

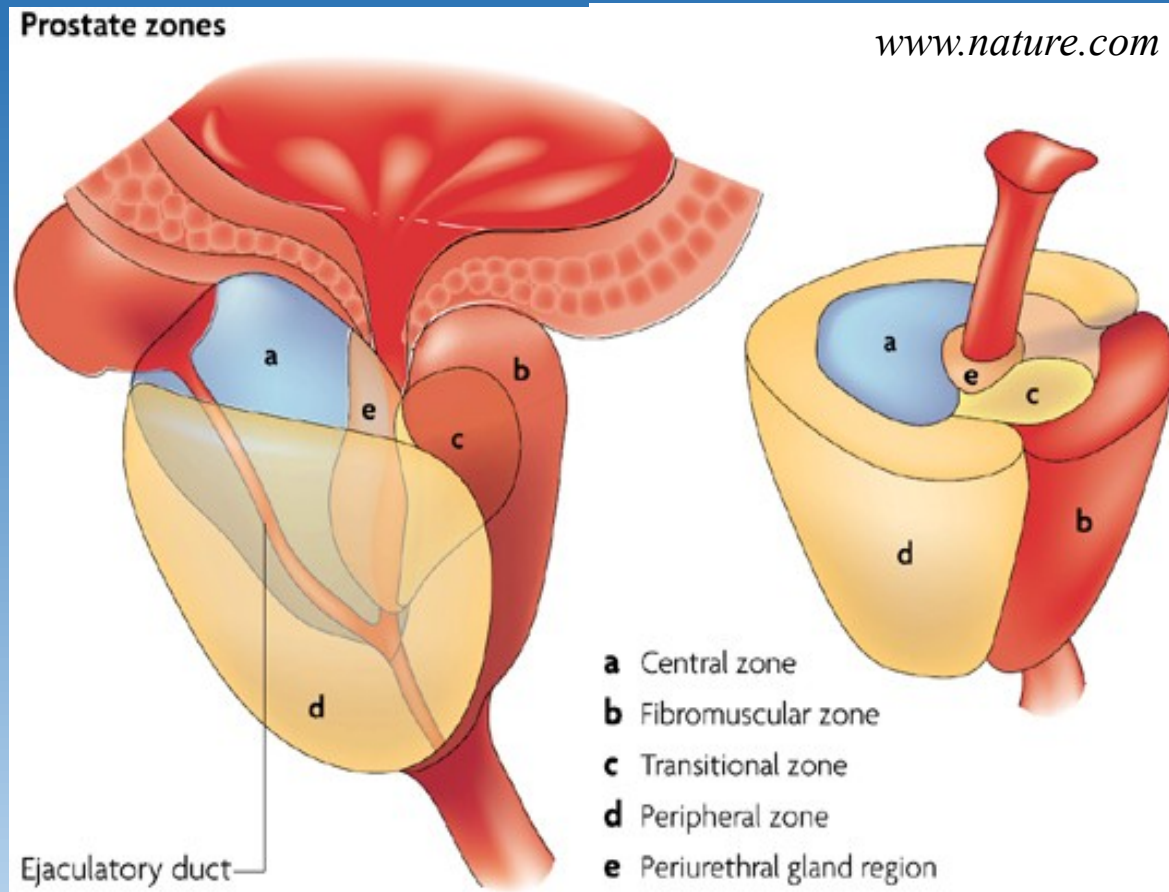
Pathology of the reproductive systems.

Pathology of the breast

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Prostatitis, benign prostatic hyperplasia



Prostatitis

- Bacterial (acute purulent)
 - Systemic symptoms, dysuria, frequency, local pain
 - Ascending infection in UTI (urinary tract infection)
 - Iatrogenic (cathetrisation, surgery, ...)
 - ATB therapy
- Chronic prostatitis/ chronic pelvic pain syndrome
 - Most common (90%)
 - Recurrent chronic genitourinary pain
 - Sexual dysfunction

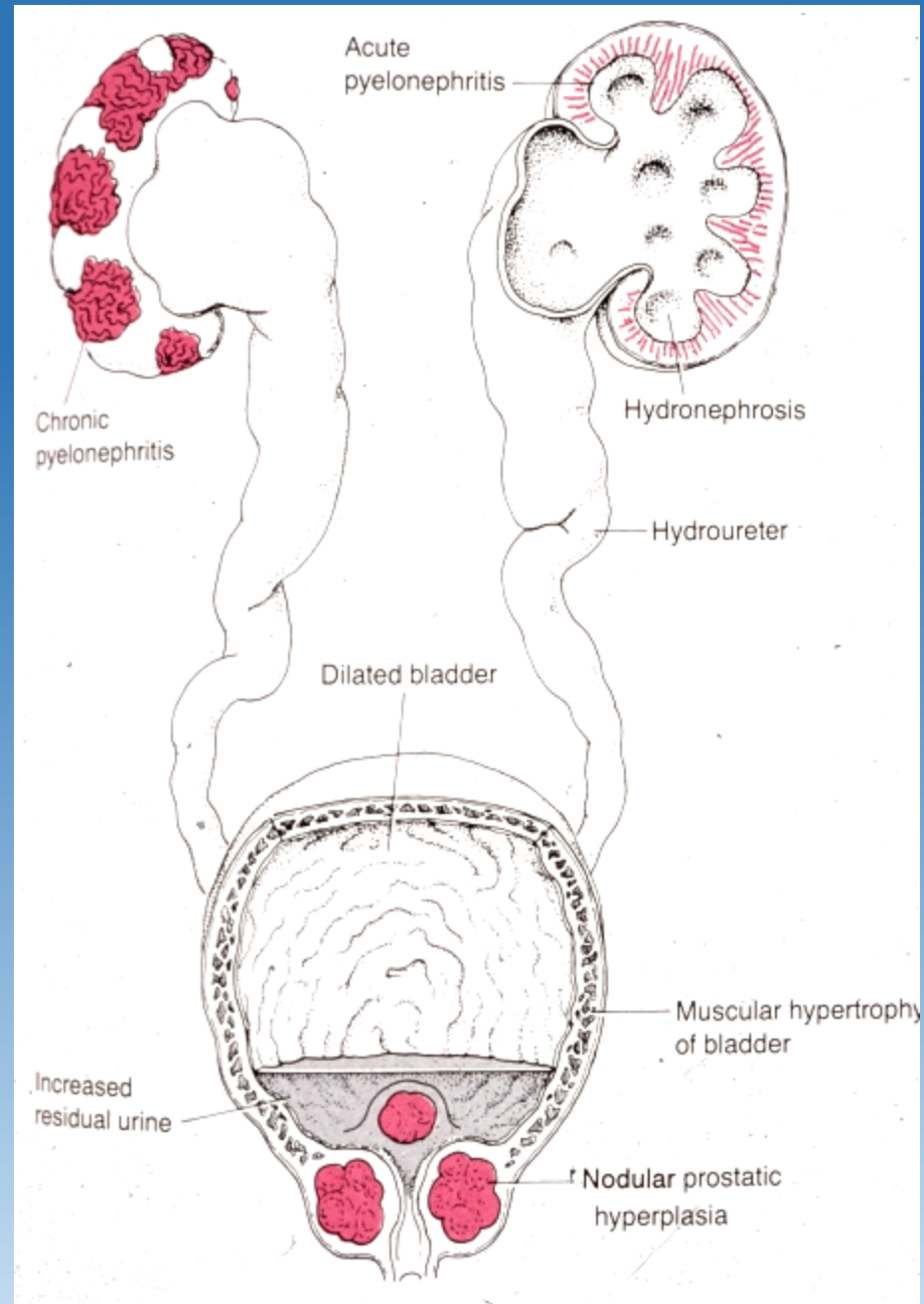
Benign prostatic hyperplasia

- **epidemiologic factors:**
 - age (BPH prevalence rising with age, 70% by age 60, 90% by 80)
 - geographic/racial (low in Asia, more common in W Europe)
- **pathogenesis:**
 - not completely clear
 - hormonal dysbalance
- **Gross: nodular hyperplasia**
 - periurethral (transition zone) mostly affected → urethral compression + obstruction

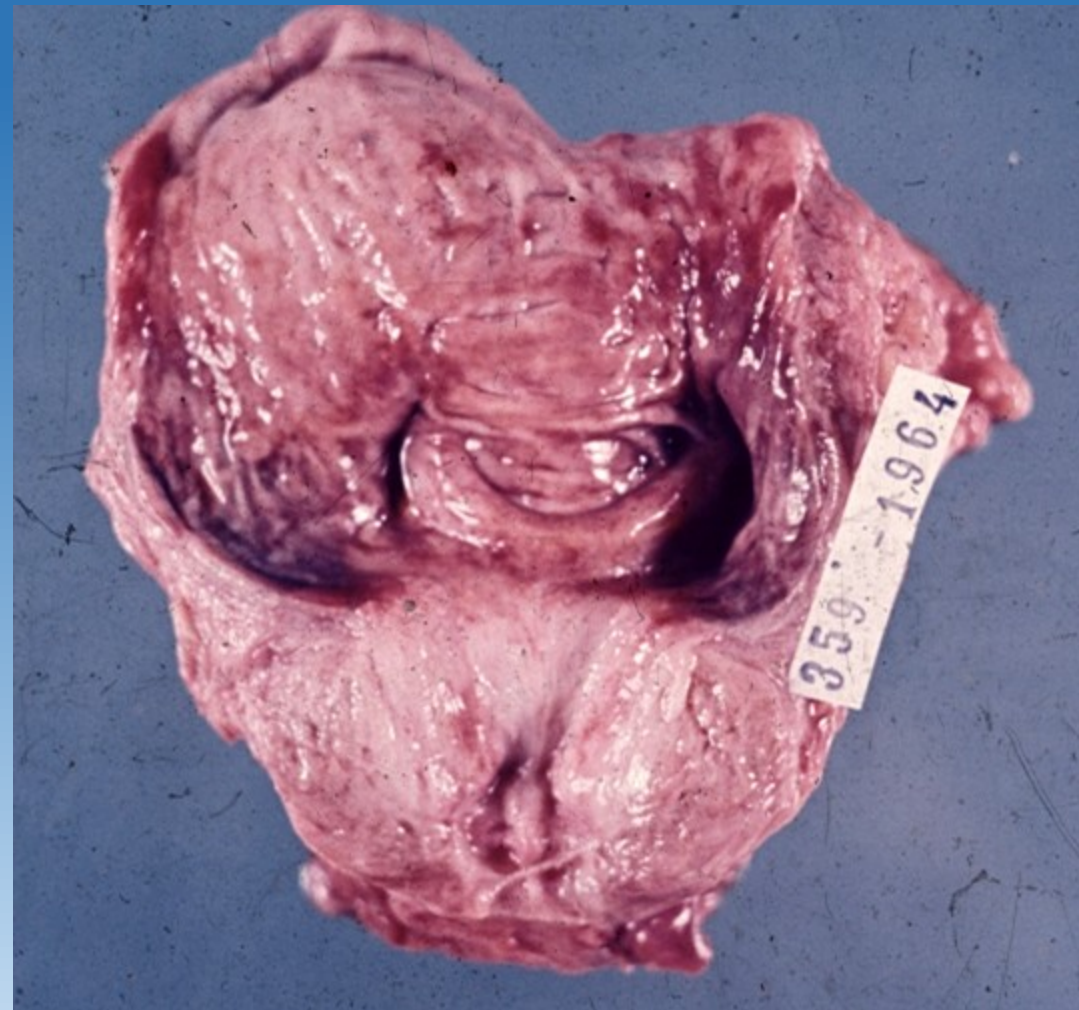
Benign prostatic hyperplasia

- **Clinical signs + complications:** partial → complete urethral obstruction, urinary residuum, risk of infection lower urinary tract symptoms (disturbances of the urine flow)
 - Storage symptoms – nocturia, frequency, urgency
 - Voiding symptoms – weak stream
- acute/chronic urinary retention, bladder trabecular hypertrophy, cystitis
- + ascending infection – pyelonephritis,
- Hydronephrosis.
- Benign, but setting for possible preneoplastic changes
- Th: surgery, drugs

Complications of prostatic hyperplasia



Benign prostatic hyperplasia



Benign prostatic hyperplasia - implications

- Urination more than every 2 hours
- More than once during the night
- Weak, interrupted urine stream
- Difficulty emptying the bladder
- Genital/pelvic pain
- Pain associated with intercourse
- Urine leakage

Possible pelvic floor disorder

Prostatic cancer

- ↑ incidence
 - 1st – 3rd of the most common male malignancies (prostate – lungs – colorectal)
- **peripheral zone of prostate**, dorsal part (palpation per rectum-digital rectal examination)
- dg.:
 - needle biopsy (by suspicion – nonspecific signs, general screening questioned)
 - transurethral resection (BHP treatment – incidental)
- Spread: regional LN, bones (!diff. dg. of pain x local mechanic origin)

Prostatic cancer

- Risk factors:
 - Age
 - African American
 - Family history
 - High-fat diet
 - Alcohol consumption
- Protective factors:
 - Physical activity
 - Tomato (lycopene)

Prostatic cancer

- Staging/grading important for therapy method choice
- Low grade tumors in older males/limited survival expectations – observation – watchful waiting
- Any tumor in younger males – therapy
 - Surgery
 - Radiation
 - Hormone therapy (androgen deprivation)
 - Chemotherapy
- Age > 50 years + unknown cause of musculoskeletal pain + past history of prostatic cancer: suspicion!!

Prostatic cancer therapy complications

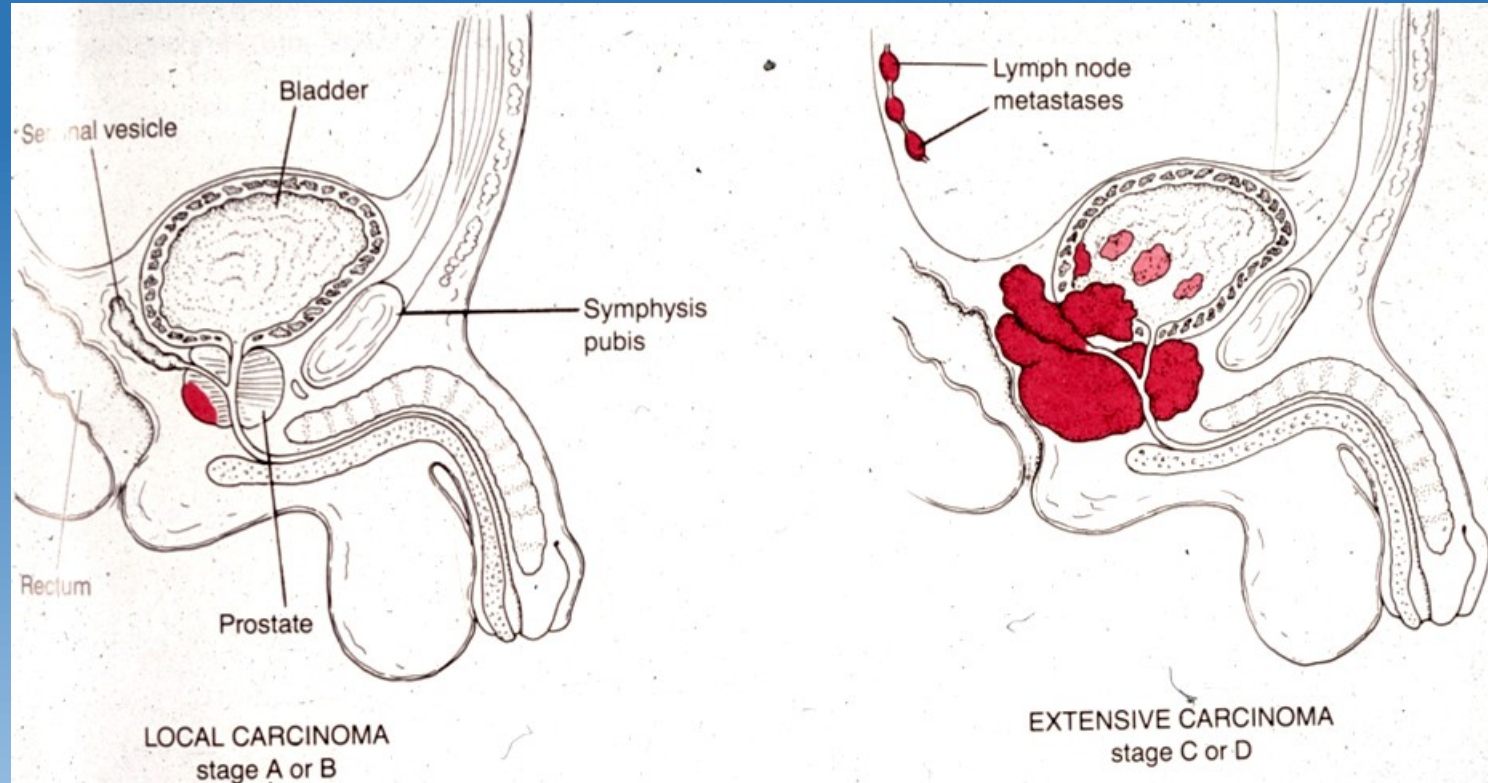
- Urinary incontinence (may be temporal)
- Impotence/sexual dysfunction
- Rectal injury with fecal incontinence, diarrhea
- Muscle atrophy, osteoporosis

- Pelvic physical therapy necessary – pre- + postoperative



Prostatic carcinoma (dorsal, blue) + benign hyperplasia (central)

Prostatic cancer



Prostatic cancer – spine metastases



Disorders of the testes

- **Congenital defects**
 - cryptorchidism (undescended testis) – infertility, ↑ risk of testicular cancer
- **Inflammation:** orchitis/epididymitis, mostly bacterial (in UTI, sepsis)
- Epididymis >>> testis
- Viral (mumps) → possible infertility
- **Testicular torsion:** sudden onset of severe scrotal pain, without immediate surgery → necrosis (haemorrhagic infarction due to twisting of vessels) – ! emergency

Testicular tumors

- **Germ cell tumors**
- Testicular enlargement, firm consistency, may be painful
- Regular testicular self-examination
- Metastasis
 - Regional (retroperitoneal) lymph nodes
 - Lung, liver
 - Bones – late metastasis (pain)

Germ cell tumors

- ~90 % of primary testicular tumors
- Most common solid organ tumors in young males (15-35 years)
- Classification:
 - Seminoma: 4th decade, good prognosis, combined therapy
 - Non-seminomatous tumors: variable types – variable age; different prognosis
- Serum tumor markers:
 - detection in serum, tissues
 - important in diagnosis, monitoring the response to therapy, patient check-up after therapy

Germ cell tumors

- Prognosis: early detection (stage I, limited to the testis) – 95% cured
- Therapy: combination of surgery (orchiectomy, LN dissection) + radiotherapy, chemotherapy
- **Implications:**
 - Possible lymphedema, infertility + sexual dysfunction
 - Side effects + toxicity of chemo/radiotherapy
 - Second malignancy possible

Penile disorders

- **Inflammations**
 - balanoposthitis (glans + inner surface of the prepuce)
 - STD (gonorrhoea, genital herpes, syphilis ...)
 - risk factors:
 - phimosis, chronic mechanical/chemical irritation
 - Immunodeficiency (DM) - candidiasis

Penile disorders

- Benign epithelial tumors
 - condyloma accuminatum – viral wart
 - HPV 6, 11
- Malignant epithelial tumors
 - invasive squamous cell carcinoma
 - geography (Latin America, East Asia)
 - circumcision - protective factor (↓HPV, carcinogenes in smegma)
 - risk factor – smoking, occupational (mineral oil, tar)
 - Macro: non-healing red patch, ulcer, verruca

Penile disorders

Erectile dysfunction: impotence

- Risk factors: age, smoking, medical history (DM, heart disease, hypertension, obesity, alcoholism, local surgery, drugs)
- Causes: organic (neurogenic, venogenic, arteriogenic) x psychogenic (more common in young)
- Sensitive situation /questions, diagnosis necessary
- Treatment: pharmacology, prosthetic devices, pelvic floor exercises

Menopause

- 1 year without menses
- Perimenopause: hormonal decline, menstrual cycle irregularity
- **Physiological changes:** reduced hormones' level incl. growth hormone, changes in tissue responsiveness mainly to estrogen throughout the body (skin, bone, muscles, heart, intestinal tract, blood vessel, brain, bladder)

Menopause

- **Clinical signs:**

- Thermoregulatory + vasomotor changes (hot flashes, night sweats)
- Sleep disturbances
- Anxiety, mood swings, irritability
- Fatigue
- Pain: headache, peripheral and/or spinal joint pain
- Vaginal atrophy, infections
- Sexual dysfunction
- Pelvic floor dysfunction / prolapse

Menopause

Musculoskeletal system changes

- Muscle mass decline, slower repair
- Osteoporosis: ↑ resorption → ↓ bone mass (density); risk factors: smoking, low calcium + vitamin D; beneficial: exercise
- ↑ peripheral (periosteal) bone growth – part of osteoarthritis
- ↑ fracture risk
- Kyphosis – spinal deformity

Menopause

Medical management:

- Hormone replacement therapy: decreasing benefits + increasing risk with the HRT duration + postmenopausal age (thrombosis, hormone-sensitive cancers, stroke)
- Alternative + complementary therapy: individual results possible; not significant benefits in studies

Menopause – implications for the therapists

- Regular physical activity (↓ the risk for weight gain, fat distribution)
 - Moderate-intensity: reduction of osteoporosis, cardiovascular disease, sleep disturbances
 - Resistance training: reduction of muscle loss (+ adequate nutrition)
- Pelvic floor muscle rehabilitation

Genital tract infections

- Genital tract – open to the outside, barriers necessary
- **Barrier function** - vaginal flora, endocervical mucus; during fertile age
- **Predisposing factors** – nonexistent barrier (age), barrier defect (loss of protective vaginal flora, menstruation, abortion, delivery + residua, instrumentation and other mucosal microtraumata, systemic diseases, drugs,...)

Genital tract infections

- **Ascending infection** most usual (sexually transmitted disease/infection – STD/STI; G- fecal bacteria – E. coli, Proteus,...)
- Lower genital tract (**STD** – HSV, molluscum contagiosum, HPV, trichomonas, chancroid, granuloma inguinale; **endogenous** – candida)
- Entire genital tract (**STD** – gonorrhea, chlamydia, mycoplasma, syphilis; **endogenous** – enteric bacteria), may end in pelvic inflammatory disease

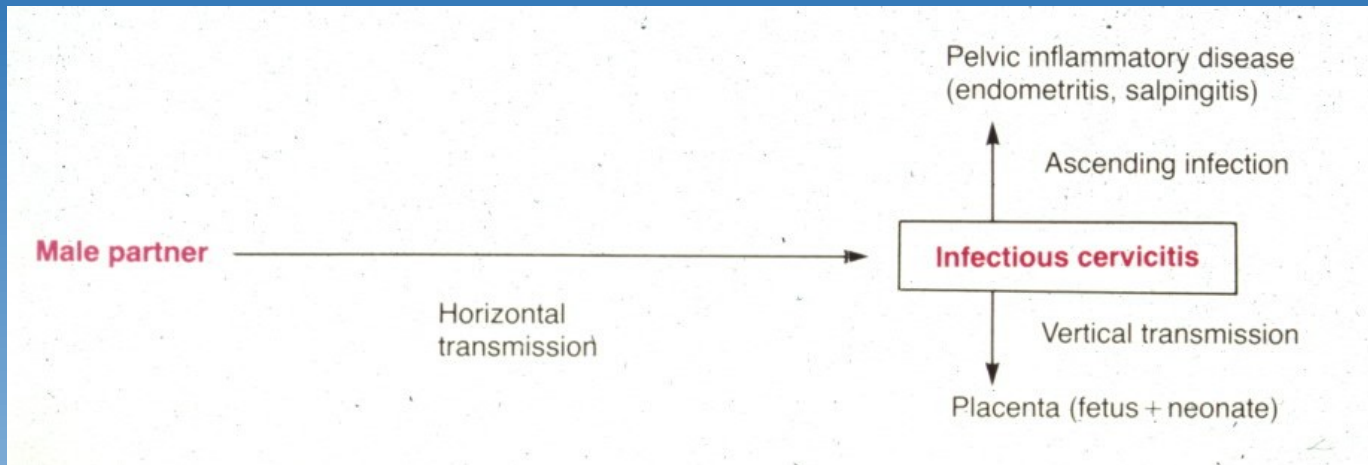
Sexually Transmitted Infections

- Sexually Transmitted Disease - **STD**
- Infection transmitted through vaginal, anal or oral sex
- Every sexually active individual is at risk
- Women acquire infections from men more than men from women
- 2/3 of STD occur in people under 25 yrs of age
- Infection by multiple agents common (↑ risk)
- Fetus or infants – vertical transplacental or perinatal transmission of STD → abortus, inborn defects, neonatal infection. Diagnosis + treatment!!

Genital warts

- May be asymptomatic; single or multiple painless cauliflower-like growths on the vulva, vagina, perineum, urethra, cervix, anus
- Productive infection – low risk types (6, 11)
- Other subtypes of HPV (i.e. 16, 18) strongly associated with cervical dysplasia and/or carcinoma
- HPV - higher risk of vaginal, vulvar, penile, anal dysplasia/carcinoma
- Some types in oral/laryngeal carcinoma
- Vaccination preferably before start of sexual activity; males + females, 2 doses sufficient

STI - complications



Pelvic inflammatory disease

- Infection + inflammation of upper genital tract (endometritis, salpingitis – fallopian tube inflammation, tuboovarian abscess, pelvic peritonitis)
- May lead to infertility, ectopic pregnancy, sepsis
- Signs: pelvic pain incl. chronic, painful intercourse, painful menstruation, vaginal bleeding; in acute stage incl. fever, chills
- Prevention of STD



PID – chronic inflammation + ovarian torsion – hemorrhagic necrosis

Endometriosis

- Foci of functional endometrium (glands + stroma) in an ectopic localisation – outside of the uterus; possible retrograde flow + migration, implantation, ?vascular spread, ?inborn
 - Ovaries, cavum Douglasi, fallopian tubes, peritoneum, bladder, umbilical skin, ... lung, bones ...)
 - Estrogen dependent, changes during menstruation cycle
 - Hemorrhagic (chocolate) cysts, hemosiderin pigmentation, scarring
 - Pain (dysmenorrhea – painful menstruation, dyspareunia), adhesions, infertility
 - Possible source of endometrioid adenocarcinoma

Endometrioid cyst



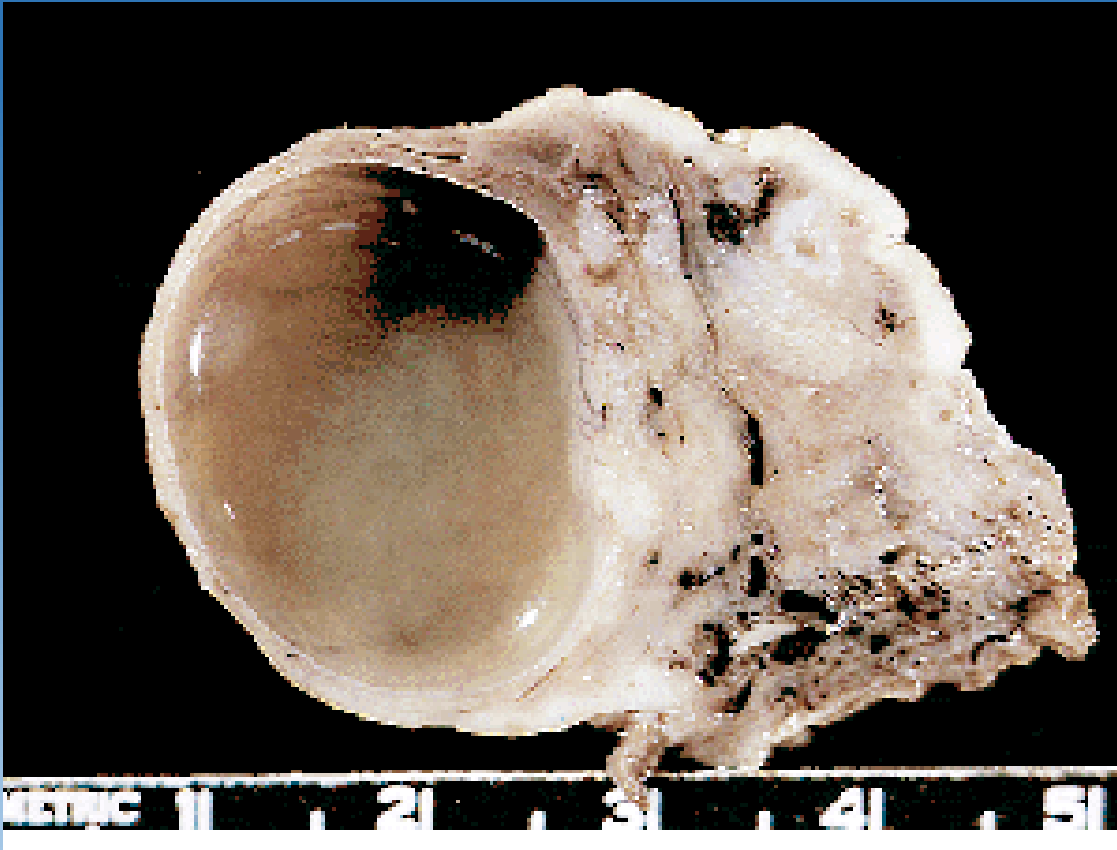
Ovarian cystic disease

- **Non-neoplastic**
 - *inclusion cyst*: small, from superficial epithelium
 - *functional cyst*: stages of ovum maturation/release: follicular, luteal
 - polycystic ovary syndrome: systemic metabolic/hormonal disorder, obesity, infertility, male type of face/body hair,
 - *endometriosis*
- **Neoplastic**: according to the tissue of origin: *surface epithelial tumors, germ cell tu, sex-cord stromal tu, metastatic tu, etc.*

Ovarian cystic disease

- Signs: according to the size + localization, hormone production
 - Pain, abdominal pressure
 - Discomfort during urination, bowel movement, intercourse
 - Sudden/sharp pain: rupture, torsion
 - Endometrial changes due to excessive hormone level (mostly estrogen)

Follicular cyst



- Non-ruptured (no ovulation) enlarging follicle
- Prolongated estrogen release without progestins
- Endometrial hyperplasia common

Ovarian tumors

- 3rd most common tumors of female genital tract
- 80% benign, mostly 20-45 years of age
- 20% malignant, 40-65 years of age, commonly late diagnosis (metastatic disease) → high mortality
- Risk factors variable, according to the type of tumor
- Familiar genetic factors (+ breast ca), nulliparity → risk of ovarian carcinoma
- 90% sporadic



Dermoid cyst – mature cystic teratoma: *most common female germ cell tumor, benign*

Ovarian cancer

- Signs: abdominal bloating/discomfort, flatulence, local pelvic pain, fatigue
- No reliable screening test, marker Ca-125 used
- Pelvic ultrasound possible
- High risk of recurrence
- Lung, liver, lymph node metastasis
- Treatment: surgery (→premature menopause), chemotherapy (side effects)

Surface epithelial tumors

Biologic potential

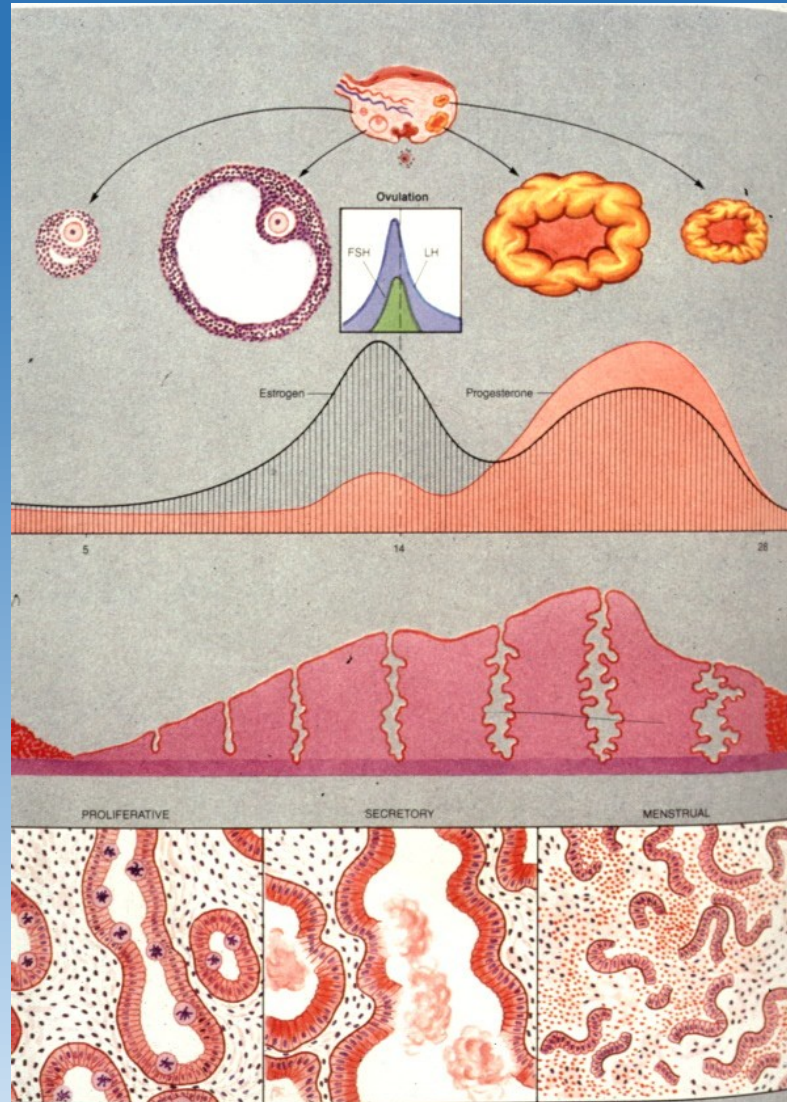
- **Benign**
 - commonly in form of cystadenoma
- **Low malignant potential**
 - borderline malignancy – moderate atypias, mitotic activity, architectonic changes (multilayering, irregular papillary budding), ! no invasion, but non-invasive peritoneal implants possible
- **Malignant**
 - carcinoma



Mucinous cystic tumor of low malignant potential

Menstruation cycle

Early proliferation
Late proliferation
Early secretion
Late secretion
Menstruation



Disorders of menstruation cycle

- **Psychogenic** – sec. amenorrhea, psychogenic sterility
- **Hypothalamic**
- **Pituitary** – idiopathic, secondary (inflammation, tumors,...)
- **Gonadal**
- **Uterine**
- **Metabolic** – endocrine (thyroid, adrenals), hepatic
- **Nutritional**

Abnormal menstruation cycle

- Usual clinical presentation – **abnormal bleeding**
- **Hormonal dysbalance, variable origin**
- **Non-secretory** ← abnormal estrogenic stimulation
 - $\uparrow E \rightarrow$ hyperproliferative \rightarrow hyperplastic endometrium (anovulatory cycle)
- **Secretory** ← abnormal progestins
 - $\downarrow P \rightarrow$ hyposecretory endometrium (luteal phase insufficiency)
 - $\uparrow P$ exogenous (contraception) - stroma-glandular dissociation – pseudo-decidualized stroma + atrophic glands
- **Irregular, mixed** ← E+P dysbalance
 - irregular shedding – mixed secretory + menstrual + proliferative

Endometrial polyp

- up to $\frac{1}{4}$ women during fertile life
- common in climacterium
- dysfunctional bleeding
- possible cause of infertility
- possible start/localisation of endometrial ca

Tumors of the uterine body

- **Endometrial lesions:**
 - Non-physiological non-invasive proliferation of endometrium, benign lesion (reactive) → premalignant condition (monoclonal)
 - Endometrial carcinoma
- **Tumors of myometrium:**
 - Smooth muscle tumor: leiomyoma (fibroid)

Endometrial carcinoma

- Most common malignant tumor of female genital tract
 - 2. cervical ca, 3. ovarian tumors
- **type I: perimenopause** (55-65 years of age)
 - Cca 80%
 - Risk factors:
 - unopposed estrogenic stimulation – endo-/exogenous
 - DM, obesity, early menarche - late menopause
 - Infertility, nulliparity (childless)
 - Precursor: atypical endometrial hyperplasia
 - Better prognosis, lymphatic spread possible

Endometrial carcinoma

- **type 2** – cca 15-20%, not directly connected with permanent estrogenic stimulation, in later postmenopause, high grade, aggressive, worse prognosis
- **Staging** – according to the invasion into the uterine wall, cervix, surrounding structures

Endometrial carcinoma

- **Signs:** abnormal bleeding – menometroragia in pre- and perimenopause, metrorrhagia in postmenopause;
uncommonly accidental finding
rarely - generalisation
- **Gross:** exophytic, ulcerated, whitish

Endometrial carcinoma



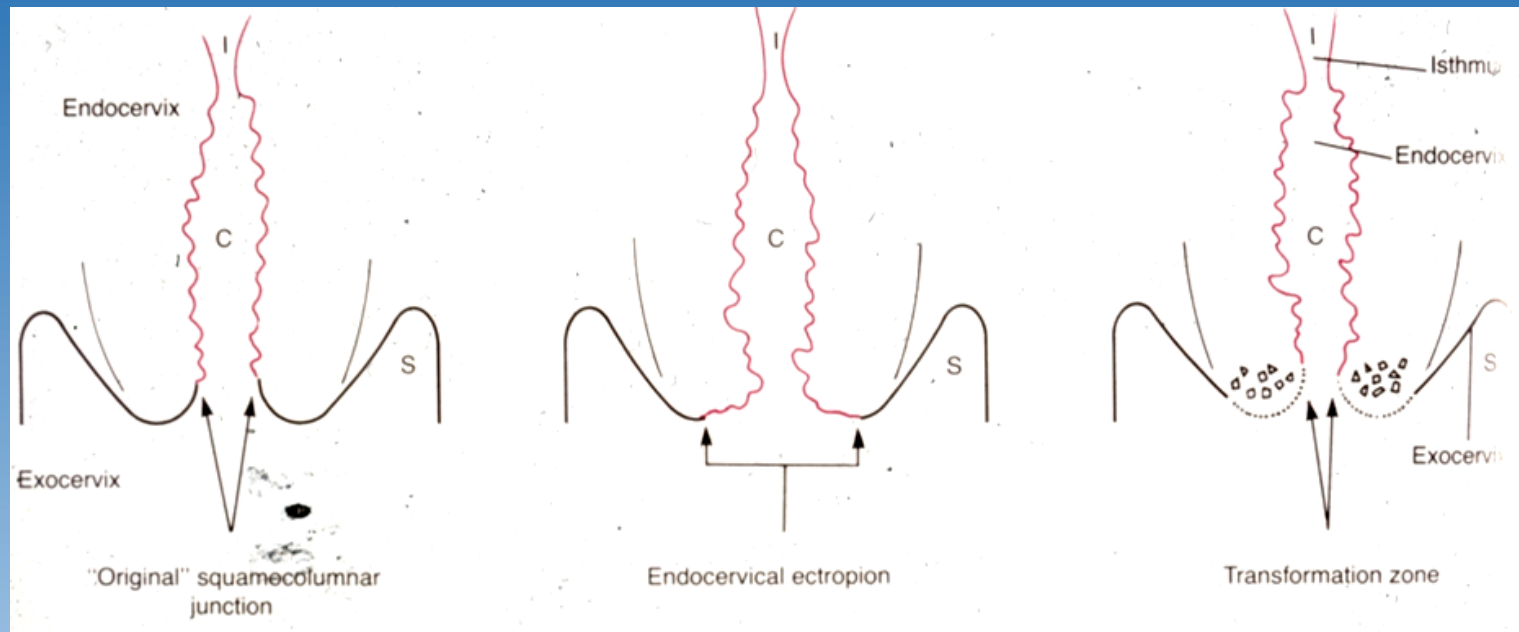
Leiomyoma

- most common benign female tumor (usual in later reproductive age), 40-70% of females
- size: mm - cca 20 cm
- symptoms due to localisation/topography (bleeding, pain, infertility, compression of adjacent organs)
- in pregnancy ↑ risk of abortion, uterine rupture, possible barrier of normal delivery
- uterus myomatosus (multiple leiomyomas)
- common regressive changes (edema, fibrosis, hyalinisation, calcification)

Leiomyoma



Cervical epithelium



Transformation zone: immature epithelium, risk zone for HPV infection, preneoplastic changes

Cervical cancer - precursors

- LR (low-risk) HPV (6,11) →→ *koilocytic atypia* of squamous cells
- Cervical dysplasia – intraepithelial neoplasia associated with **HR (high-risk) HPV**:
 - HR HPV:
 - 16, 18, 31, 33, 35
 - deregulation of the cell cycle, ↑ proliferation, ↓ or arrested maturation
- Other risk factors: smoking, high number of births, multiple sexual partners, young age at 1st intercourse (<17 years), oral contraceptives (in combination with other risk factors), ↓ immunity, other STD

Cervical cancer - precursors

- 2 categories of cervical epithelial lesions, according to the risk of progression and clinical management:
 - **LSIL** (low-grade squamous intraepithelial lesion)
= CIN I (cervical intraepithelial neoplasia), exophytic or flat condylomatous lesion
 - mostly self-limited (viral clearance), productive infection, lower rate of progression
 - only regular check in young, local excision in older females
 - **HSIL** (high-grade squamous intraepithelial lesion)
= CIN II/III + carcinoma in situ (non-invasive carcinoma)
 - majority persists or progresses to invasive carcinoma
 - treatment necessary in any age (very careful observation in pregnancy, CIN II in young females)

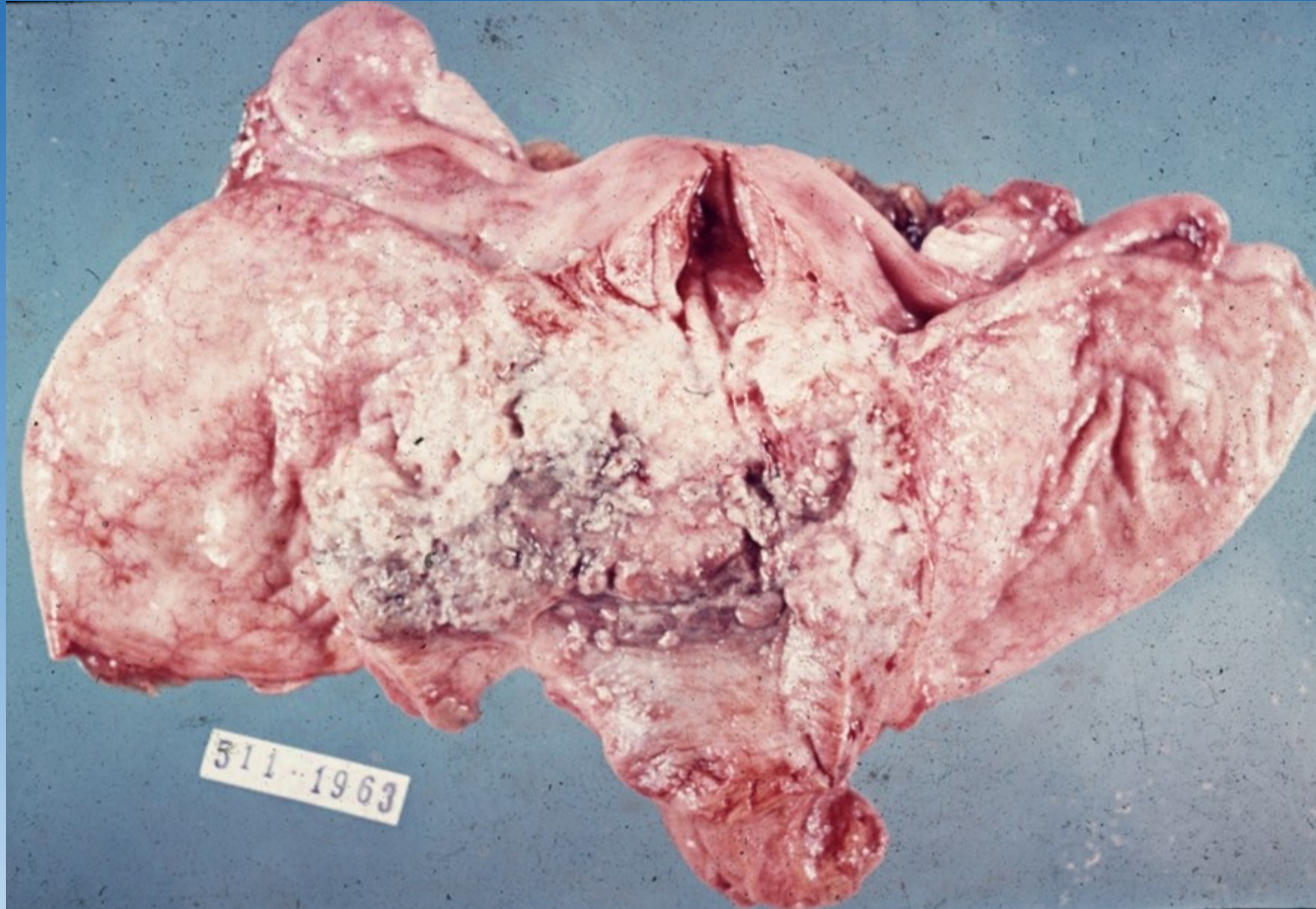
Invasive cervical squamous cell carcinoma

- almost always by HSIL progression
- mostly starts in the transformation zone
- growth:
 - local progression
 - size + depth of the invasive component (bleeding)
 - direct invasion into adjacent organs (bladder, rectum), fistulae
 - regional LN metastases
 - distant metastases via blood (lung, liver, bone marrow)
- ↑ incidence, but mostly lower stages (if screened), ↓ mortality
- Treatment side effects common
- Prevention: vaccination (incl. males), most common types are covered by the immunization, crossed immunity possible; further evolution ? – spread of less common types possible

Cervical cancer



Cervical cancer – late stage



Pelvic floor disorders

- Lesions of variable pelvic structures:
 - Organ based / medical treatment (UTI, PID, ...)
 - Common musculoskeletal disorders (lumbar, sacroiliac dysfunction) – treated by most physical therapist
 - Special musculoskeletal disorders (painful bladder syndrome, pelvic floor muscles dysfunction) - treated by specialist physical therapist

Pelvic floor disorders

Pelvic organ prolapse

- **Cystocele**: bladder prolapse (loss of support), displacement of the bladder, bulging of anterior vaginal wall
- **Rectocele**: rectum prolapse, bulging of posterior vaginal wall
- **Uterine prolapse**: herniation of the uterus into vagina, variable stages, protrusion to the outside possible

Pelvic floor disorders

- Risk factors: multiple pregnancies, familial risk, aging, history of heavy weight lifting, obesity, chronic constipation, chronic cough
- Signs variable, not directly related to the stage
 - Sense of heaviness/pressure in perineum
 - Foreign „lump“ in the vagina
 - Backache, bleeding (irritation)
 - Cystocele: frequency/urgency, incontinence
 - Rectocele: incomplete emptying, constipation

Pelvic floor disorders

- Treatment:
 - surgery,
 - mechanical treatment (pessary)
 - Conservative: pelvic floor muscles rehabilitation/strengthening, biofeedback, stimulation
- ! Exacerbation of prolapse during other exercises (increased intraabdominal pressure)

Benign breast disorders

Benign epithelial lesions

- **benign alterations in ducts and lobules**
- **common lesions** (benign breast changes)
- classification according to the risk of developing subsequent breast carcinoma
 - Nonproliferative/non-atypical lesions (cyst, fibrosis, usual hyperplasia, ...) no risk
- palpable irregularities (lumps, granularity), +/-tender
- etiology:
 - hormone dependent
 - inflammation-associated
- diff. dg.: malignant tumors

Benign breast disorders

- Symptom + findings
 - Cyclical swelling, tenderness
 - Breast pain
 - Cysts
 - Nodularity
 - Nipple discharge
 - Infections, inflammations

Benign breast disorders

- **Fibroadenoma**

- Most common breast tumor in young females (peak incidence before 30 years)
- Benign, circumscribed, mobile, rubbery
- May be painful before menses
- Proliferating ducts + increased amount of stroma

Breast cancer

Atypical hyperplasia (ductal, lobular)– 5x ↑ risk of invasive cancer

Carcinoma in situ: intraductal (DCIS)

lobular carcinoma in situ (LCIS)

- Monoclonal neoplastic lesions
- Direct precursors of invasive cancer
- High relative risk of subsequent invasive carcinoma (10x)
- Histopathological diagnosis necessary

Breast cancer

- **commonest malignancy in females in high-income countries**
- **rising incidence**
- **falling mortality**
 - screening + better diagnostics
 - known modifiable risk factors
 - more effective therapy
- **metastases**
 - lymphatic spread – regional LN (mostly axillary)
 - haematogenous spread (bones, lung, liver, brain...)

Breast cancer

- Risk factors:

- Age (65+ x younger)
- High endogenous estrogen levels, chronic inflammation (incl. obesity)
- Early menarche (<12 years), late menopause (>55 years)
- No full-term pregnancy, no breastfeeding
- Late age (>30 years) at first full term pregnancy
- Smoking, alcohol
- Radiation exposure
- Hormone replacement therapy (long-term)

Breast cancer

- **Sporadic carcinomas** ($\approx 95\%$)
 - accidental sequential mutations
 - mostly perimenopausal/postmenopausal, old age (50-75)
- **Familial carcinomas** ($\approx 5\%$)
 - hereditary mutations in some TSG (BRCA1, BRCA2...)
 - typical in young females (after age of 20)
 - possible multicentric, bilateral \rightarrow prophylactic mastectomy
 - \uparrow risk of ovarian carcinomas

Breast cancer

- Invasive carcinoma of non-specific type (former invasive ductal carcinoma)
- Invasive lobular carcinoma
- Others

- Screening: mammography, ultrasound
- Signs: palpable mass, firm, irregular, painless
 - New asymmetry, distortion
 - Nipple discharge
 - Axillar lymphadenopathy

Breast cancer

- Diagnosis by histopathology
 - Core-cut biopsy
 - Excision
- Molecular markers important for diagnosis, prognosis, treatment
- Combined treatment:
 - Surgery
 - Radiation
 - Hormonal therapy
 - Biologic therapy
 - Chemotherapy

Breast cancer - implications

- Possible help with diagnosis
 - Upper quadrant symptoms of unknown origin
 - Axillar lymphadenopathy – compression of adjacent structures
 - Signs of recurrence; local/regional/distant metastasis
- Preoperative assessment of general and local functional status
- Postoperative rehabilitation, complications and their prevention (lymphedema, decreased range of movements, scarring)
- Side effects of chemo-, radiotherapy, hormonal therapy, ...