LYMPHATIC SYSTEM
T-lymphocytes (activated in the thymus) identify aggressors and try to destroy them through the production of lymphokines (synthesized proteins)

- Killer T-cells
- Helper T-cells
- Suppressor cells
B-lymphocytes (from the bone marrow) synthesize immunoglobulins which function as antibodies combining with foreign antigens (bacteria and viruses):

- IgG – major immunoglobulin (80%)
- IgM – mostly intravascular
- IgA – in body secretions, GI and respiratory tract
- IgE – active in hypersensitivity (allergy)
- IgD
DISEASES OF THE LYMPHATIC SYSTEM

• Obstruction to the lymph flow ➢ Edema

• Draining infected areas ➢ Lymphadenitis

• Cancer: Lymphomas, Hodgkin’s disease, Leukemia
DISEASES THAT COMPROMISE THE HOST DEFENCE MECHANISM

Hodgkin’s disease
Lymphomas
Leukemias
Multiple myeloma
Carcinomas and sarcomas
Inherited or acquired primary immunodeficiency disease
LYMPH NODE STRUCTURE - SCHEMA

- afferent lymph vessels
- lymph follicle
- medullary sinusoids
- intermediary sinusoids
- subcapsular sinusoids
- efferent lymph vessels
- capsule
- trabecula
PREFERENTIAL SITES OF CANCER SPREAD

LUNGS ⇒ Lymph nodes, Adrenal glands, Bones, Liver, Brain

BREAST ⇒ Lymph glands, Lungs, Liver, Bones, Brain

PROSTATE ⇒ Lymph glands, Spine, Bones, Lungs

COLON ⇒ Lymph glands, Liver, Lungs

BRAIN - Rarely to lymph nodes
Lymphatic Spread of Cancer

Intra-thoracic organs drain mostly to the right cervical and supraclavicular lymph nodes.

Intra-abdominal organs drain mostly to the left cervical and supraclavicular lymph nodes.
ENLARGED GLANDS (LYMPHADENOPATHY)

**Subjective:** tender or painless

**Objective:** Acute or chronic
- Local or general
- Isolated or matted glands

**Differential diagnosis:** Chronic infections
- Cancer

**Diagnosis:** Biopsy and pathologic examination

*No needle biopsy*
Left cervical lymphadenopathy (Enlarged lymph nodes) – Chronic lymphatic leukemia (CLL)
Right Cervical (Neck) Enlarged Lymph Nodes - Lymphoma
Swollen glands – Hodgkin’s disease
Burkitt’s lymphoma
Relapse of “Testicular Cancer”
On pathology review: Large cell lymphoma
Use of Gallium$^{67}$ scan in Hodgkin’s disease
High-grade lymphoma involving the floor of the mouth
HIGH-GRADE LYMPHOMA OF THE LT. TONSIL
Liver scan with focal areas of involvement
Abdominal CT Scan of a Patient with Lymphoma
EVALUATION OF HODGKIN’S DISEASE AND LYMPHOMA

Physical examination
Laboratory profile
CT or PET–CT scan
Other tests as indicated by the presentation
LYMPHOMAS OTHER THAN HODGKIN’S DISEASE

Classified by their rate of proliferation:

• Low-grade
• Intermediate grade
• Hi-grade
TREATMENT OF LYMPHOMAS

Low-grade (Indolent) lymphomas:

Observation
Chemotherapy at time of progression +/- Radiation

High-grade (aggressive) lymphomas:

Chemotherapy
Bone marrow transplantation

Multiple myeloma: Chemotherapy + BMT
CANCER of BLOOD FORMING ORGANS

LEUKEMIA
Active (Normal) Bone Marrow
Active (Normal) Bone Marrow
**Neutrophilic Lineage**

- **Pluripotent Stem Cell**
  - IL-1
  - IL-6
  - IL-3
- **Myeloid Stem Cell**
  - IL-3
  - GM-CSF
- **CFU-GEMM**
- **CFU-G**
- **CFU-GM**
- **Myeloblast**
  - GM-CSF
  - G-CSF
- **Neutrophilic Myelocyte**
  - GM-CSF
  - G-CSF
- **Polymorphonucleated Neutrophil**
  - GM-CSF
  - G-CSF
Stem Cell and Blood Cells

- Multipotential hematopoietic stem cell (Hemocytoplasm)
  - Common myeloid progenitor
    - Megakaryocyte: Thrombocytes
    - Basophil
    - Neutrophil
    - Eosinophil
    - Myeloblast
  - Common lymphoid progenitor
    - Natural killer cell (Large granular lymphocyte)
    - Small lymphocyte
    - T lymphocyte
    - B lymphocyte
    - Plasma cell
    - Macrophage
Blood film (smear) to show:
Red blood cells, white blood cells (neutrophils), and a platelet
LIFETIME OF BLOOD CELLS

RBC  120 days
WBC  8.5 -14 days
Platelets  ~ one week
Homeostasis of the White Blood Cells
Leukemia – Microscopic view of the bone marrow
ACUTE VS. CHRONIC LEUKEMIA

Clinically:

**Acute leukemia:** Acute course, with bleeding, infections

**Chronic leukemia:** Course is chronic - years

Microscopically:

**Acute:** Primitive bone marrow cells in the bone marrow and in the blood

**Chronic:** Relatively differentiated bone marrow cells in the blood
Table 1. A Classification of Acute Leukemia

1. Myelogenous Leukemia
   - Myeloblastic
   - Promyelocytic
   - Myelomonocytic (and monocytic)
   - Di Guglielmo syndrome
     - Erythroleukemia
     - Erythremic Myelosis
2. Lymphoblastic Leukemia
3. Undifferentiated Leukemia
# LEUKEMIA

## BURDEN OF SUFFERING

### US 2015 Est. new cases  54,270

<table>
<thead>
<tr>
<th>Type</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lymphocytic leukemia</td>
<td>6,250</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>14,620</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>20,830</td>
</tr>
<tr>
<td>Chronic myeloid leukemia</td>
<td>6,660</td>
</tr>
<tr>
<td>Other leukemias</td>
<td>5,910</td>
</tr>
</tbody>
</table>
ACUTE LEUKEMIA
ETIOLOGY

• Genetic factors
• Viral infection
• Radiation exposure
• Chemicals exposure
ACUTE LEUKEMIA - ETIOLOGY
GENETIC FACTORS

Chromosome imbalance: Down’s syndrome
Other aneuploidies

Chromosome breakage: Bloom’s syndrome
Fanconi’s syndrome
Ataxia telangiectasia

Genetic “susceptibility”: Familial (?)
Coexistent neoplasm (?)
ACUTE LEUKEMIA ETIOLOGY
VIRAL LEUKEMOGENESIS

In animals: Experimental evidence

In humans: Viruses and virus-like particles in leukemic cells and plasma of patients

- Are viruses bystanders?
- Are viruses co-carcinogens?
- Koch’s postulate not fulfilled
ACUTE LEUKEMIA - ETIOLOGY
RADIATION EXPOSURE

In the general population:

• Survivors of the atomic bomb explosions (Japan, 1945)
• Radiologists exposed to ionizing radiation

In patients treated for other diseases:

• Ankylosing spondylitis
• Thymus radiation in childhood
• Diagnostic tests: Unknown dose threshold
LEUKEMIA - SYMPTOMS

• Weakness, fatigue
• Recurrent infections
• Bleeding, gum bleeding
• Bone pain
• Anorexia
Polycythemia rubra vera (P. vera)
Chronic myeloid leukemia (CML or CGL)
Agnogenic myeloid metaplasia (AMM)
Essential thrombocythemia (ET)
Myelodysplastic syndromes (MDS)
ACUTE VS. CHRONIC LEUKEMIA

Clinically:

**Acute leukemia:** Acute course, with bleeding, infections

**Chronic leukemia:** Course is chronic - years

Microscopically:

**Acute:** Primitive bone marrow cells with poor differentiation in the bone marrow and in the blood

**Chronic:** Relatively differentiated bone marrow cells in the blood
A child with bleeding in the mouth mucosa had low platelets in the blood
Petechiae in Leukemia
View of the eye fundus showing multiple spot bleeding caused by low platelets in a patient with acute leukemia

Fig. 28-2. Retinal hemorrhages in a 19-year-old man with acute myelogenous leukemia. The white spots at the center of the hemorrhage are leukocytes.
BLEEDING INTO THE BRAIN IN LEUKEMIA
B/O LOW PLATELETS
LEUKEMIA
Treatment

Acute leukemia (lymphatic and myeloid):
  - Chemotherapy
  - Bone marrow transplantation

Chronic lymphatic leukemia: Chemotherapy

Chronic myeloid leukemia: Chemotherapy
  - BMT (?)

Polycythemia rubra vera: Phlebotomies
  - Chemotherapy
LUNG CANCER
Air Pollution and Cancer

- Combustion of fossil fuels
- Smoking
- Asbestos
AIR POLLUTION BY COMBUSTION
Epidemiologic Studies

Silesia (Poland) ➔ PAH ➔ genotoxic effects

Yunan (China) - lung cancer in women

Shanghai - lung cancer in non-smoking women
LUNG CANCER
RISK FACTORS

• Active tobacco smoking (87%)

• Passive smoking

• Environmental factors (asbestos, metals)
LUNG CANCER

Karolinska Institute:

- **Protective effect** of *dietary vegetables*, primarily carrots (RR=0.07)
- **Protective effect** of *non-citrus fruits* (RR=0.6)
LUNG CANCER

African Americans

Cases = higher daily mean total fat intake (p<.001)
Controls = higher daily mean fiber intake (p<.001)
and fruits (p=.02)

Mexican Americans

- less total fat intake (p<.002)
- more fiber (p<.001)
- more vegetables (p=.08)

Independent of cigarette smoking, high fat consumption & low fruit and vegetables contribute to the excess of lung cancer in African American men
Nutrition – Cancer Relationship
The Evidence

Cancer Protective Agents

- Fruits
- Vegetables
- Foods with:
  - Lycopene
  - Selenium
  - Folate
  - Fiber
Cancer Prevention

WCRF & AICR Recommendations

1. Be as lean as possible (normal weight range).

2. Be physically active every day.

3. Limit foods that promote weight gain:
   - Limit intake of processed, energy dense foods.
   - Avoid sugary drinks.
   - Consume fast foods sparingly, if at all.
Cancer Prevention

WCRF & AICR Recommendations

4. Eat mostly plant foods.
   - At least 5 servings of a variety of non-starchy vegetables and of fruits every day.
   - Eat unprocessed grains and/or legumes with every meal.
   - Limit refined starchy foods.
Cancer Prevention

WCRF & AICR Recommendations

6. Limit alcohol intake to
   Not more than:
   - 2 drinks per day for men.
   - 1 drink per day for women.

1 drink = 1 ½ oz liquor, 5 oz wine, or 12 oz beer
Cancer Prevention

WCRF & AICR Recommendations

8. Aim to meet nutritional needs through diet.

- Dietary supplements are not recommended for cancer prevention.

Food is!
CANCER SCREENING
GUIDING PRINCIPLES

Burden of Suffering
Risk Factors
Family History (?)
Effective Methods of Early Detection
Results - reliability
Ideal Cancer Screening Method

- Inexpensive
- Safe
- Highly accurate
- Easy to use in community
LUNG CANCER SCREENING

• Intense counseling against tobacco smoking

• Routine screening is not recommended in asymptomatic patients
NLST: National Lung Screening Trial

September 2002 – February 2004
50,000 participants randomized
Monitor through 2009

Current or former heavy cigarette smoker
(>1 ppd x 30 years)
Age 55-74

Low-dose fast spiral CT

Randomized

CXR

Years

0 1 2
Population: 53,454 adults 55-74 y.o.

Smoking history: > 2 pack/day for 30 pack/yrs.

Method: Routine Chest X-ray vs. spiral CT three exams/year

Duration of study: 2002 – 2010

Results: published in 2011

20% reduction in mortality of the group given Spiral CT
## LUNG CANCER

### SYMPTOMS DURING COURSE OF DISEASE

<table>
<thead>
<tr>
<th>Symptom</th>
<th>% Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>COUGH</td>
<td>48-71</td>
</tr>
<tr>
<td>CHEST PAIN</td>
<td>28-50</td>
</tr>
<tr>
<td>DYSPNEA</td>
<td>23-42</td>
</tr>
<tr>
<td>HEMOPTYSIS</td>
<td>9-63</td>
</tr>
<tr>
<td>WEIGHT LOSS</td>
<td>31-49</td>
</tr>
</tbody>
</table>

*Data culled from 3 series (2404 patients)*
Several histologic types each with specific:

- Growth
- Natural history
- Complications
- Response to treatment
- Survival
LUNG CANCER

PROGNOSTIC FACTORS

EXTENT

METASTATIC SITES

PERFORMANCE STATUS

WEIGHT LOSS

CELL TYPE
Normal Chest X-ray
Chest CT Scan Showing Metastases
PET/CT scan

Positron Emission Tomography/Computer Tomography
Surgery for curative intent
Surgery for palliative intent
Radiation therapy
Systemic chemotherapy
Intra-cavity (intra-pleural) chemotherapy
LUNG CANCER SURGERY

Provided that PFT’s are minimally OK:

Wedge resection

Segmental resection of small peripheral lesions.

Lobectomy

Pneumonectomy
LUNG CANCER: Localized or not?

Lung cancer localized to the thorax: 70,000 cases annually.

- T1N0: 28%
- T1N1, T2N0, T2N1: 37%
- IIIB Unresectable: 10%
- IIIA Partially Resectable: 10%
- IIIA Resectable: 15%
LUNG CANCER
RADIATION THERAPY

Effective as used alone or in combination with systemic chemotherapy

Dose depends on the histologic type of the cancer

New modalities showed increased effectiveness
NON-OAT CELL CARCINOMA
CHEMOTHERAPY

Problems Related to Patient

1. Blood supply - prior surgery
   - prior radiotherapy
2. Coexistent lung infection
3. Metabolic status
4. Treated vs. untreated
LUNG CANCER COMPLICATIONS

Atelectasis (collapse of lung tissue)
Infection > Bronchopneumonia
Pleural effusion
Metastases to brain, adrenals, bones, liver
Paraneoplastic syndromes with metabolic alterations