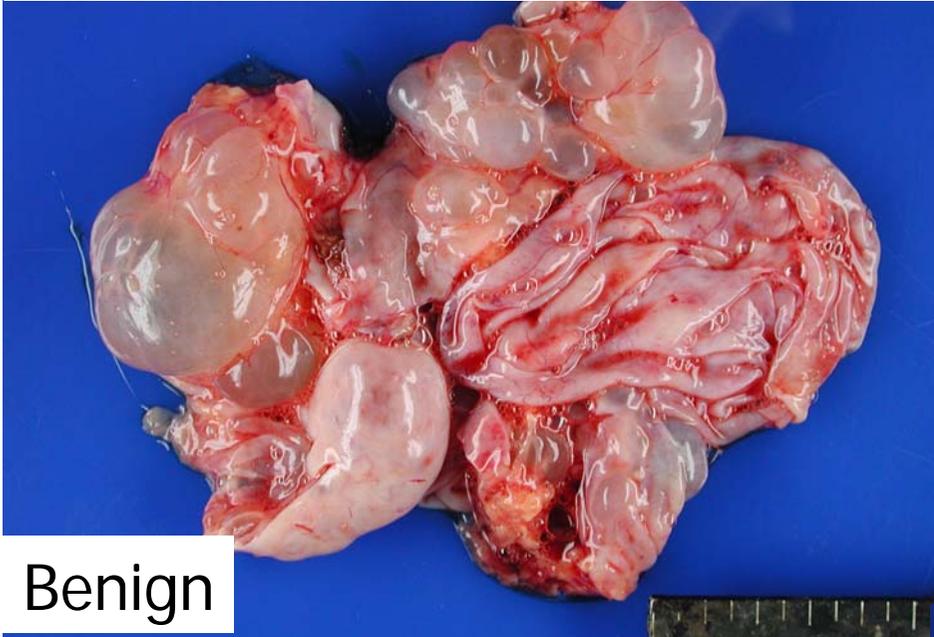
- **Benign:** 80%, 20~45 yrs
- **Malignant:** 20%, 40~65 yrs, high mortality
- **S/S:** abdominal pain, abdominal distension, ascites, GI and GU discomfort
- Peritoneal seeding (0.1 ~ 0.5 cm. nodules)
- **CA-125:** 80% serous & endometrioid ca.
- **Risk factors:** nulliparity, family history (BRCA1 gene)
- **Cystadenoma; cystadenocarcinoma**



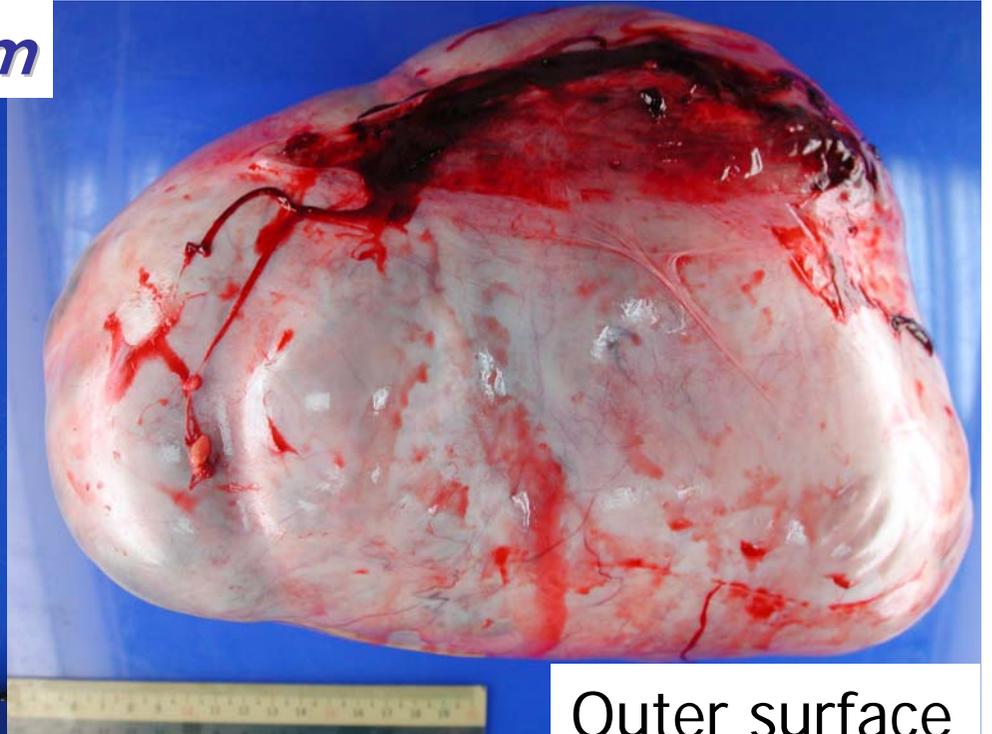
Tumors of Surface Epithelium

- **Incidence:** 65 – 70% of ovarian tumors
- **Micro:**
 - Benign, Borderline malignant, Malignant
- **Classification:**
 - Serous tumors (53%)
 - Mucinous tumors (31%)
 - Endometrioid tumors (6%)
 - Others

Tumors of Surface Epithelium



Benign



Outer surface



Malignant



Borderline

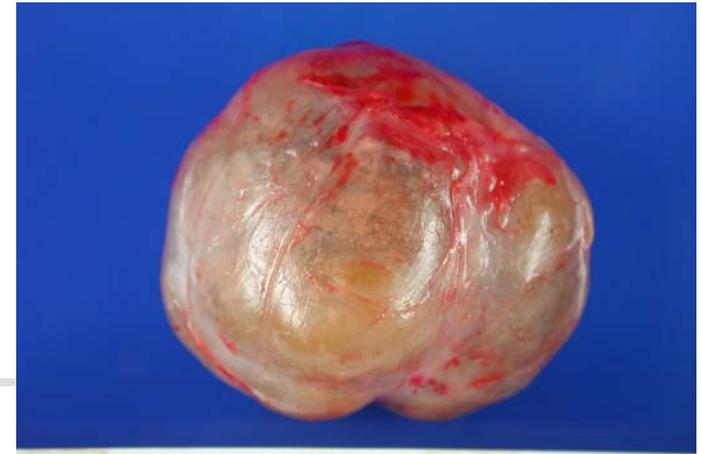
Teratoma

■ Mature Teratoma

- 發生於生育年齡期
- 含三胚層構造
- 俱成熟性分化
- 大部分是囊狀
- 又稱dermoid cyst

■ Immature Teratoma

- 含 immature tissue
- < 20 y/o
- 生長快速, 會轉移



■ Dysgerminoma

- = seminoma of testis
- 75% 10~30 y/o
- most common in malignant germ cell tumor (1/2)



■ Endodermal Sinus Tumor (Yolk Sac Tumor)

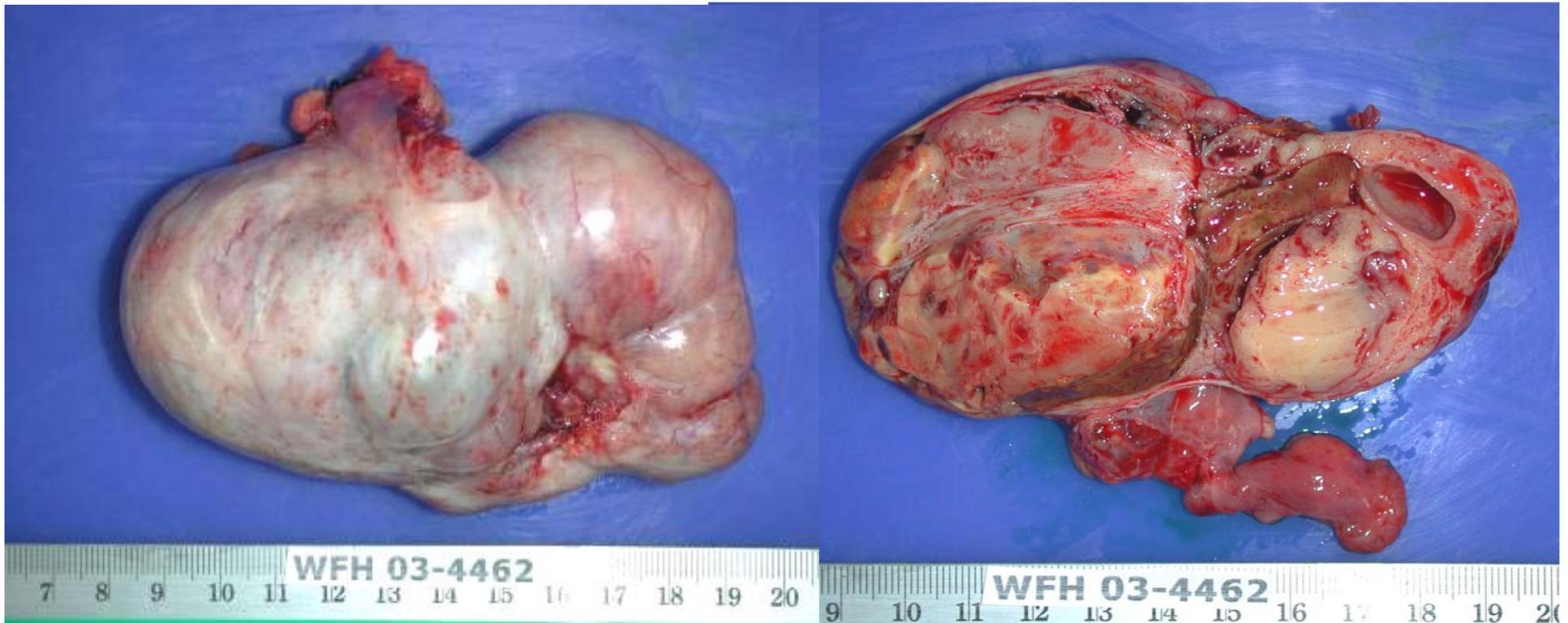
- 小孩及年輕婦女
- α -fetoprotein (α -FP) \uparrow
- 生長快速, 相當具侵襲性



Sex Cord-Stromal Tumors

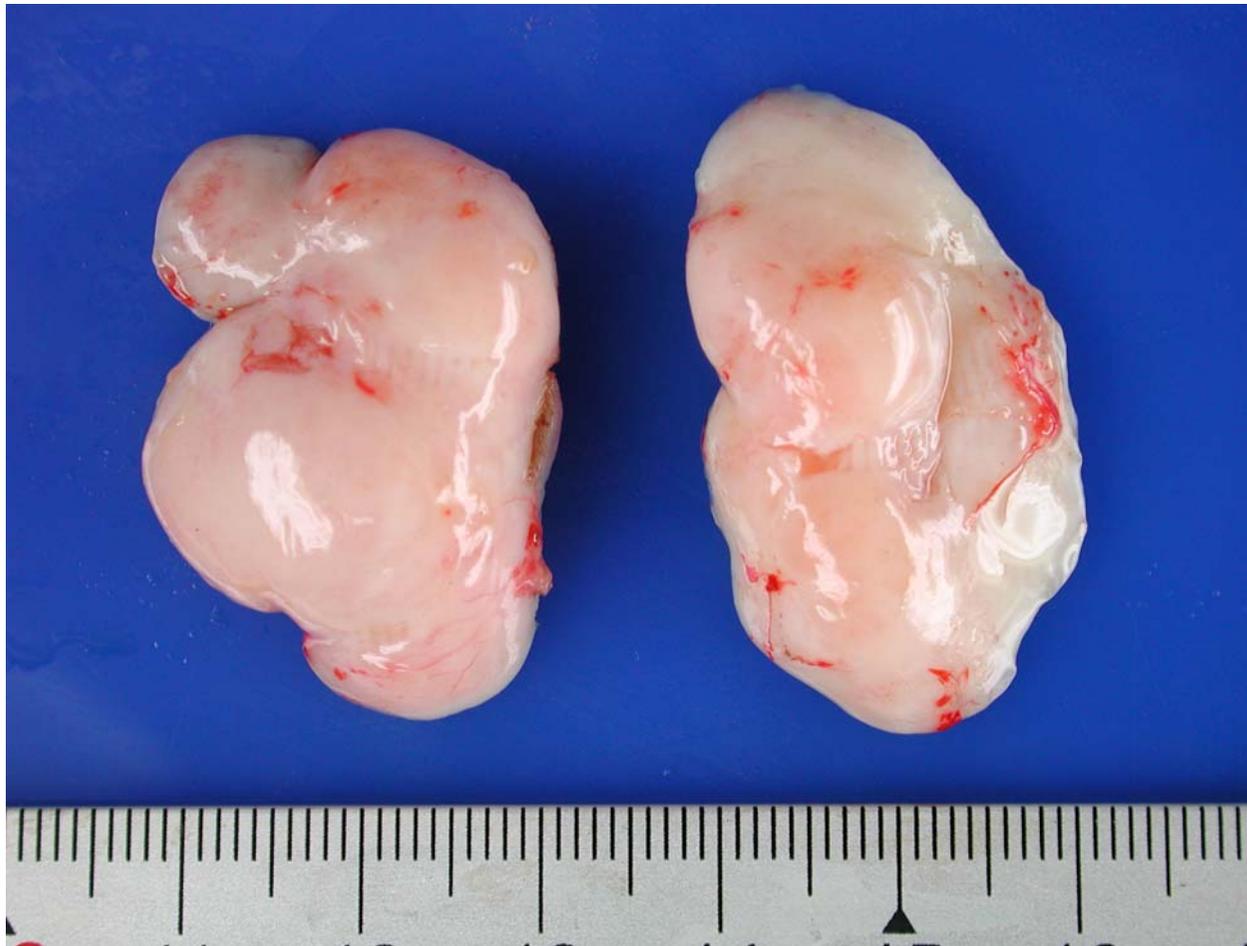
Granulosa Cell Tumor

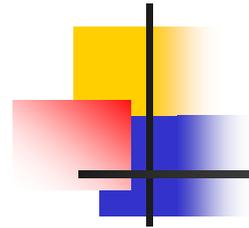
- ■ 2/3 postmenopause, *estrogen effect*
- Malignant potential (5 ~ 25%)
- Prognosis: good, 10 yrs survival rate: 85%



Metastatic Tumors

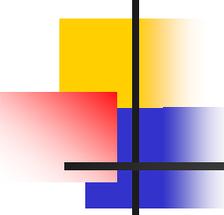
- **Krukenberg's tumor:** GI tract, bilateral, mucin-producing signet-ring cells





Gestational and Placental Disorders

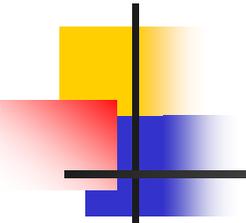
- **Pathology of fertilization**
- **Pathology of implantation**
- **Pathology of placentation**
- **Abortion**
- **Gestational trophoblastic disease**
- **Toxemia of pregnancy**



Pathology of Fertilization

- **Ovum-related factors: older women**
- **Sperm-related factors: azoospermia, oligospermia**
- **Genital organ factors: PID**
- **Systemic factors: immune mechanism, etc.**

Pathology of Implantation



Ectopic Pregnancy

- 1/150

- fallopian tube (90%)

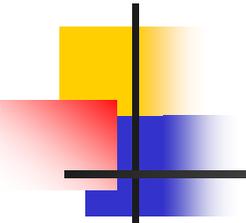
- ovary

- abdominal cavity

- **Causes:** PID, IUD, peritubal adhesion, normal (50%)

- **S/S:** severe abdominal pain

- **Diagnosis:** HCG, U/S, laparoscopy, endometrial Bx



Pathology of Placentation

- **Placental anomalies**

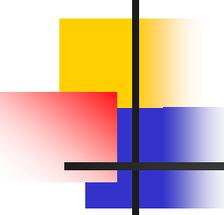
 - size, shape

- **Placental accreta:**

 - Absence of the decidua with adherence of the placenta directly to the myometrium

- **Placenta previa:**

 - Implantation in the lower segment of the uterus



Abortion

- **Interruption of pregnancy prior to the term of fetal viability (500gm or 20wks)**
- **Spontaneous or Induced**

Gestational Trophoblastic Diseases

Hydatidiform Mole

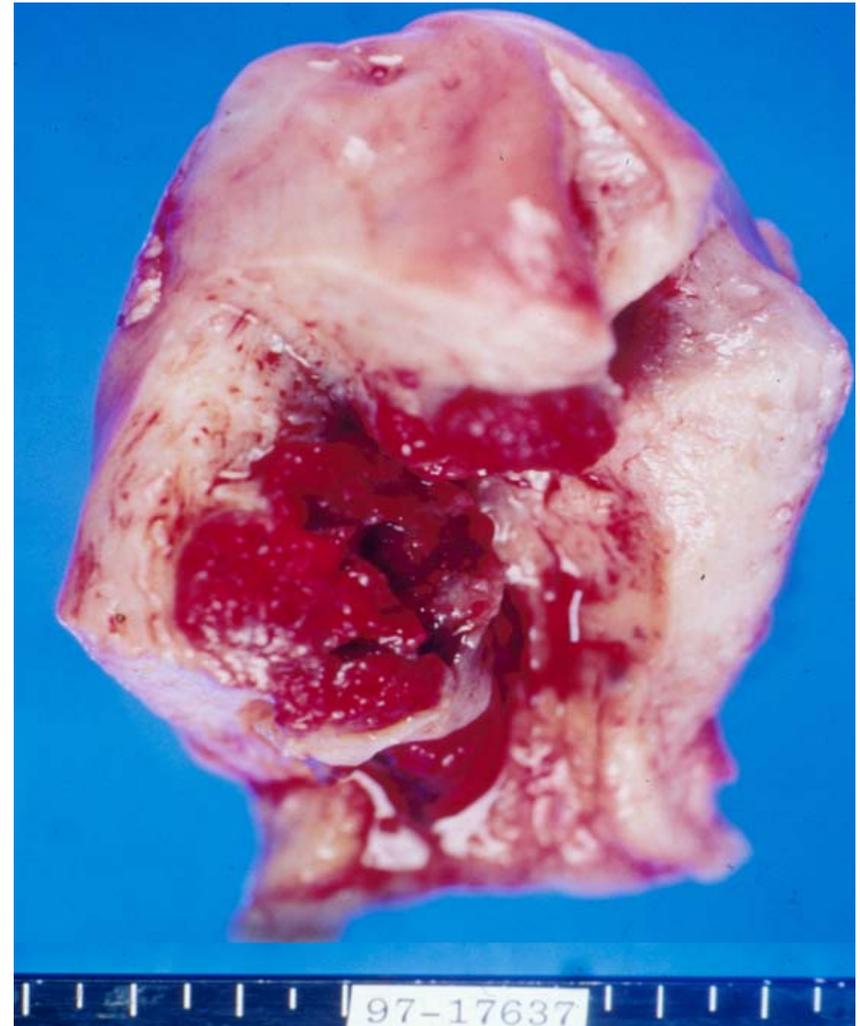
- 1/2000 pregnancy
- Complete mole:
 - 46, XX, paternal origin
- Incomplete mole:
 - oocytes fertilized with two spermatozoa, 69
- 陰道出血, HCG↑, 超音波
- 2.5% choriocarcinoma

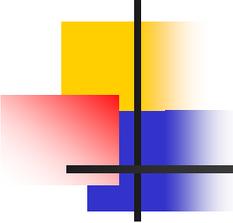


Choriocarcinoma

- **Malignant tumor** composed of cytotrophoblasts & syncytiotrophoblasts

- 50% hydatidiform mole
25% abortion
25% normal pregnancy
- **HCG**↑
- Bulky hemorrhagic nodules
- Invades the vein
- Metastasizes to lung, brain, liver
- Responds well to chemotherapy



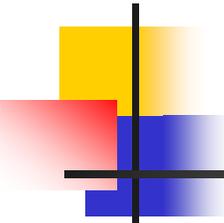


Toxemia of Pregnancy

- Preeclampsia: hypertension, proteinuria, edema
- Eclampsia: more severe, convulsion, coma
- 初產婦較常見
- 妊娠第三期, 但有高血壓, 腎臟病, hydatidiform mole較早發生
- 治療: 輕度: 臥床休息, 飲食, 抗高血壓藥
嚴重: 誘導分娩

Diseases of the Breast

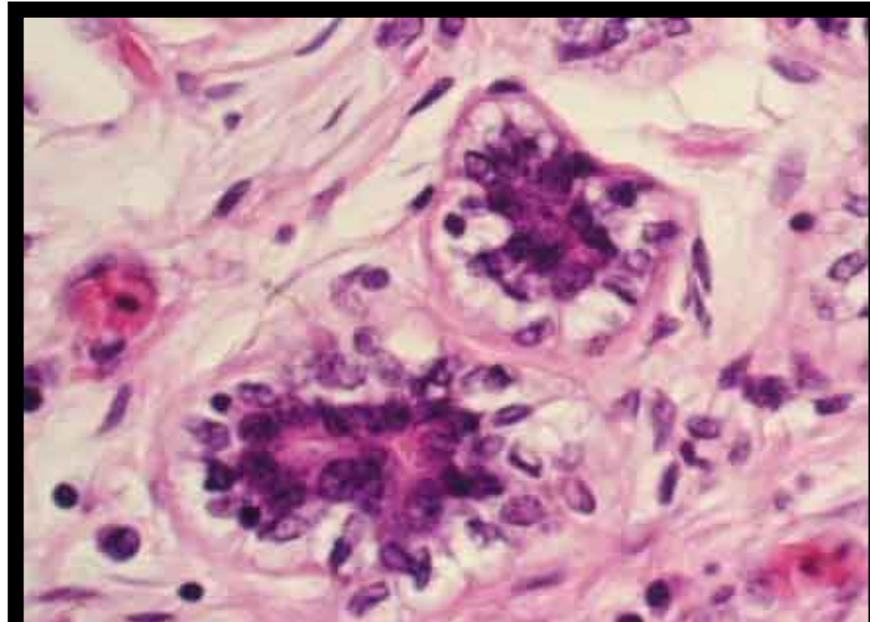
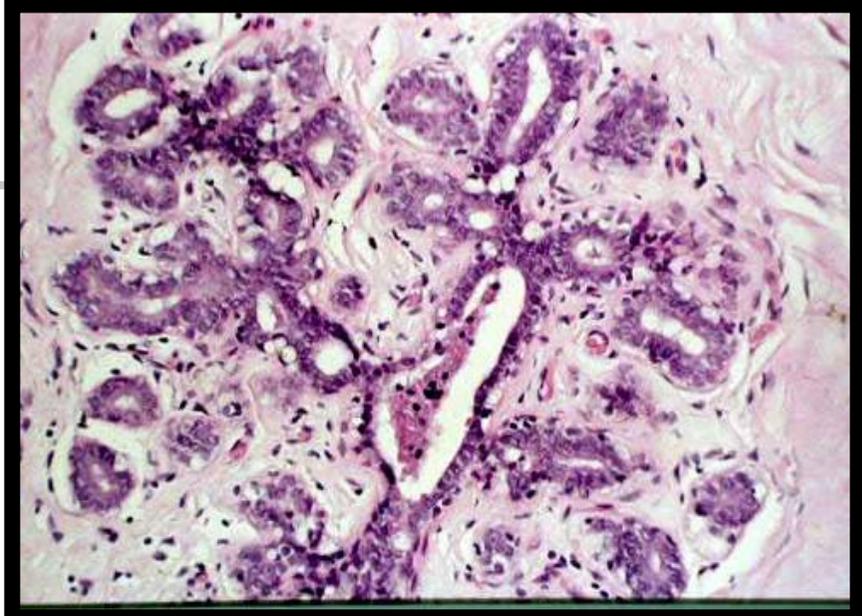
乳房疾病



Overview of major disease

- **Tumors:** cancer is the most important disease affecting the breast
- **Hormonally induced diseases**
- **Inflammatory diseases**

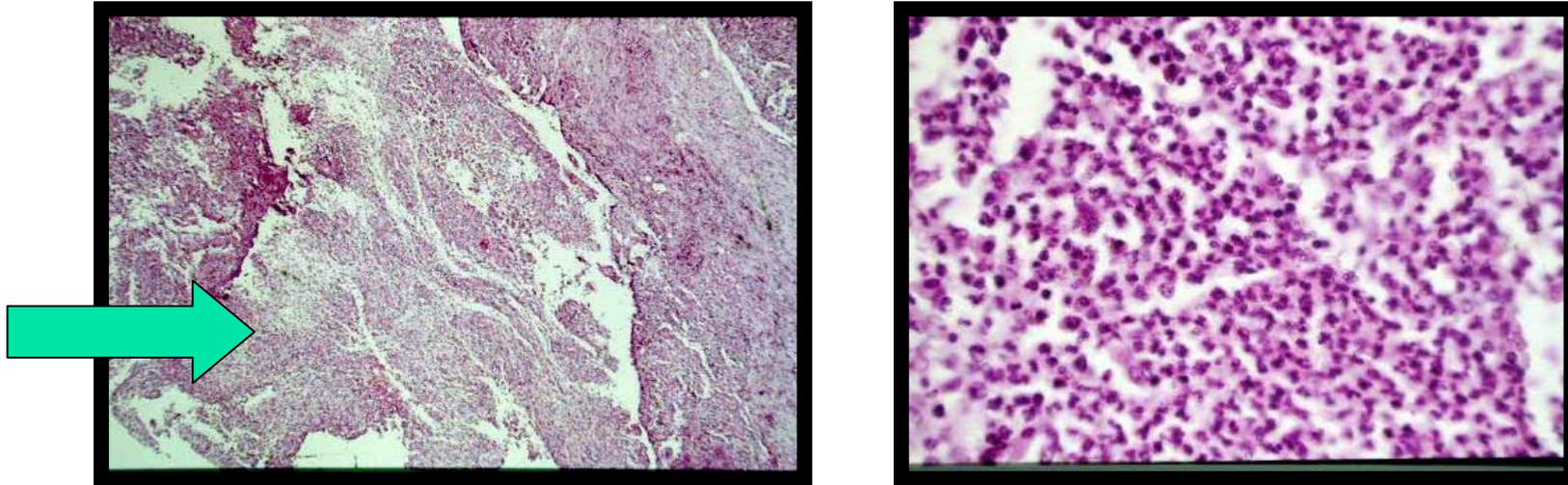
Histology of the Breast



Inflammations

- **Acute mastitis**

- Lactating period, staphylococcus aureus, streptococcus

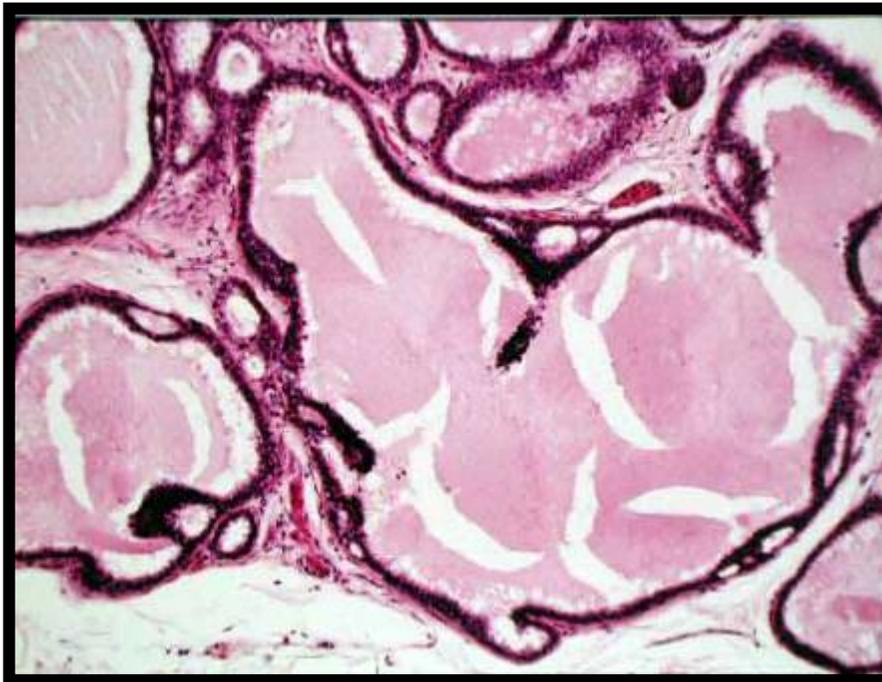


Breast abscess

- **Chronic inflammation**

Hormonally induced changes

- **Pubertal change:** juvenile hyperplasia of the breast
- **Fibrocystic changes**
 - Most common change, hormone imbalance
 - Three dominant patterns of morphologic changes: **Cyst, Fibrosis, Adenosis**

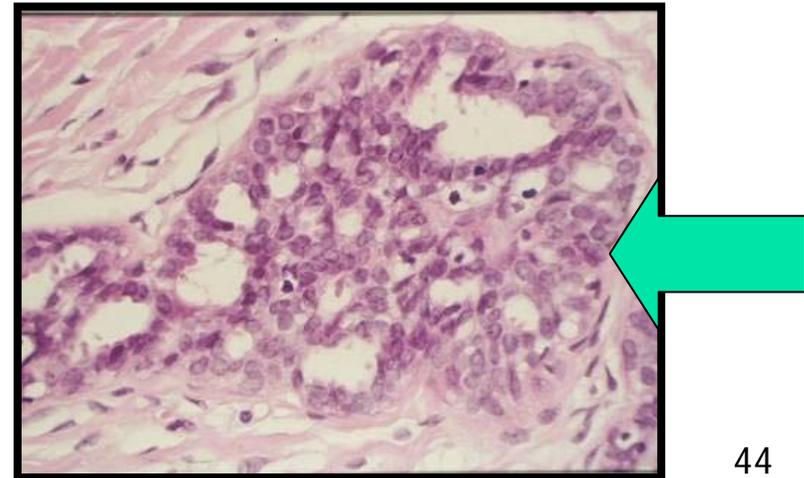


Epithelial Hyperplasia

- Mild hyperplasia: no increased risk
- Moderate and florid hyperplasia: 1.5 ~ 2X
- Atypical hyperplasia: 5X

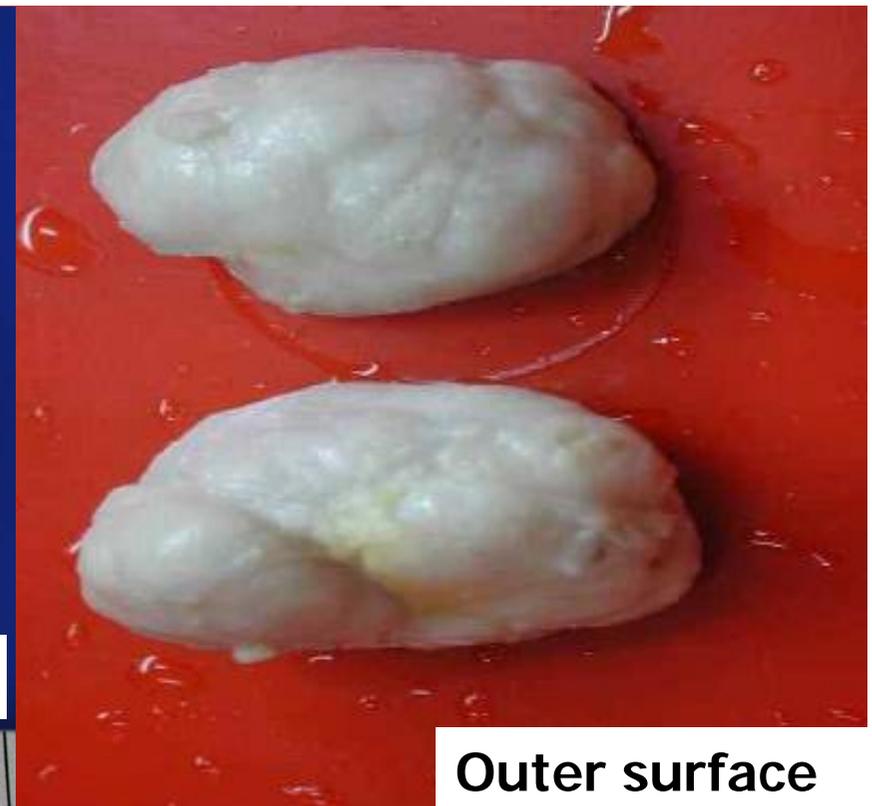
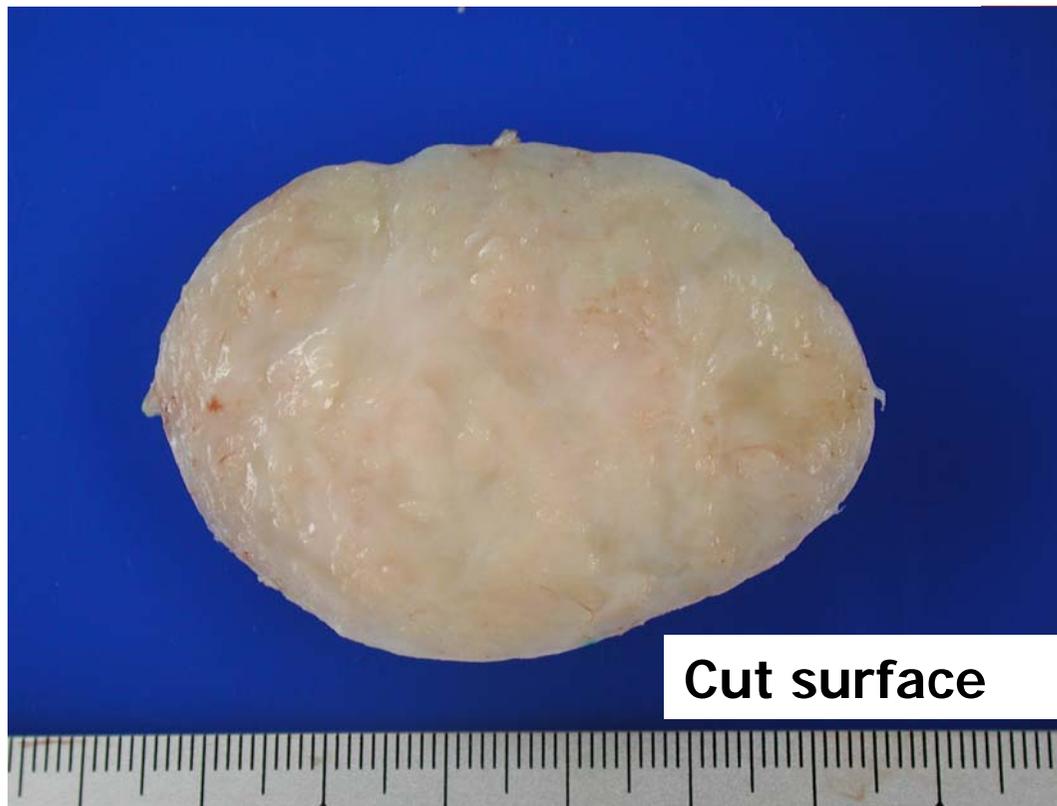
Clinical significance

- Elevate the risk of developing carcinoma
- Differentiation from carcinoma



Fibroadenoma

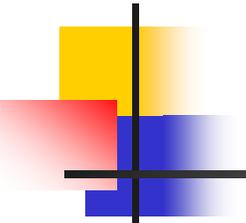
- Most **common** benign tumor
- Occurring at any age within the reproductive period, mainly in **young women** (<30 y/o)
- Well circumscribed





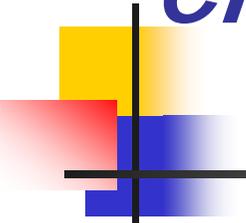
Risk Factors of Breast Cancer

- **Age**
- **Age at Menarche**
- **Pregnancy: first full-term pregnancy**
- **First degree relatives with breast cancer**
- **Proliferative breast disease**
- **Race**
- Exogenous estrogens
- Radiation exposure
- Ca. of contralateral breast or endometrium
- Geographic factors
- Diet
- Obesity
- Cigarette smoking



Clinical Presentation of Breast Carcinoma

- Breast mass discovered by palpation
- Tumor discovered by mammography
- Pain (mastodynia) or painful breast mass
- Nipple retraction, eczematoid reaction, or discharge
- Distant metastases

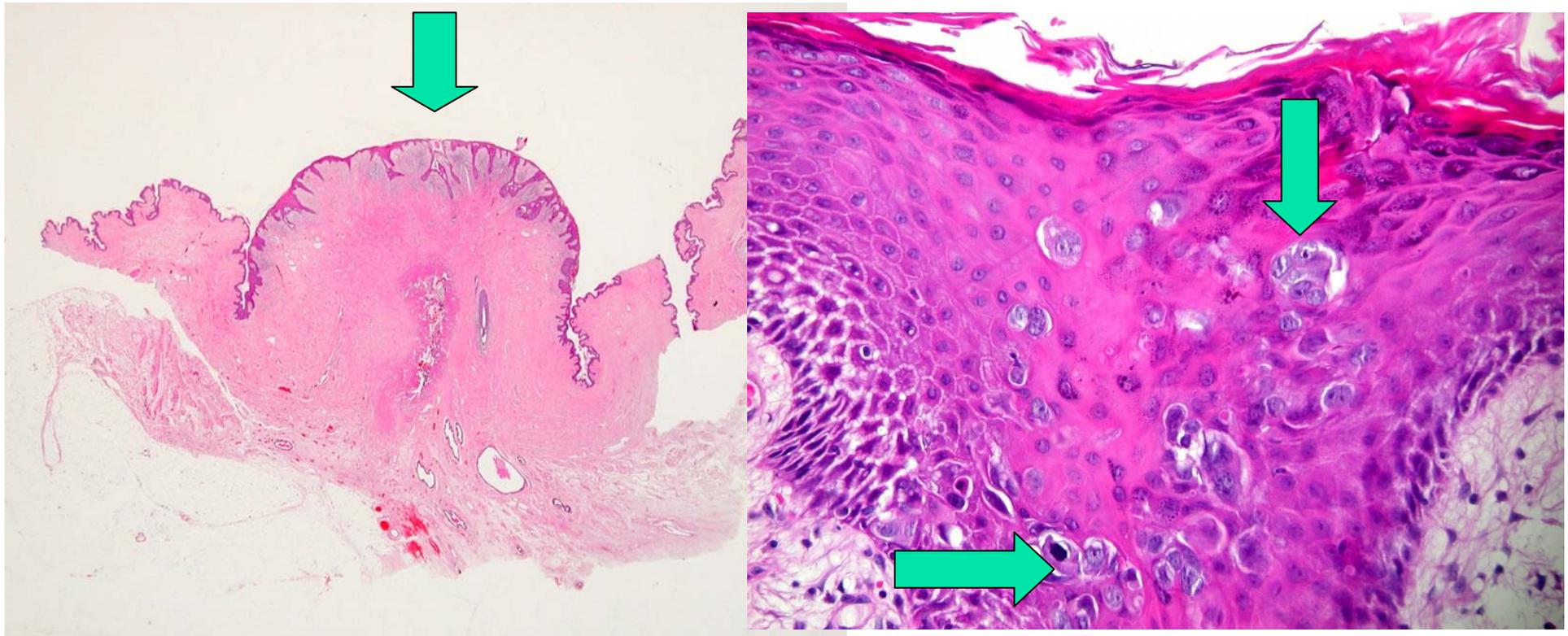


Classification of Breast Carcinoma

- **Carcinoma in situ**
 - **Ductal Carcinoma In Situ (DCIS, Intraductal carcinoma)**
 - **Lobular Carcinoma In Situ (LCIS)**
- **Invasive**
 - **Invasive (infiltrating) ductal carcinoma: 80%**
 - **Invasive lobular carcinoma**
 - **Others**

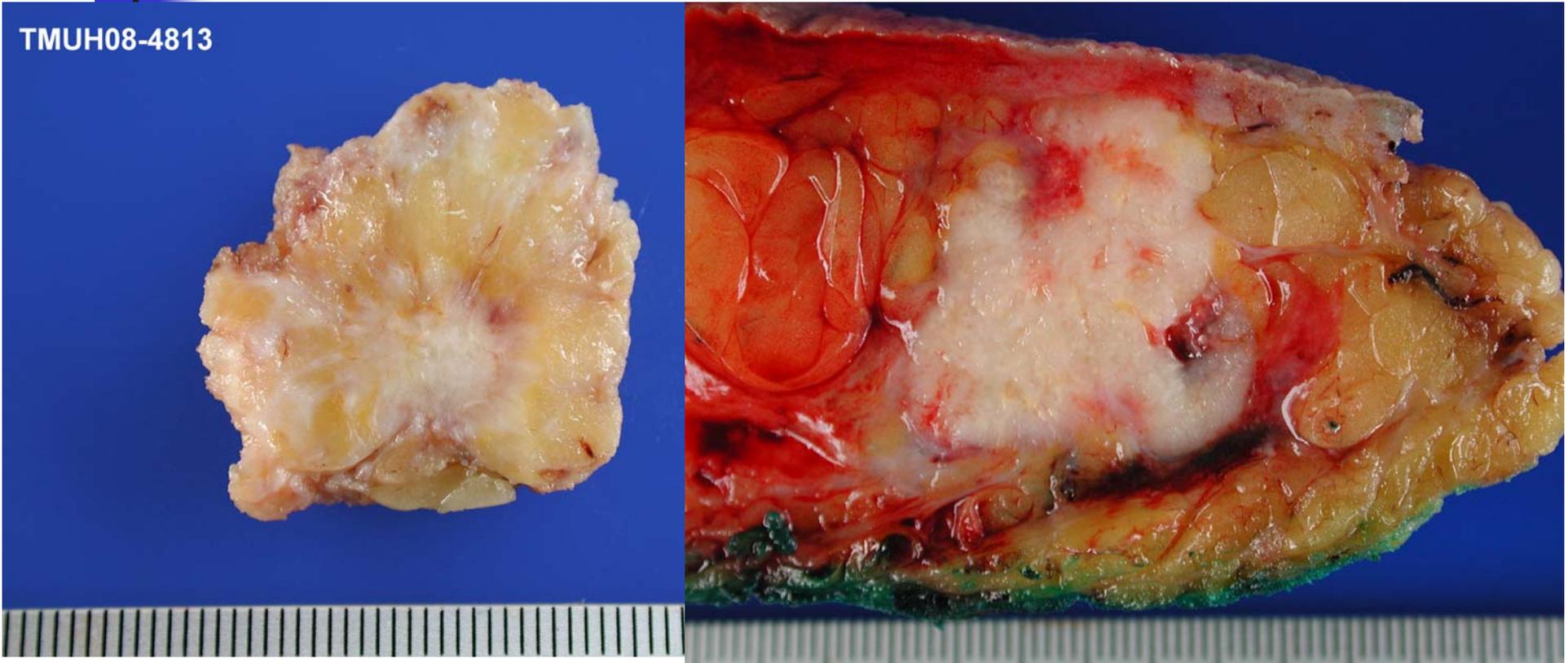
Paget's disease of the nipple

- Rare manifestation of breast cancer

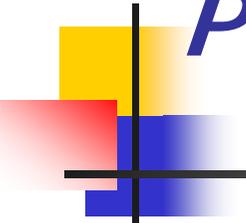


Invasive ductal Carcinoma

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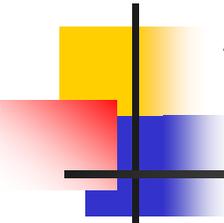


Usually firm to hard in consistency, irregular border



Prognostic and Predictive Factors

- 1. Invasive carcinoma or in situ disease**
- 2. Distant metastases**
- 3. Axillary LN status**
- 4. Tumor size**
- 5. ER & PR**
- 6. Histologic type**

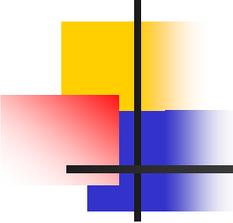


Pathology of Male Breast

Gynecomastia:

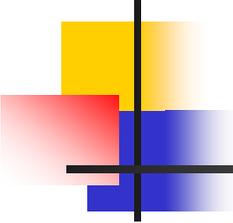
- **Unilateral or bilateral**
- **Causes: indicator of hyperestrinism**
 - **Liver cirrhosis**
 - **Functioning testicular tumor**

Carcinoma



Summary (I)

- **Cervical cancer** is one of the common cancer in women. Nearly all cervical cancer is HPV-related.
- **Endometriosis** refers to location of endometrial glands and stroma outside the uterus. It occurs commonly in the ovary.
- **Adenomyosis** refers to growth of endometrium into the myometrium.
- **Endometrial carcinoma** is associated with estrogen excess and endometrial hyperplasia.



Summary (II)

- The most common benign tumor of female genital tract is **leiomyoma**.
- The **neoplasms of ovary** may be of epithelial, germ cell and sex-cord stromal origin.
- **Fibroadenoma** is the most common benign tumor of the breast.
- The prognosis of **breast cancer** is related to the stage, histological type, estrogen receptor status, etc.