HMM 4401–Cancer
Cancer

• A group of diseases characterised by unregulated cell growth: (i) invade locally; (ii) produce distant satellites (metastases)

• The "cancer epidemic": if all tobacco-related cancers were removed from statistics, there would have been a decline in age-adjusted cancer incidence among women (but not men)
Carcinogenesis

• Initiation: a carcinogen (chemical, virus, radiation, sunlight) changes the cell’s genetic material to make the cell cancerous

• A promotor (a genetic flaw or another agent) may make the cell more susceptible to carcinogens
THE CELL CYCLE

Cell divides (mitosis)

Cell prepares to divide

Cell replicates its DNA

Beginning of cycle

Cell enlarges and makes new proteins

Restriction point: cell decides whether to commit itself to the complete cycle

G0

G1

G2

M

R

S

Cell rests
**Stimulatory Pathways**

- Growth factor ("go" signal)
- Neighboring cells release growth stimulatory factors
- Receptors at cell surface
- Cytoplasmic relay proteins
- Transcription factors
- DNA
- Proteins that trigger cell division
- Cell cycle clock decides whether cell should proliferate

**Inhibitory Pathways**

- Inhibitor ("stop" signal)
- Neighboring cells release growth inhibitory factors
- Receptors at cell surface
- Cytoplasmic relay proteins
- Transcription factors
- DNA
- Proteins that inhibit cell division
- Cell divides when it should not, because inhibitory signal fails to reach nucleus

**Example of Stimulatory Abnormality**

- No growth factor attaches
- Receptor fires away
- Cell divides in the absence of stimulation by external growth factors

**Example of Inhibitory Abnormality**

- Receptor
- Relay molecule is lost
- Signaling stops
- Cell divides when it should not, because inhibitory signal fails to reach nucleus
Risk factors and causes

- Genetics (Philadelphia chromosome): Breast cancer and ovarian cancer ($\text{BRA}_1, \text{BRA}_2$ (some women have 80-90% risk of breast cancer)), colon cancer, Down’s syndrome
- Smoke (lung, mouth, larynx, bladder)
- Radiation: X-rays and other ionizing radiation, non-ionizing radiation? (sunlight, mobile phones?)
- Diet (fibre, smoked food)
- Place of living (Japan, USA)
- Infections
Colonoscopic view of bleeding colon cancer
Basal cell carcinoma, most common form of cancer
Terms

• Carcinoma, adenocarcinoma
• Sarcoma
• Hematogenic and lymphatic metastases
• Hepatoma
• Seminoma
• Hypernephroma
• Lymphoma
• Leukemia
Diagnosis

• Screening
• Biopsy: fine needle and lump
• Cytology (Papanicolaou, other)
• Examination of any opening: oral, bronchial, esophageal, gastric, rectal, colonic, vaginal, urethral
• Examination of stool and urine
• X-ray
• CT
• MRI
Screening

• Screening: a test to detect the possibility of cancer
• Aim: early diagnosis
• Sensitivity: The probability that a patient with cancer will have a positive test
• Specificity: The probability that a patient without cancer has a negative
• Predictive value positive: the probability that a patient with a positive test has cancer
Treatment

• Surgery for solid tumours (not diffuse cancers such as leukemia, lymphomas, etc)
Treatment

- Surgery
- Radiation; curing: lymphomas, seinomas, others; palliation for painful metastases
- X-rays (electromagnetic radiation), proton beam radiation
- Side effects: nausea, skin burns, tissue damage
Treatment

• Surgery
• Radiation
• Chemotherapy (cytostatics etc.). Note side effects: nausea, vomiting, fatigue, hair-loss
• Combination therapy
• Investigational therapy: high dose radiation combined with later infusion of stem cells
• Adjuvant therapy

• Great improvements in therapy: some lymphomas, some childhood cancers, seminoma,
Tumour markers/antigens

- PSA – prostata specific antigen
- CEA - Carcinoembryonic antigen (colon, breast, pancreas, smoking, etc)
- Alpha-fetoprotein (liver cancer, testis, ovary)
- Others
Herceptin®

- Human Epidermal growth factor Receptor 2 (HER2) gene results in HER2 protein overexpression
- HER2 overexpression occurs in approximately 25% of breast cancer patients
- HER2 protein overexpression correlates with several negative prognostic variables, including estrogen receptor-negative (note: tamoxiphen)
- Herceptin™ (Trastuzumab) monoclonal antibody
- Mechanism: cytotoxic, cytostatic
Monoclonal antibodies targeting a HER2 protein overexpressing cell
Improvements in Median Time to Disease Progression

Combined Chemotherapy Results
- Chemotherapy Alone*: 4.5 months (n=234)
- Herceptin + Chemotherapy*: 7.2 months (n=235)
- Paclitaxel Subgroup
  - Paclitaxel Alone: 2.5 months (n=96)
  - Herceptin + Paclitaxel: 6.7 months (n=92)

*Chemotherapy = either doxorubicin or epirubicin plus cyclophosphamide, or paclitaxel.
Improvements in One-Year Survival

![Graph showing improvements in one-year survival.](image)

- **Chemotherapy Alone**: 68% (n=234)
- **Herceptin + Chemotherapy**: 79% (n=235)

*Chemotherapy = either doxorubicin or epirubicin plus cyclophosphamide, or paclitaxel.*
Herceptin®

- HER2 protein overexpression correlates with several negative prognostic variables, including estrogen receptor-negative
- Herceptin® (Trastuzumab) monoclonal antibody
- Mechanism: cytotoxic, cytostatic
- Side effects: fever, chills, nausea, vomiting, cardiomyopathy, anaphylaxis
- Costs NOK 250,000 per patient
Breast cancer
Breast anatomy, normal and abnormal
Breast cancer

- Symptoms/occurrence: lump, 1/10,
- Risk factor: age, genetics (BCA1-2), nullipareous, amenorrhea, long menstruating period, late pregnancies, use of estrogens (but hardly p-pills), lack of physical activity
- Screening: mammography
- Diagnosis: palpation, mammography, biopsy, ultrasound, CT, chest X-ray, isotope examination
- Therapy: surgery, radiation, chemotherapy, adjuvant therapy
Breast cancer incidence and mortality by age
Age-adjusted incidence rate 1956–2001 (world std.)
Breast, females

Rate per 100,000

Year of diagnosis

Breast cancer screening – is it effective?
Colon cancer
Age-adjusted incidence rate 1956–2001 (world std.)
Colon

Rate per 100 000

Year of diagnosis


Males
Females
5-year relative survival by period and stage
Colon, males

- Localized
- Regional
- Distant
- Total

Period of diagnosis:
- 1958-62
- 1963-67
- 1968-72
- 1973-77
- 1978-82
- 1983-87
- 1988-92
- 1993-97
Urinary tract cancer

- Definition: tumor of kidney or lower urinary tract. Hypernephroma. 2% of all cancers, more often in men
- Causes: smoking
- Symptoms: (microscopic) hematuria, pain in the side, fever,
- Diagnosis: CT, MR, biopsy, cytology, cystoscopy, ultrasound, intravenous urography
- Treatment: surgery, chemotherapy, radiation
- Prognosis: kidney – not so good; bladder:
Age-adjusted incidence rate 1956–2001 (world std.)
Bladder and other urinary organs

Rate per 100,000

Year of diagnosis

Males
Females
Male reproductive system

- Penis, three erectile tissue/bodies
- Testes: two functions: producing sperm/semen and testosterone
- Priapism – what is it
Benign Prostatic Hyperplasia

- Definition: Benign growth of the prostate gland
- Cause: age, unknown
- Diagnosis: hesitation, frequent urination, nocturia, less urination force, dribble at end of urination, infections, rectal examination, cystoscopy, biopsy
- Treatment: expectation, drugs, transurethral surgery, abdominal surgery
Prostatic Cancer

• Definition: malignant tumor of the prostate gland (found in 50% of men aged 70 and all men aged 90)
• Diagnosis: symptoms largely as for BPH, back pain (metastases), rectal examination, urinary retention, cystoscopy, biopsy, PSA
• Treatment: watchful waiting, brachytherapy, external beam radiation, radical surgery, orchidectomy, estrogen, other drugs
• Prognosis: fewer than 3% die from it
Age-specific incidence rate 1997–2001
Prostate
1–5-year relative survival by stage 1993–97
Prostate

- Localized
- Regional
- Distant
- Total

% survival over time:

- Diagnosis: 100%
- 1 year: 80%
- 2 years: 60%
- 3 years: 40%
- 4 years: 20%
- 5 years: 10%

Diagnosis vs. years.
Female genital cancer
Cancer of the female genital organs

• Uterus: age 50+, abnormal bleeding
• Cervix: caused by sexual activity/virus, abnormal bleeding
• Ovaries: 40+, no symptoms, abdominal swell,
• Diagnostics: colposcopy, curettage, ultrasound
• Treatment: conization, surgery, chemotherapy, radiation
Age-adjusted incidence rate 1956–2001 (world std.)
Uterine cervix

Rate per 100,000

Year of diagnosis

1–5-year relative survival by stage 1993–97
Uterine cervix

- Stage I
- Stage II
- Stage III
- Stage IV
- Total

Survival rates over 5 years:
- Diagnosis: 100%
- 1st year: 90%
- 2nd year: 75%
- 3rd year: 60%
- 4th year: 45%
- 5th year: 30%

Graph shows the decreasing survival rates across different stages.
Age-specific incidence rate 1997–2001
Ovary
Immunology
The immune system

- Cells
- Soluble substances (immunoglobulins, antibodies)
Antibodies

- Produced by T-lymphocytes
- igM: the initial substance
- igG: the most prevalent
- igA: surface antigen
- igE: causes immediate allergic reactions
Terms

- Antigen
- Antibody (immunglobulin)
- Complement
- Cytokines
- HLA antigens
- Leucocytes (neutrophile, lymphocyte, eosonophilic)
Allergy

- Allergic reactions – hypersensitivity reactions (atopic diseases)
- Immune reactions in which normal body tissue is damaged
- Types: seasonal rhinitis/conjunctivitis, food allergy, (asthma), anaphylaxis, urticaria (hives, elveblest)
- Diagnosis: history, blood tests (igE), skin tests