LECTURE #4

LYMPHATIC SYSTEM

CELL-MEDIATED IMMUNITY

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

HUMORAL IMMUNITY

B-lymphocytes (from the bone marrow) synthesize immunoglobulins which function as **antibodies** combining with foreign **antigens** (bacteria and viruses):

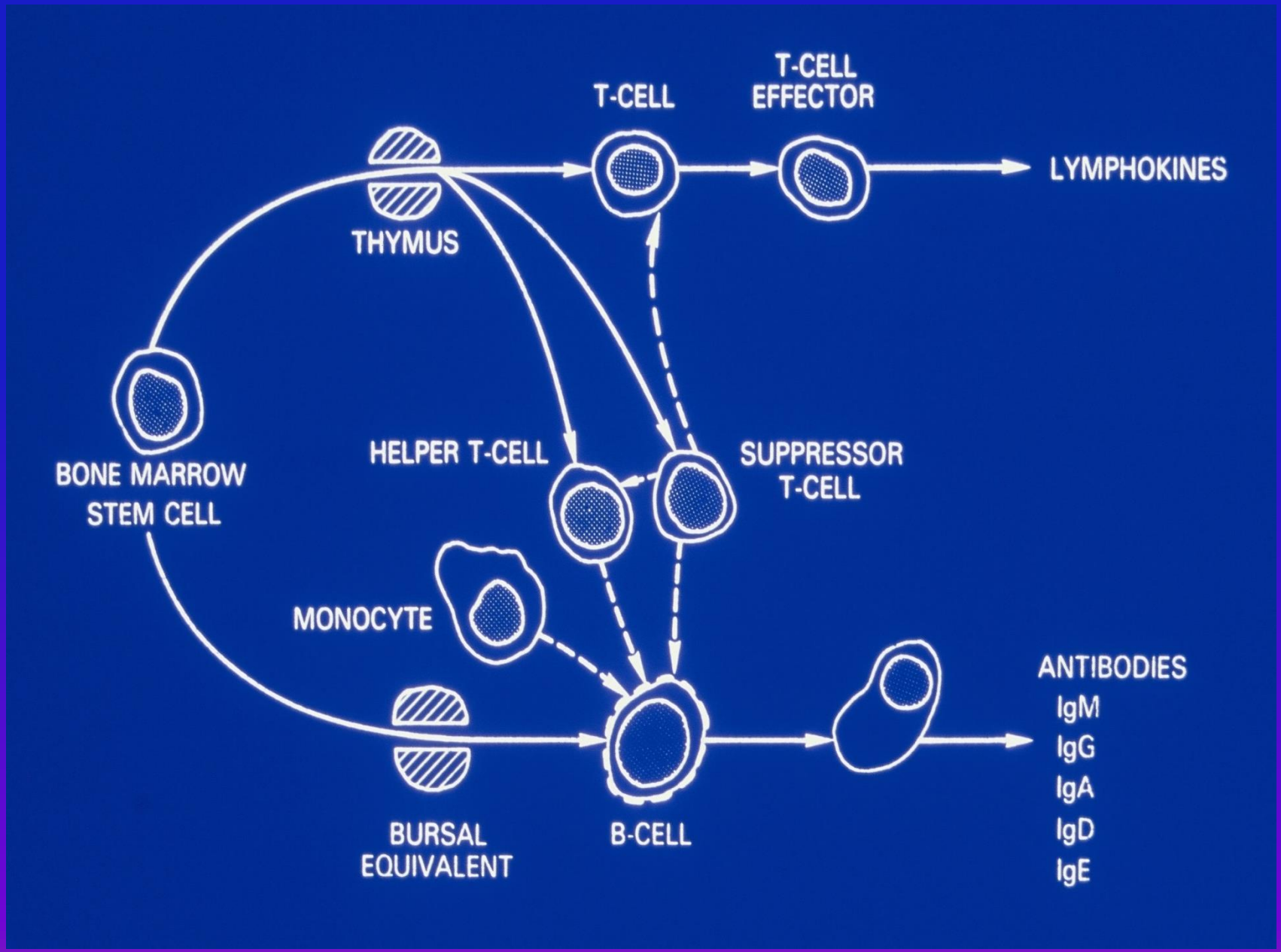
IgG – major immunoglobulin (80%)

IgM – mostly intravascular

IgA – in body secretions, GI and respiratory tract

IgE – active in hypersensitivity (allergy)

IgD


T-CELL
T-CELL EFFECTOR
LYMPHOKINES
THYMUS
BONE MARROW STEM CELL
HELPER T-CELL
SUPPRESSOR T-CELL
MONOCYTE
ANTIBODIES
IgM
IgG
IgA
IgD
IgE
BURSAL EQUIVALENT
B-CELL

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

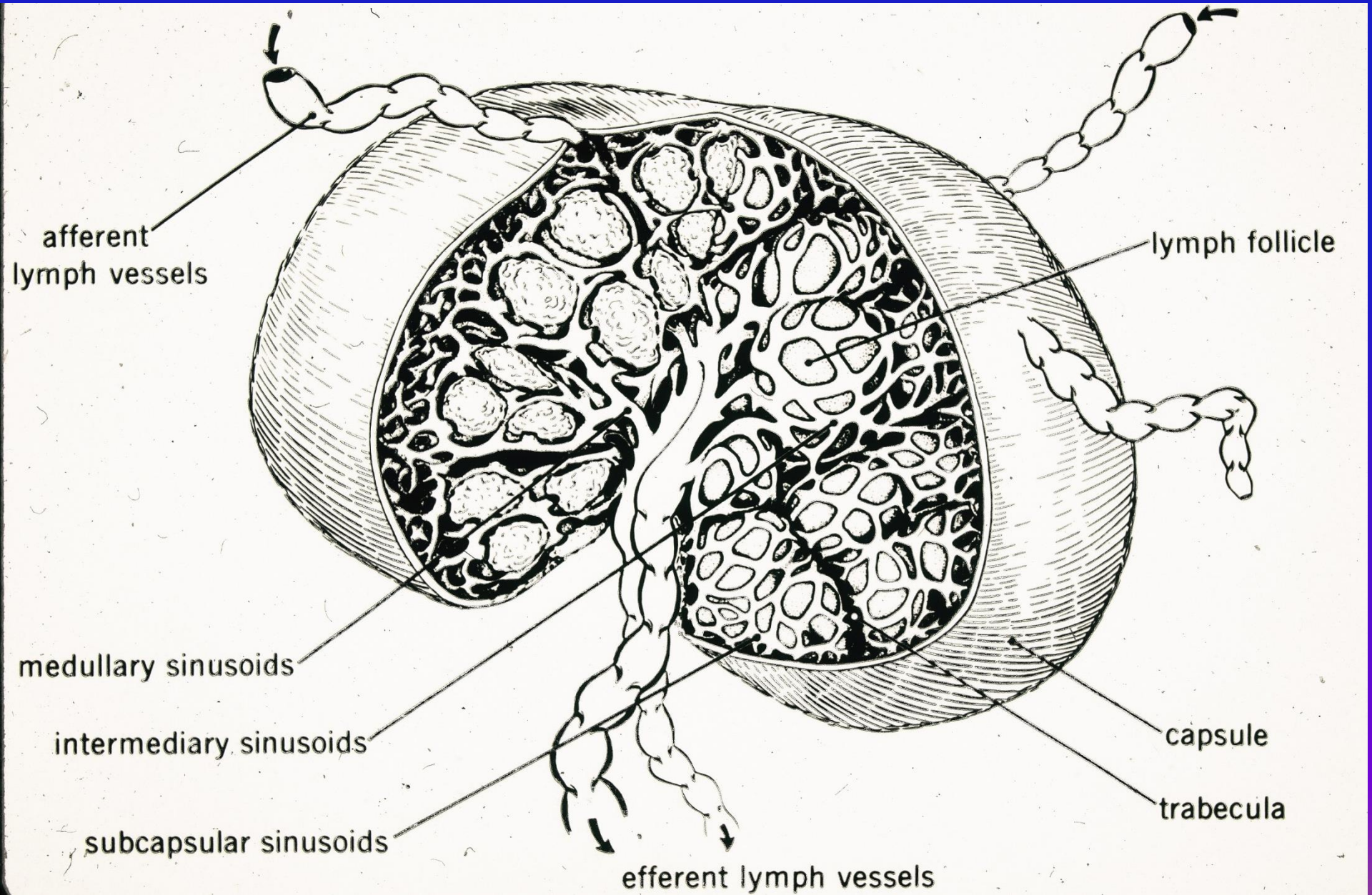
Leukemias

Multiple myeloma

Carcinomas and sarcomas

Inherited or acquired primary immunodeficiency disease

LYMPH NODE STRUCTURE - SCHEMA



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

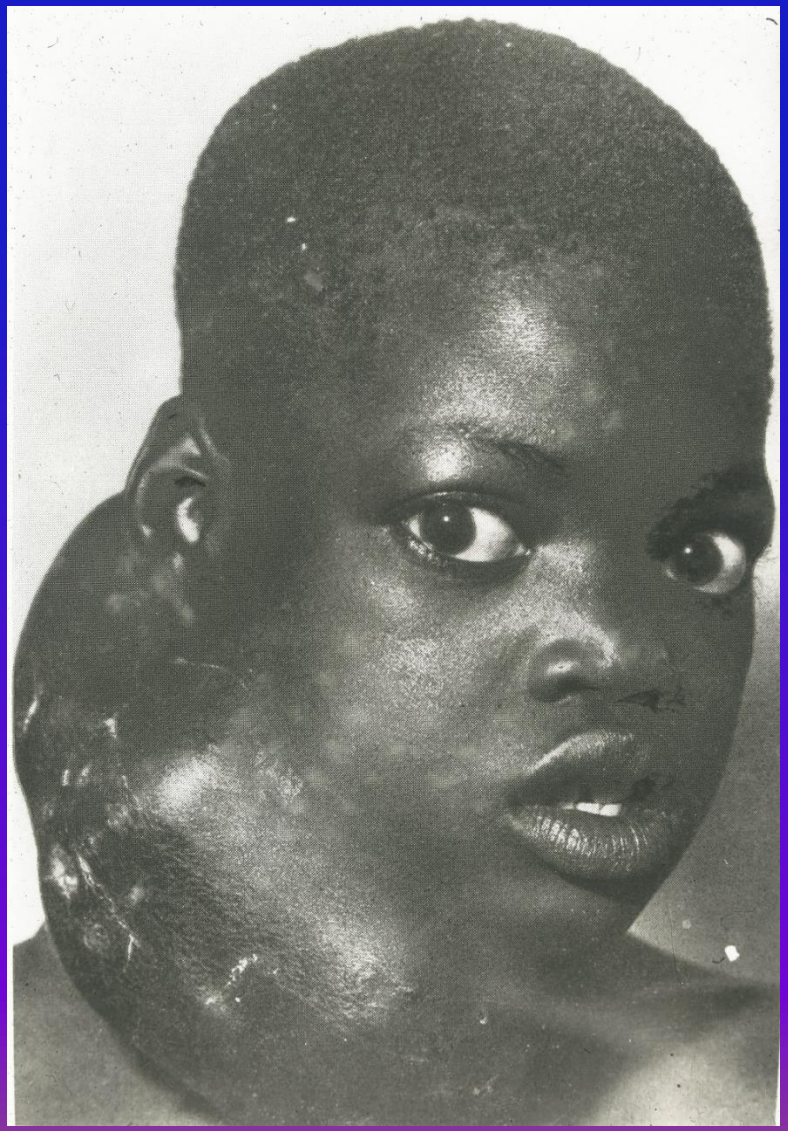
No needle biopsy

Left cervical lymphadenopathy (Enlarged lymph nodes) – Chronic lymphatic leukemia (CLL)

Right Cervical (Neck) Enlarged Lymph Nodes - Lymphoma

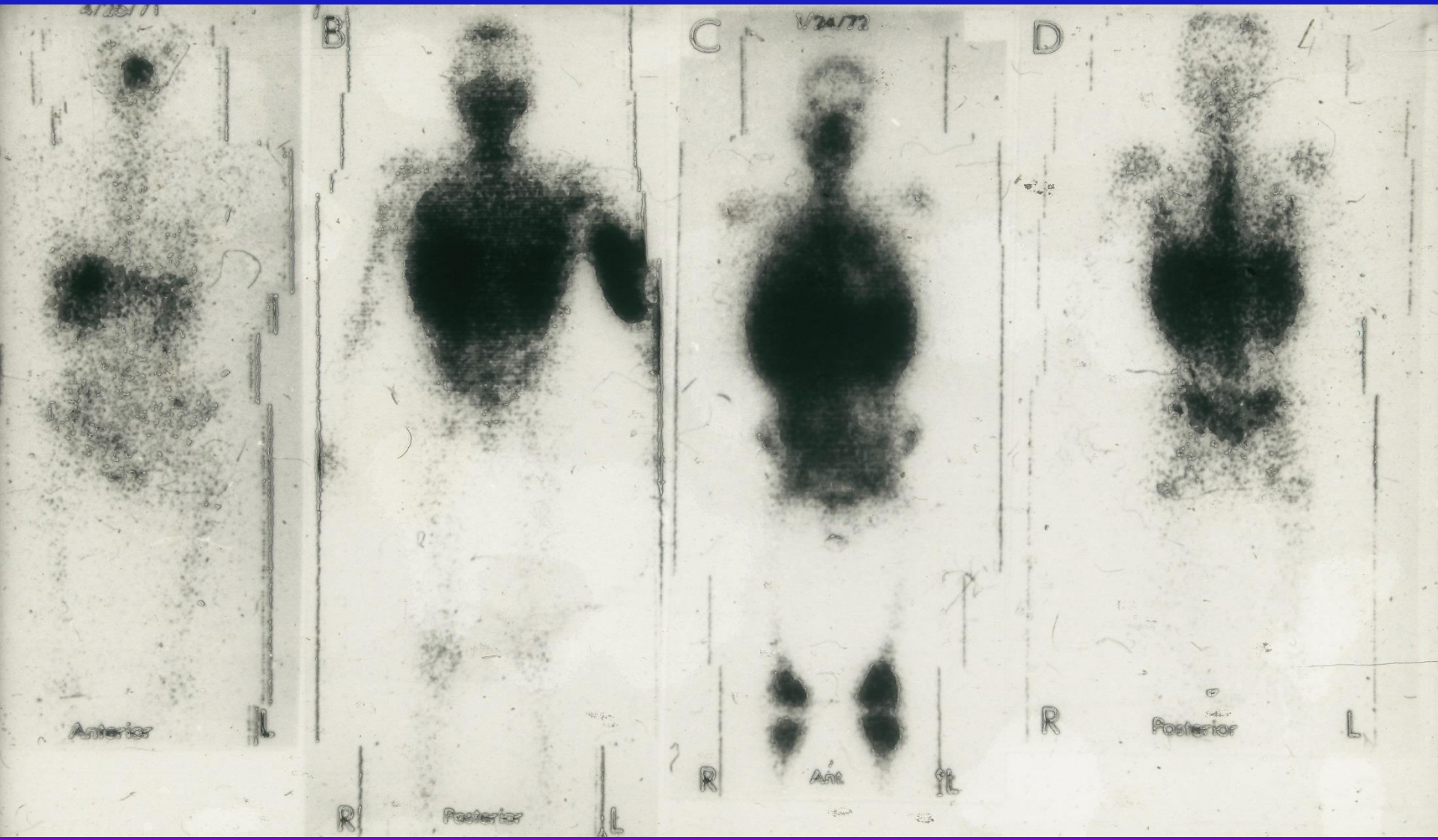
Swollen glands – Hodgkin's disease

Burkitt's lymphoma



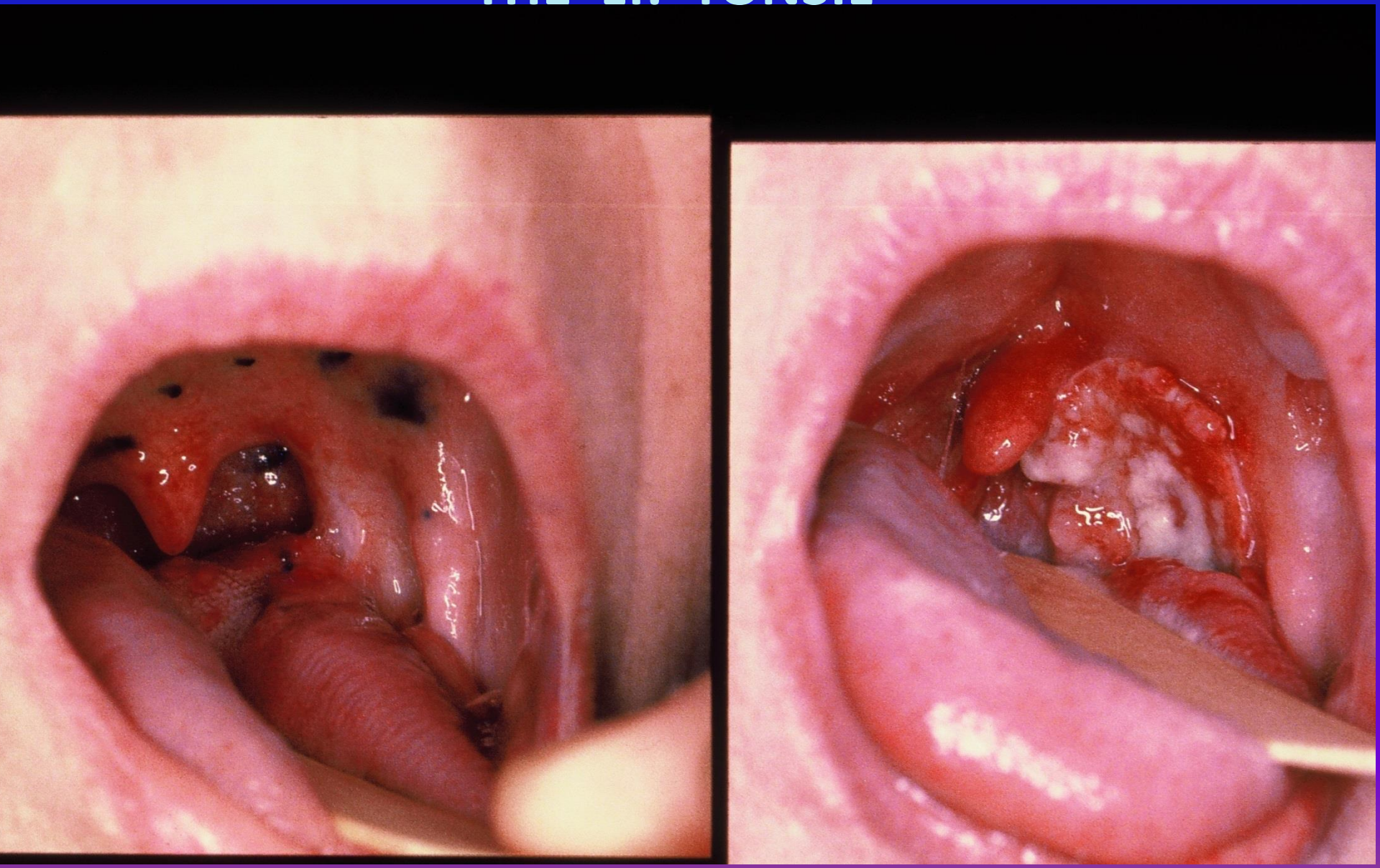
Relapse of "Testicular Cancer"
On pathology review: Large cell lymphoma

Use of Gallium^{67} scan in Hodgkin's disease

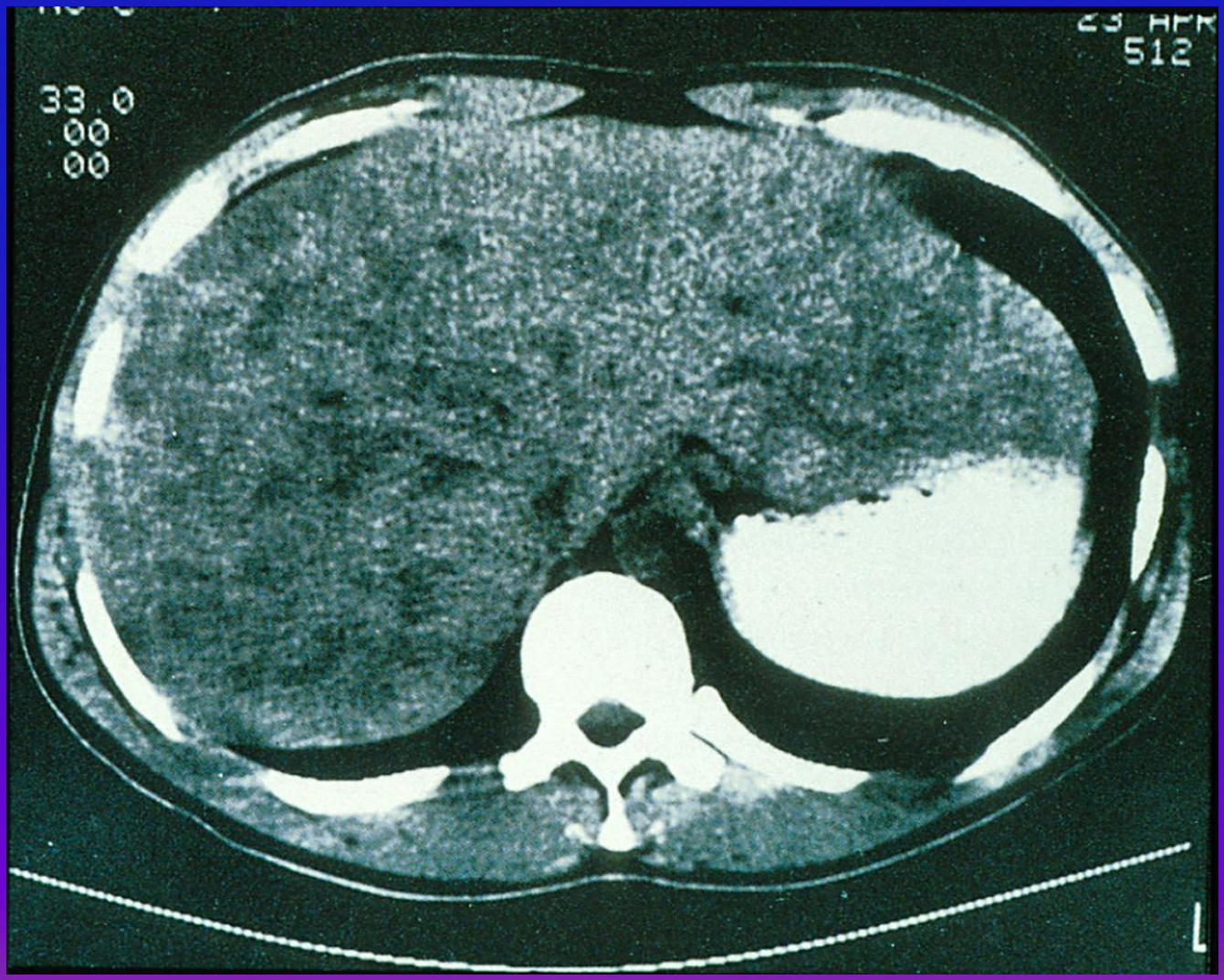


High-grade lymphoma involving the floor of the mouth

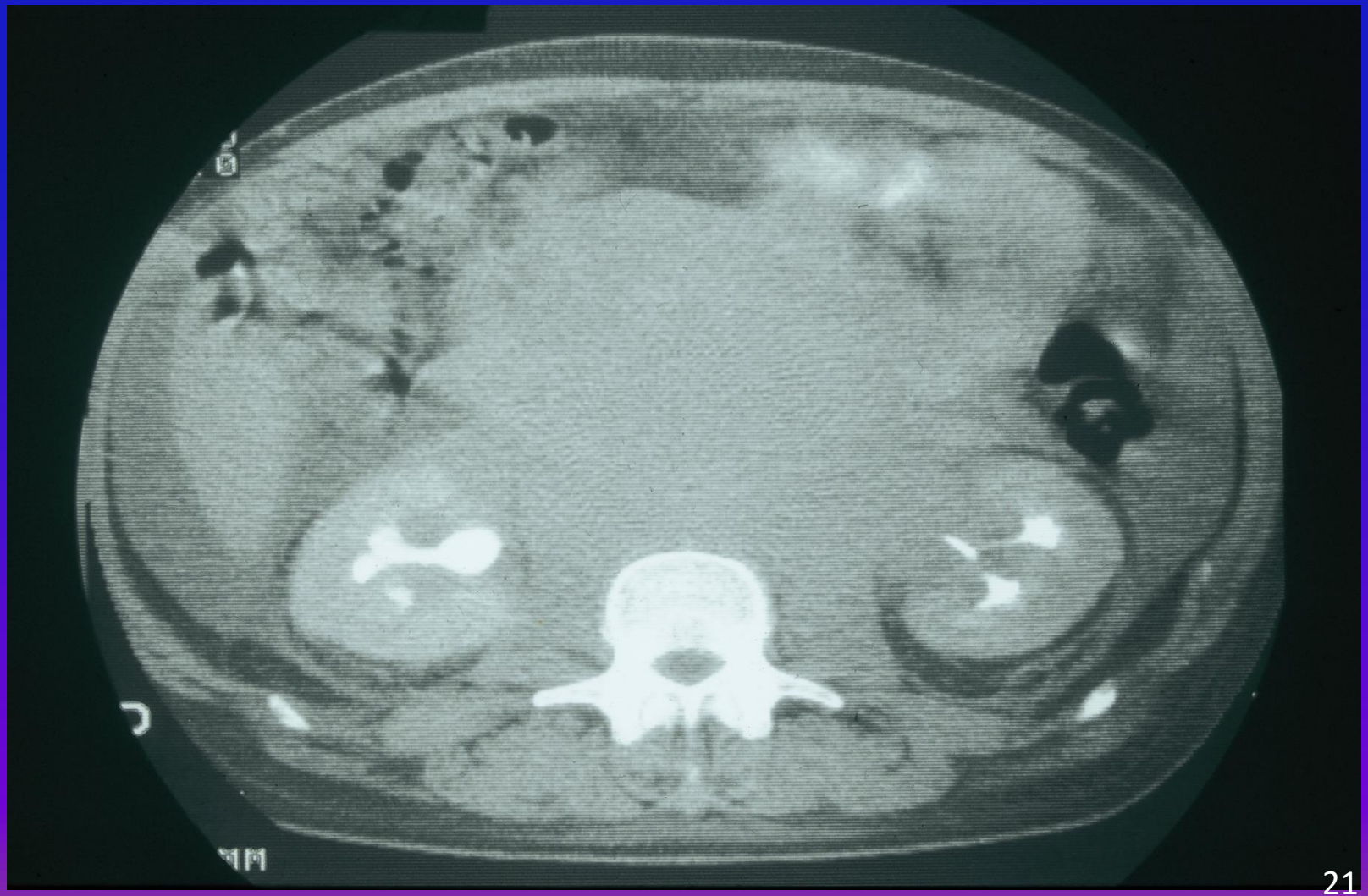
HIGH-GRADE LYMPHOMA OF THE LT. TONSIL



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

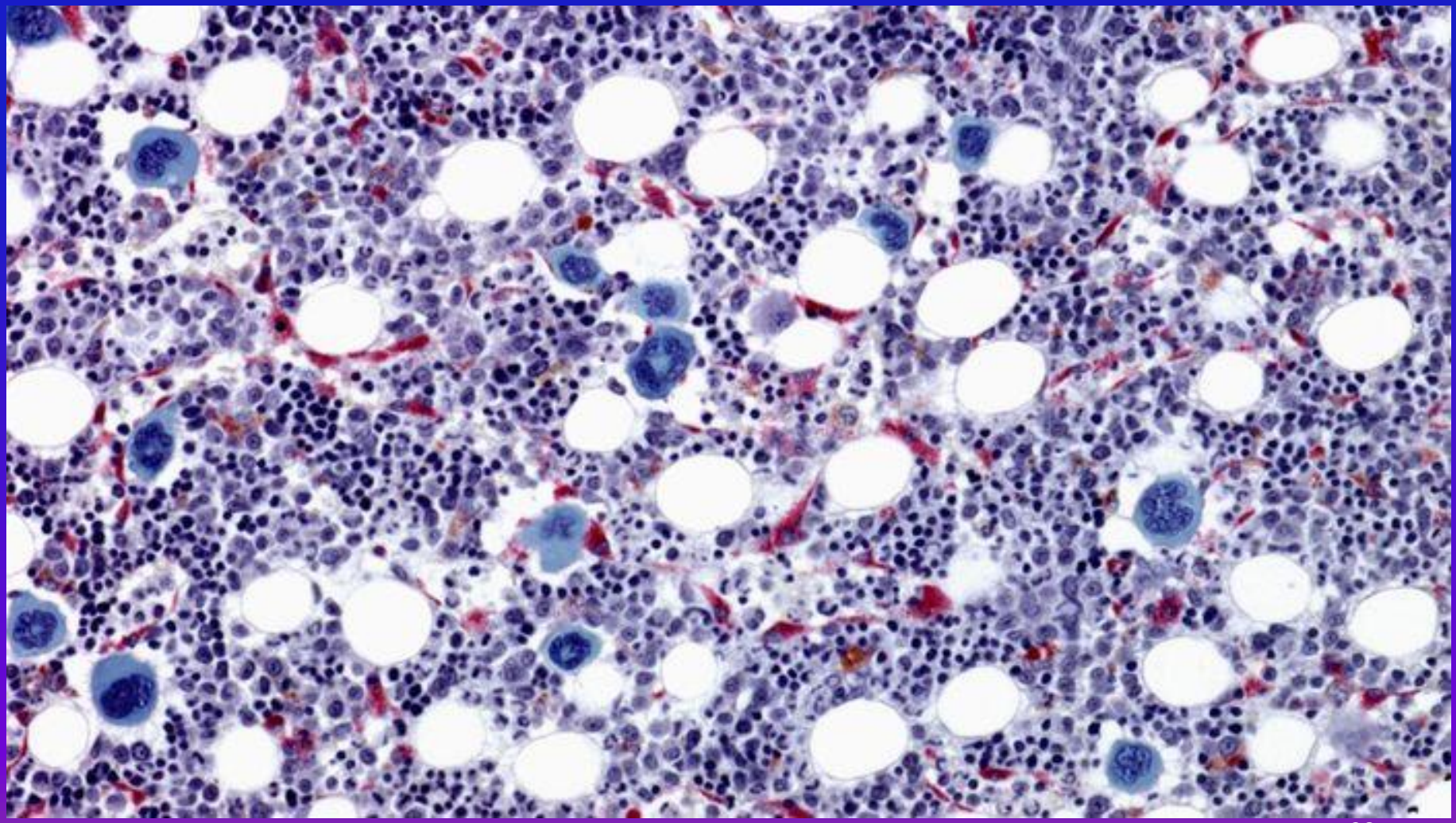
Multiple myeloma: Chemotherapy + BMT

CANCER of BLOOD FORMING

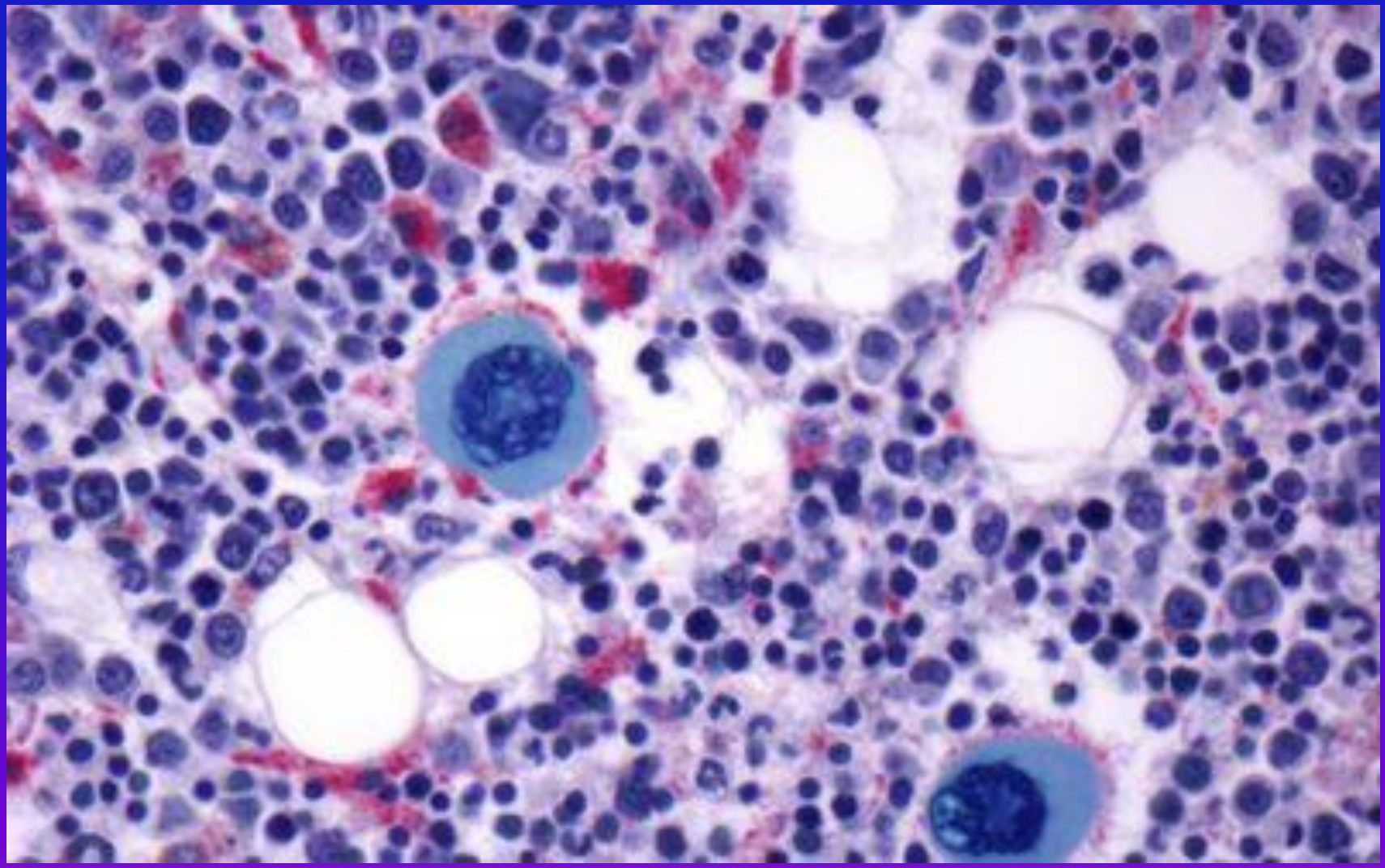
ORGANS

LEUKEMIA

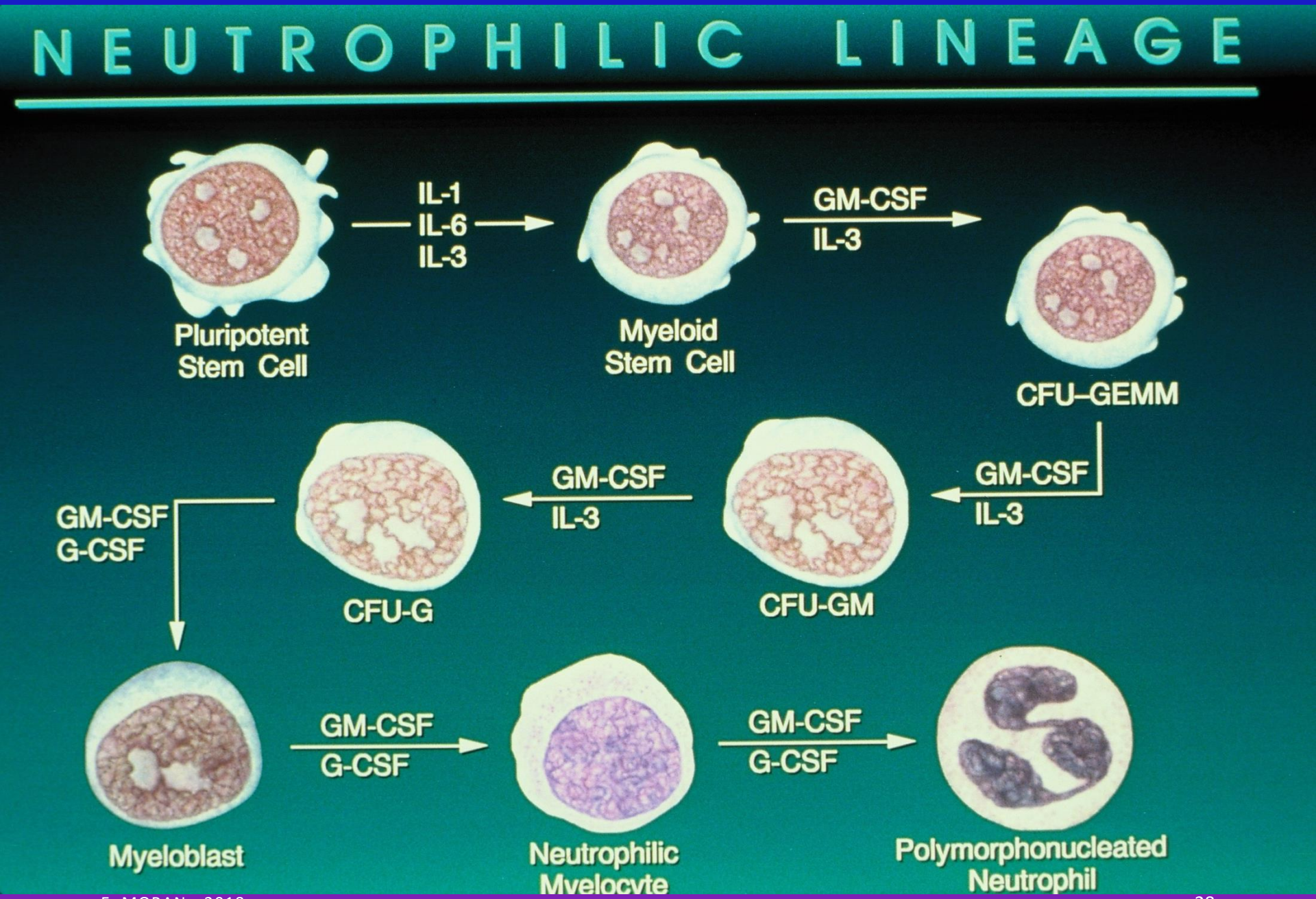
Active (Normal) Bone Marrow



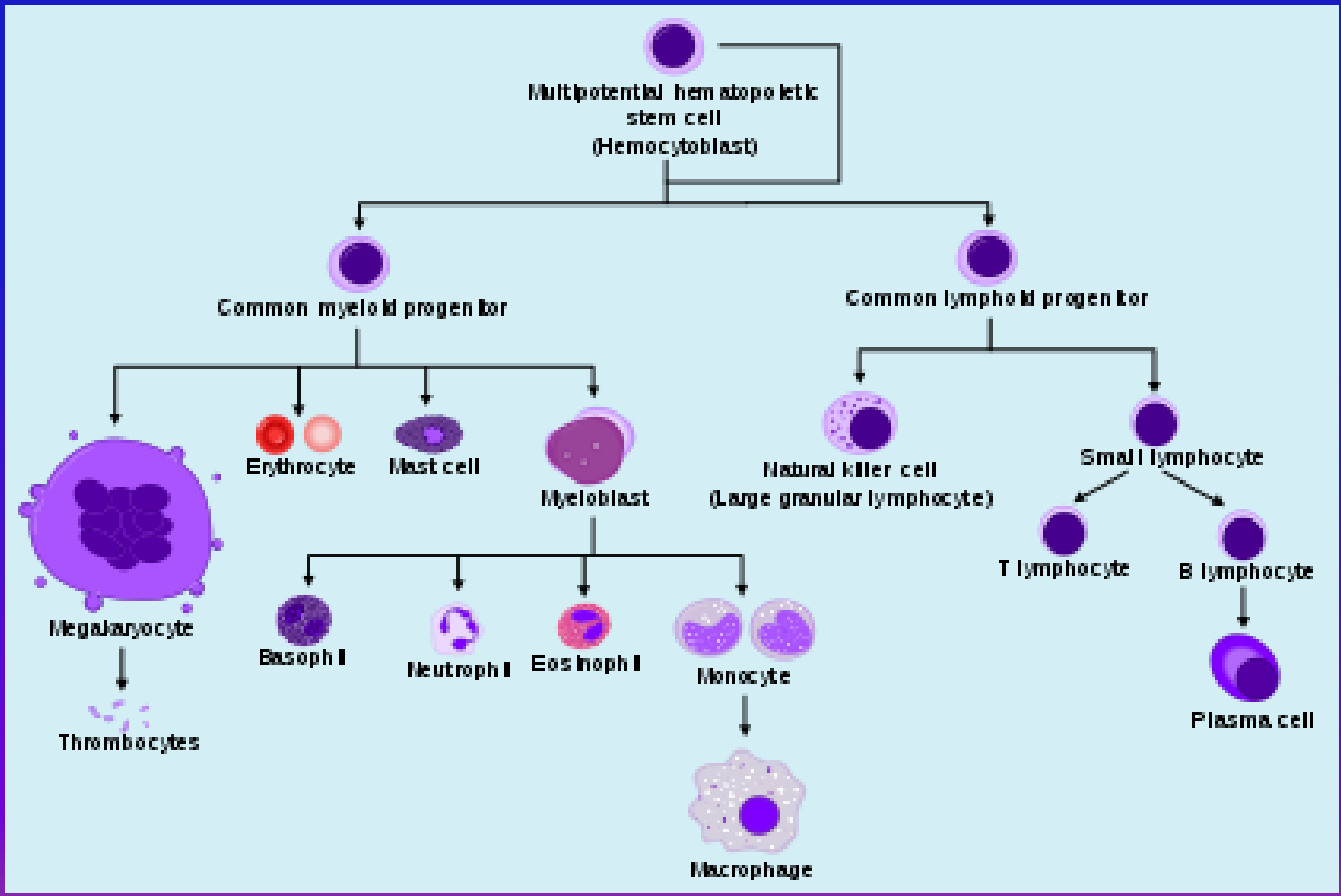
Active (Normal) Bone Marrow



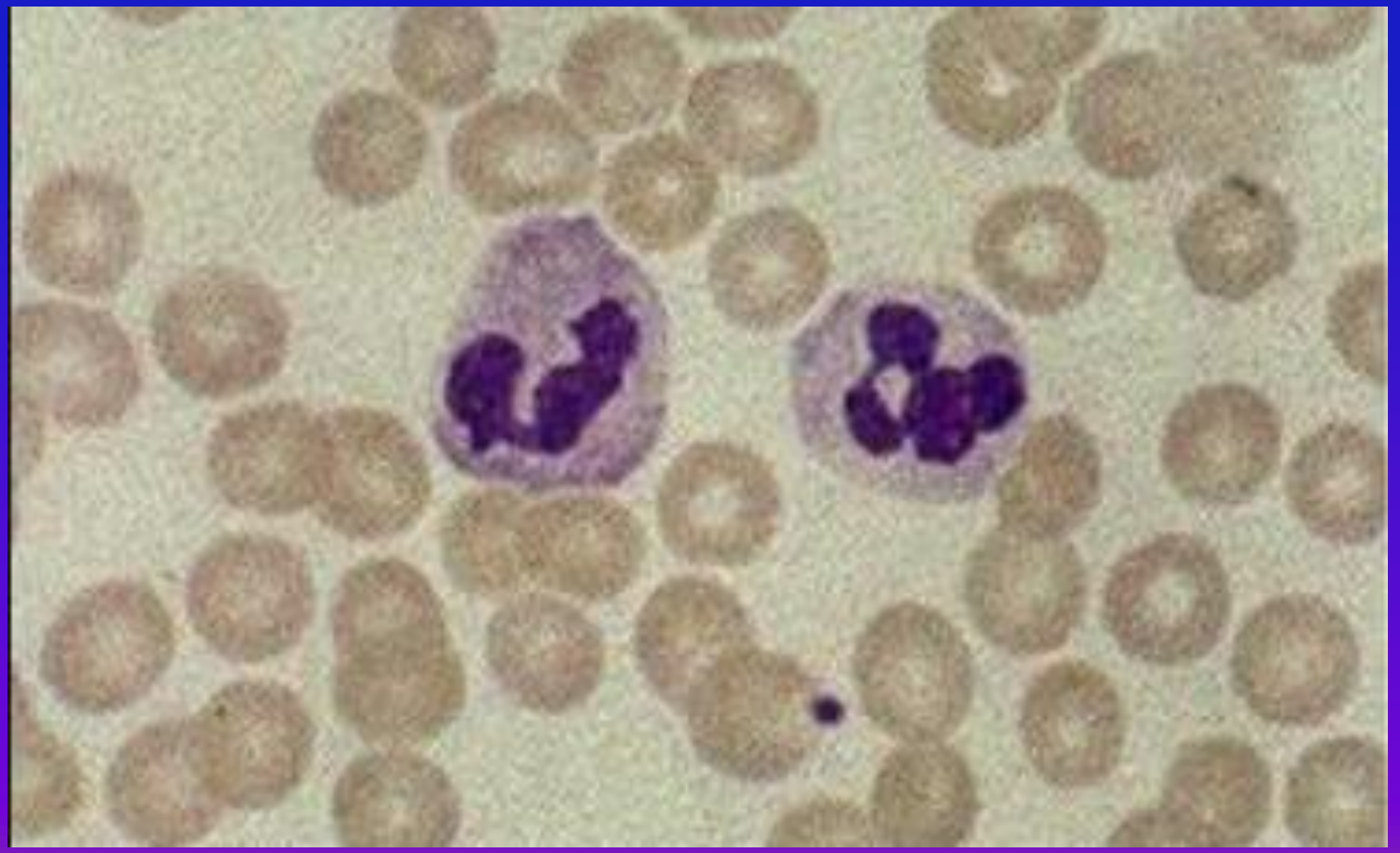
NEUTROPHILIC LINEAGE



Stem Cell and Blood Cells



Blood film (smear) to show: Red blood cells, white blood cells (neutrophils), and a platelet



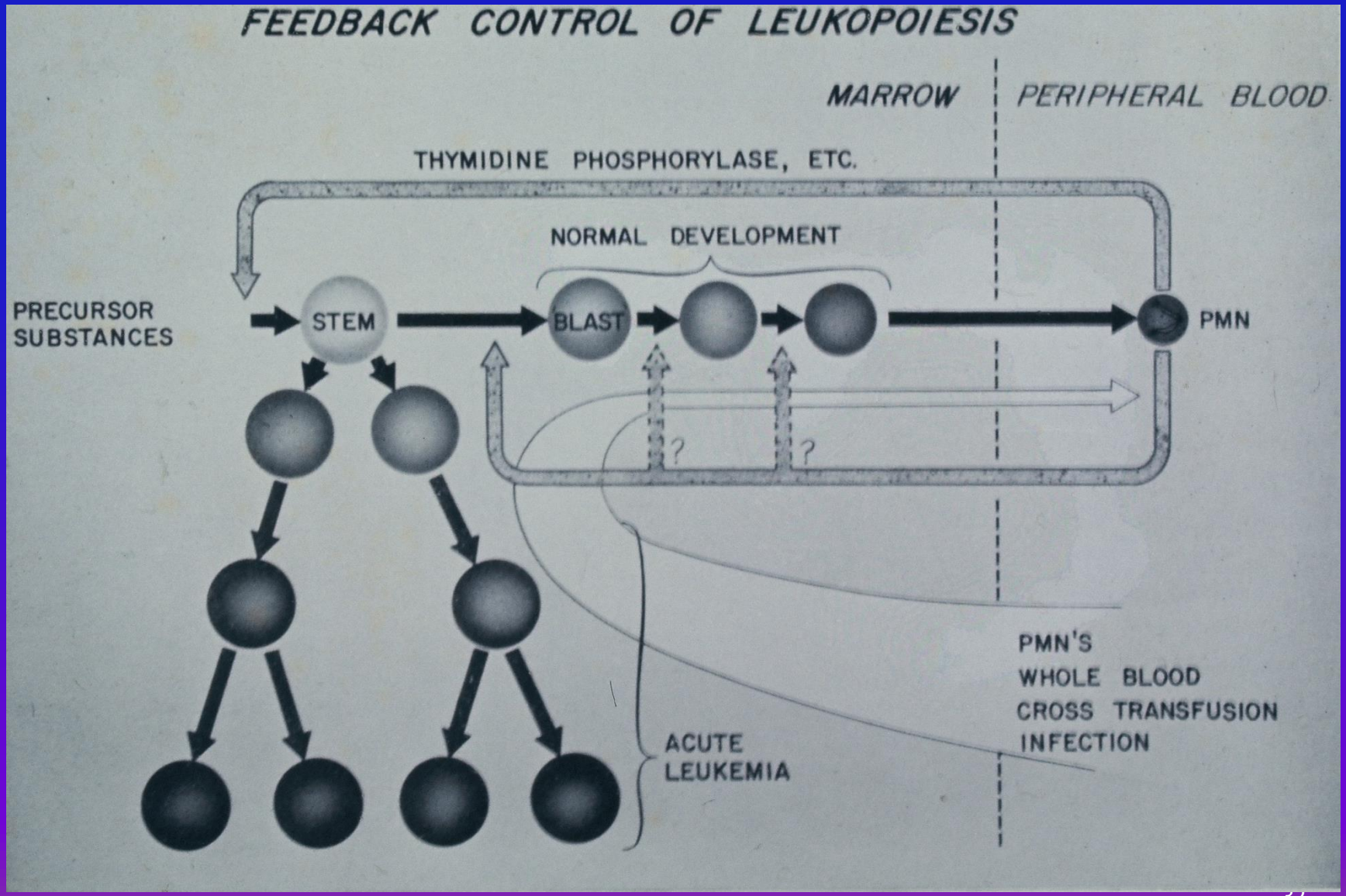
LIFETIME OF BLOOD CELLS

RBC 120 days

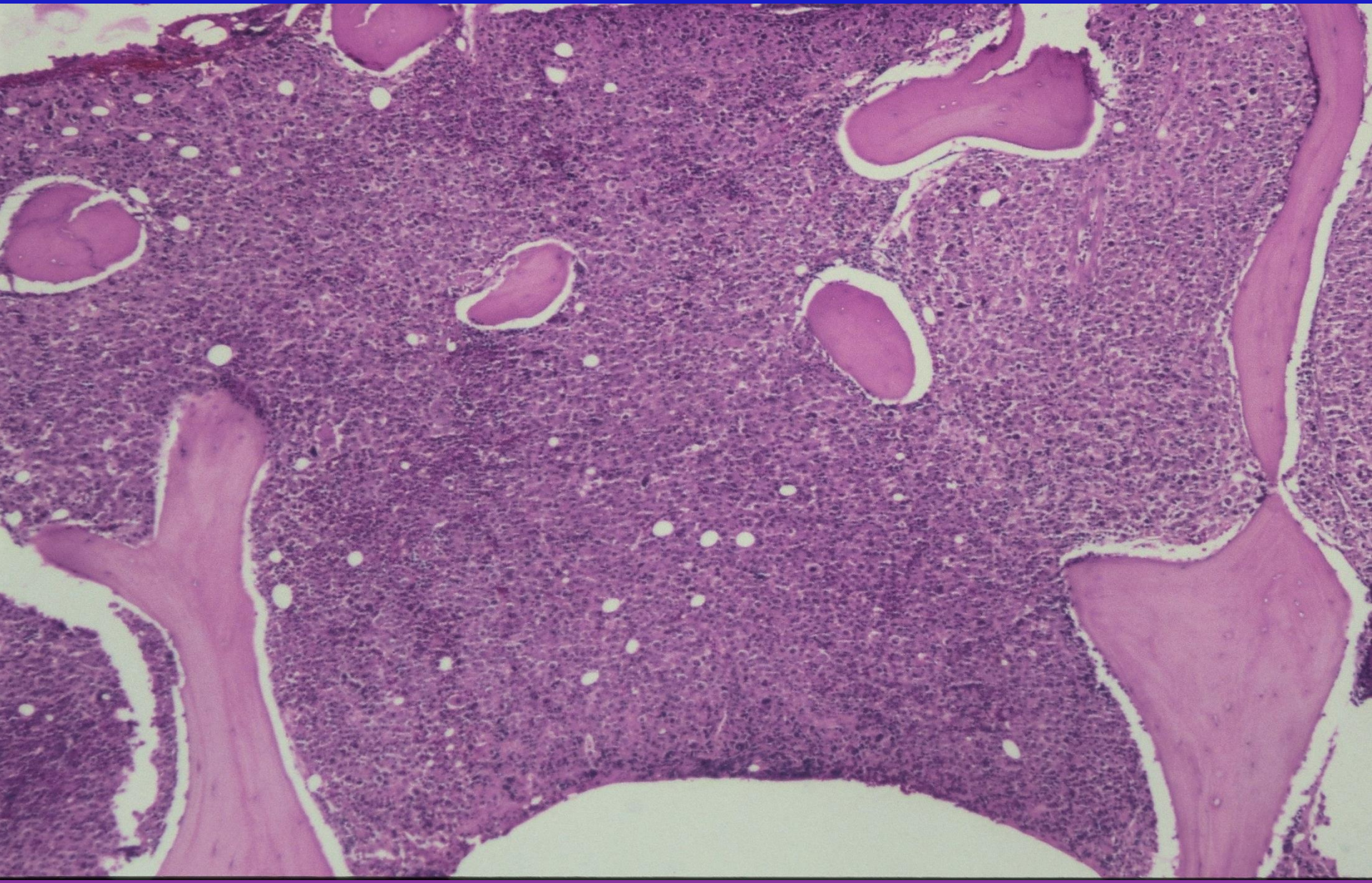
WBC 8.5 -14 days

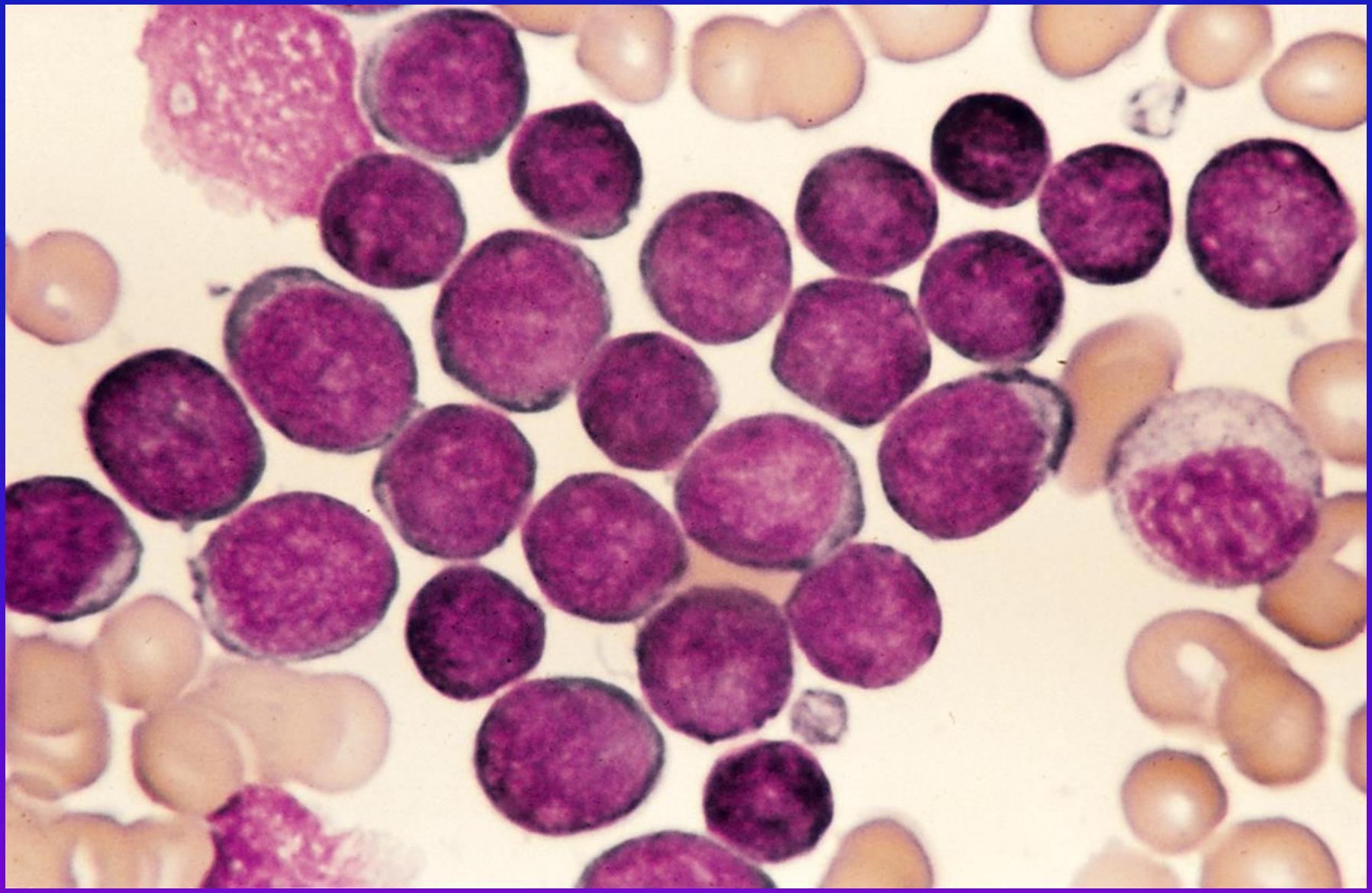
Platelets ~ one week

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

Acute lymphocytic leukemia	6,250
Chronic lymphocytic leukemia	14,620
Acute myeloid leukemia	20,830
Chronic myeloid leukemia	6,660
Other leukemias	5,910

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

CHRONIC MYELOPROLIFERATIVE DISORDERS

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

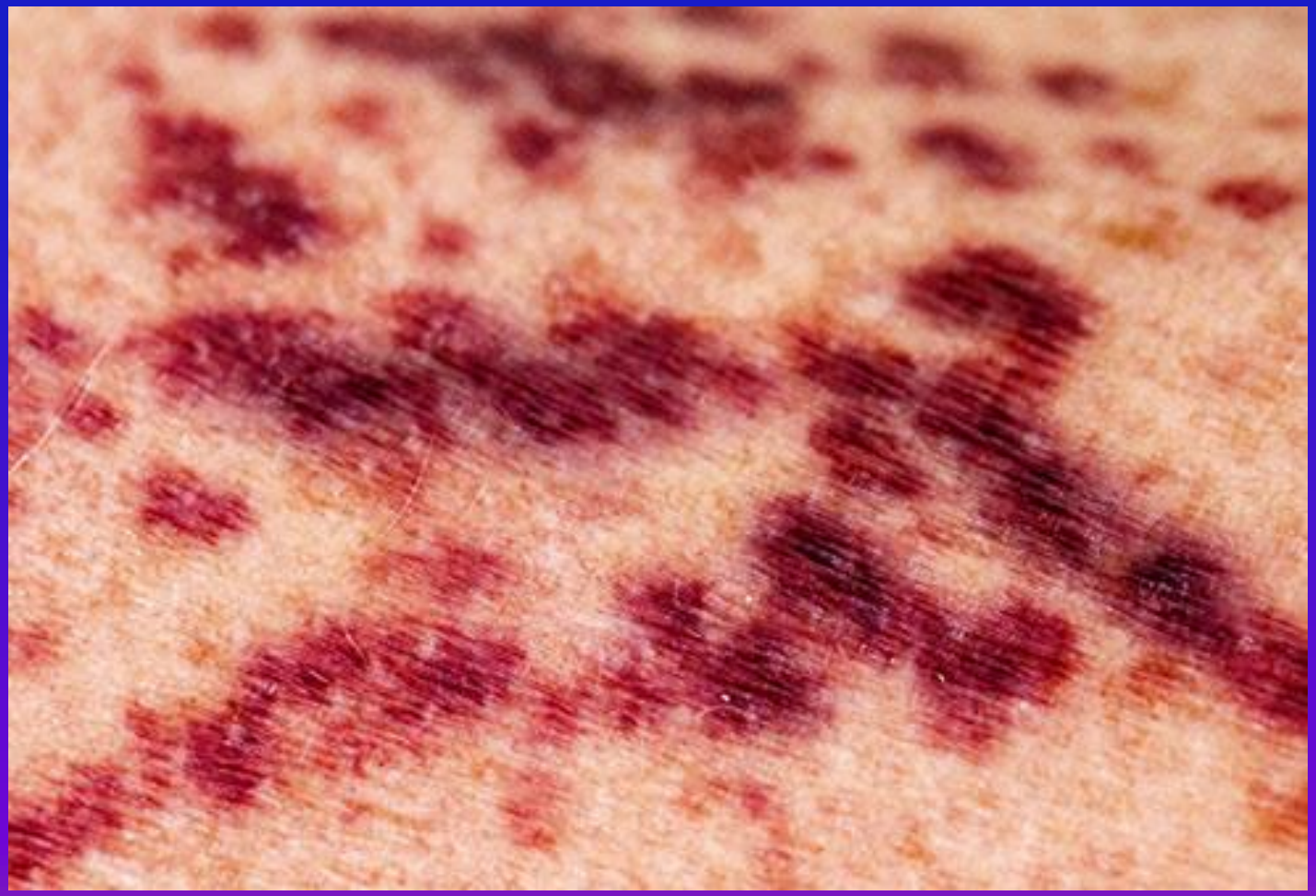
Microscopically:

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

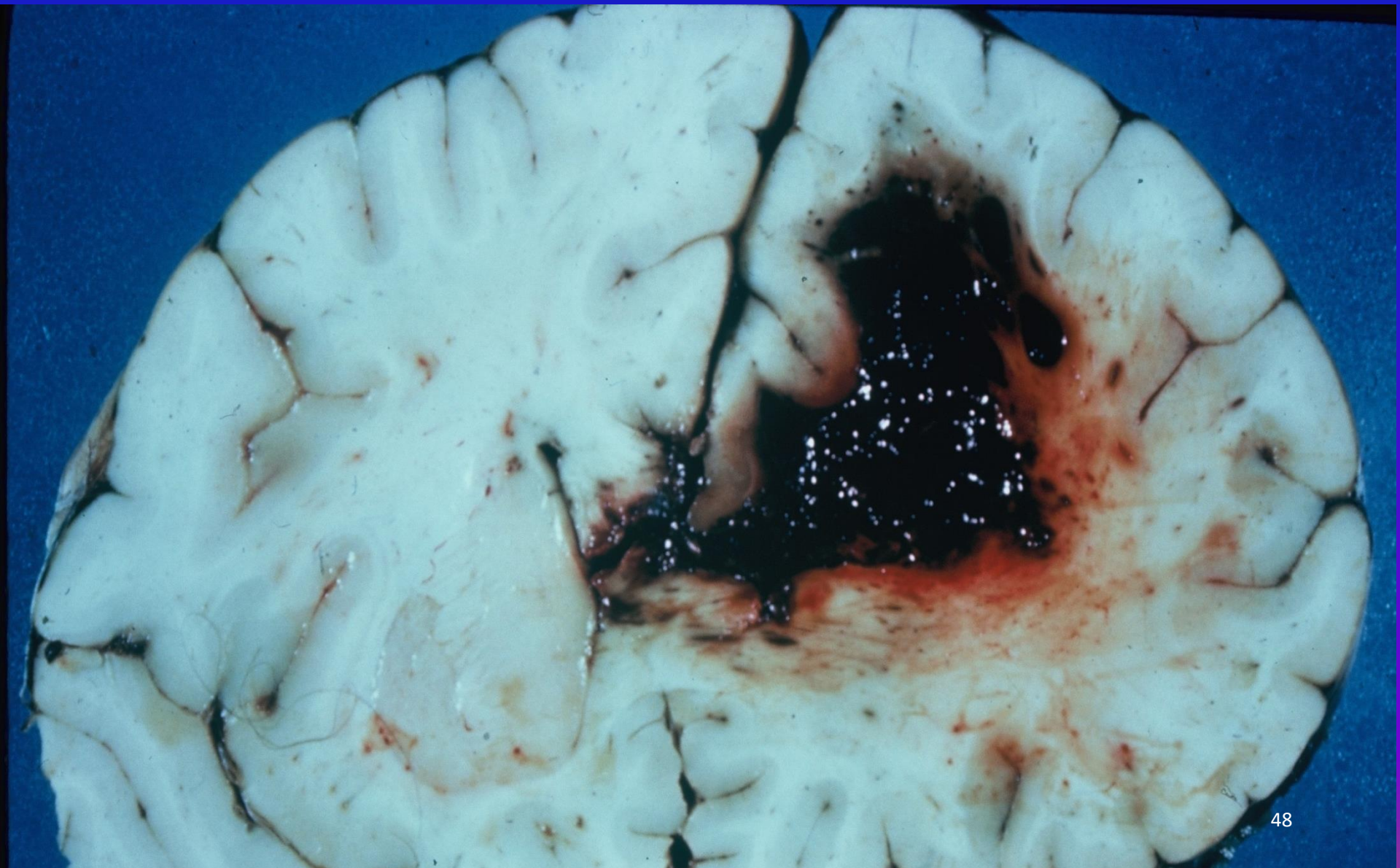
Petechiae in Leukemia



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=.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

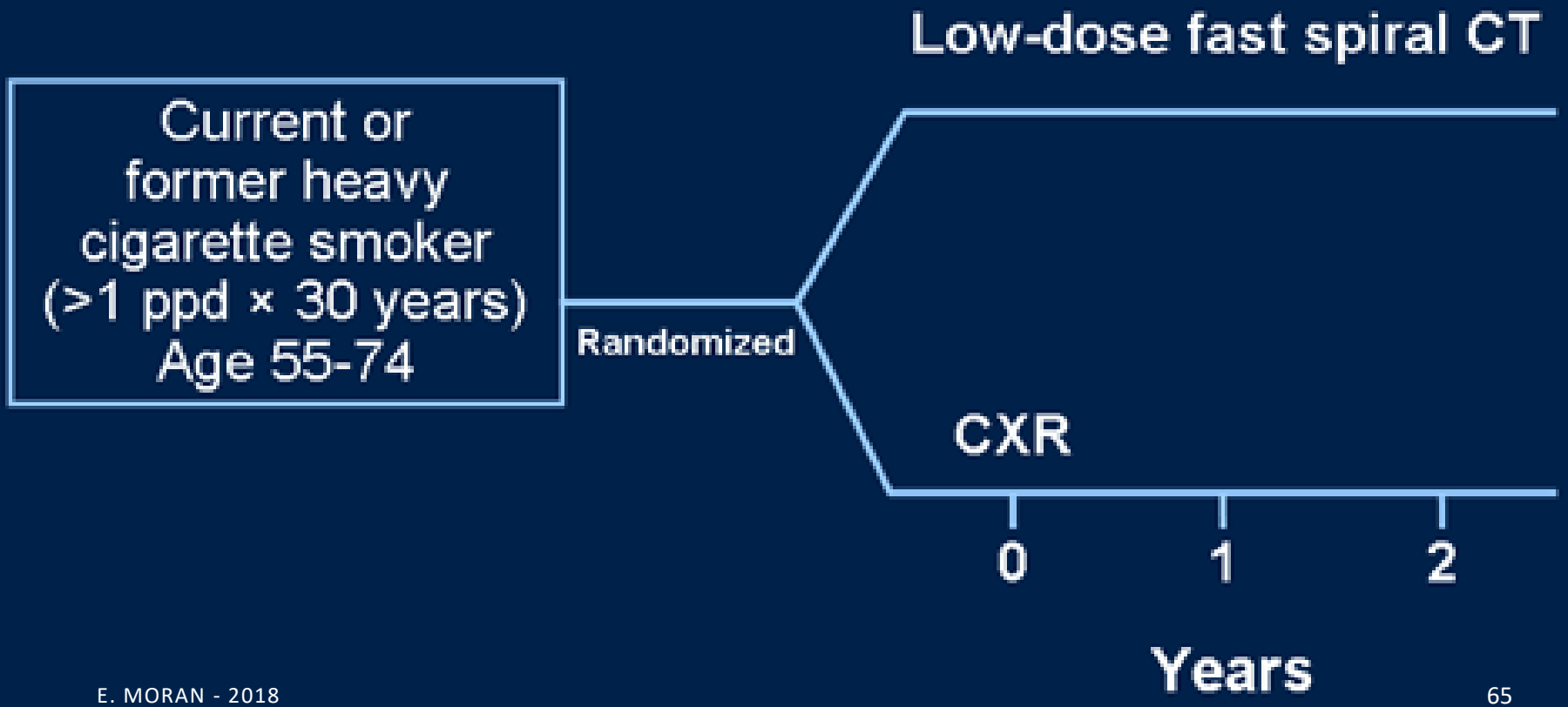
- Inexpensive
- Safe
- Highly accurate
- Easy to use in community

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



NLST

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

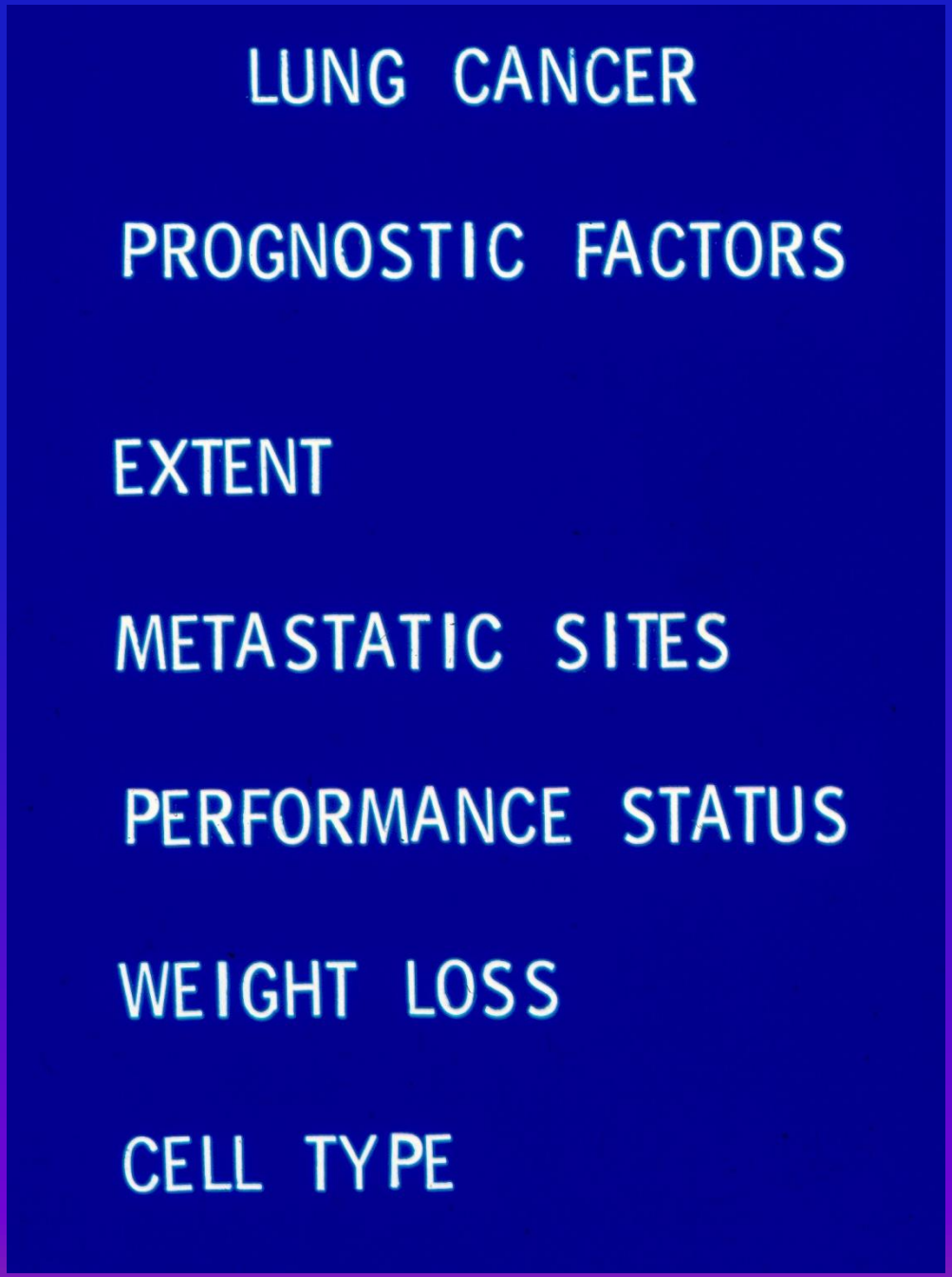
	% INCIDENCE*
COUGH	48-71
CHEST PAIN	28-50
DYSPNEA	23-42
HEMOPTYSIS	9-63
WEIGHT LOSS	31-49

*Data culled from 3 series (2404 patients)

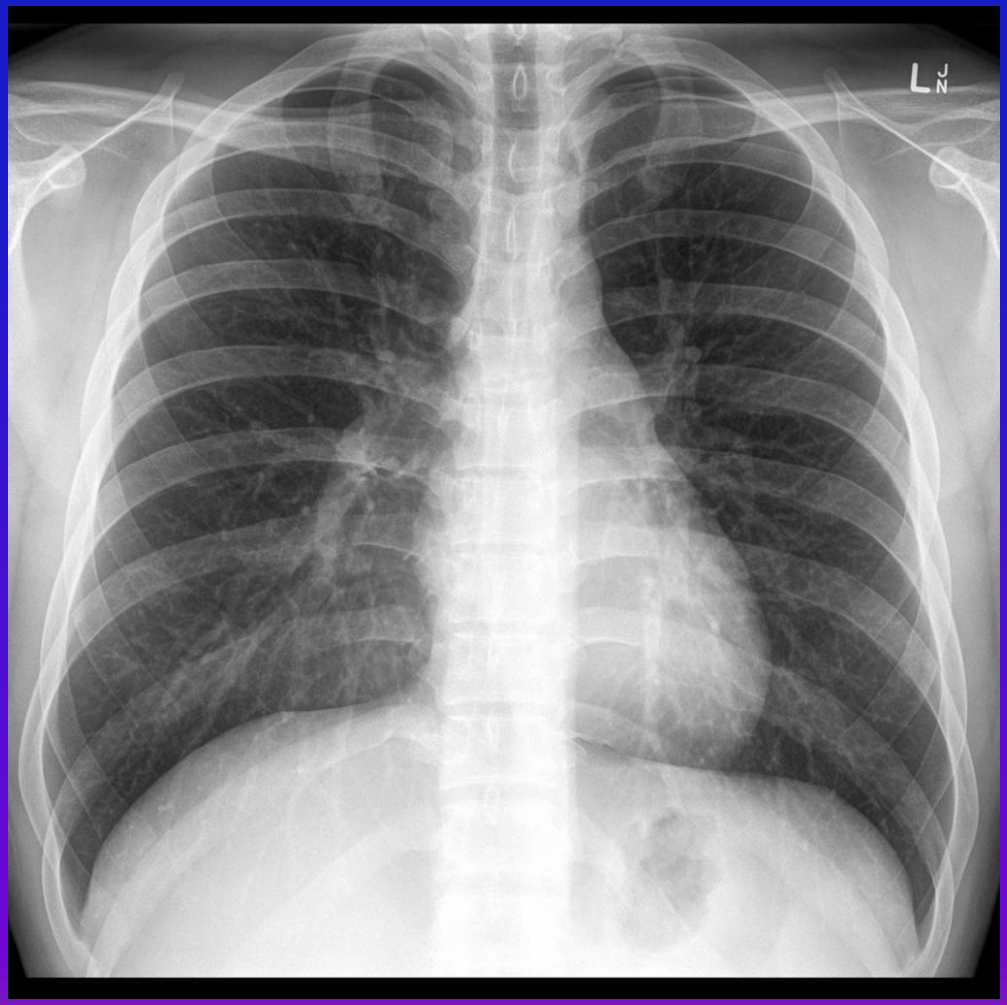
LUNG CANCER

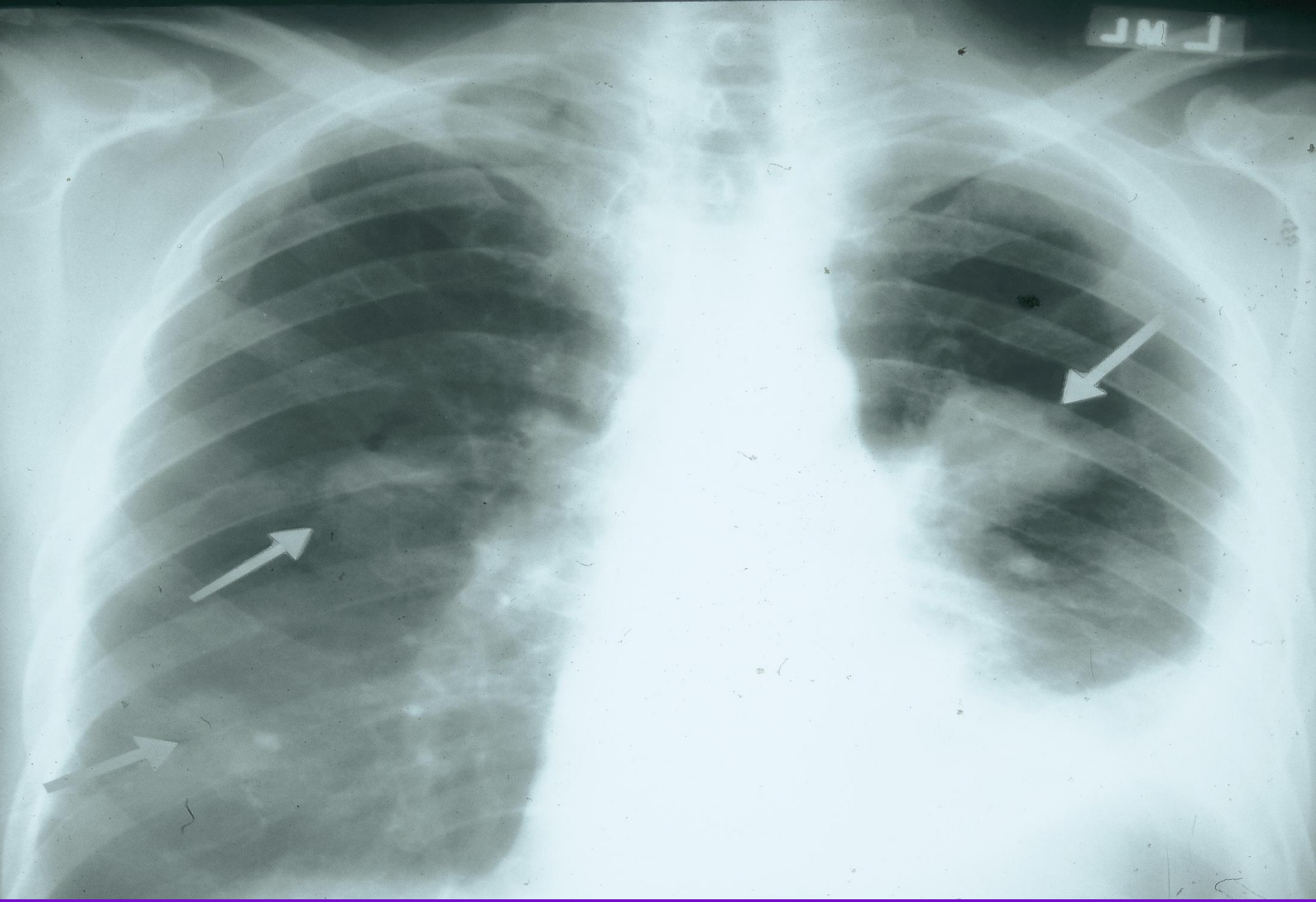
Several histologic types each with specific:

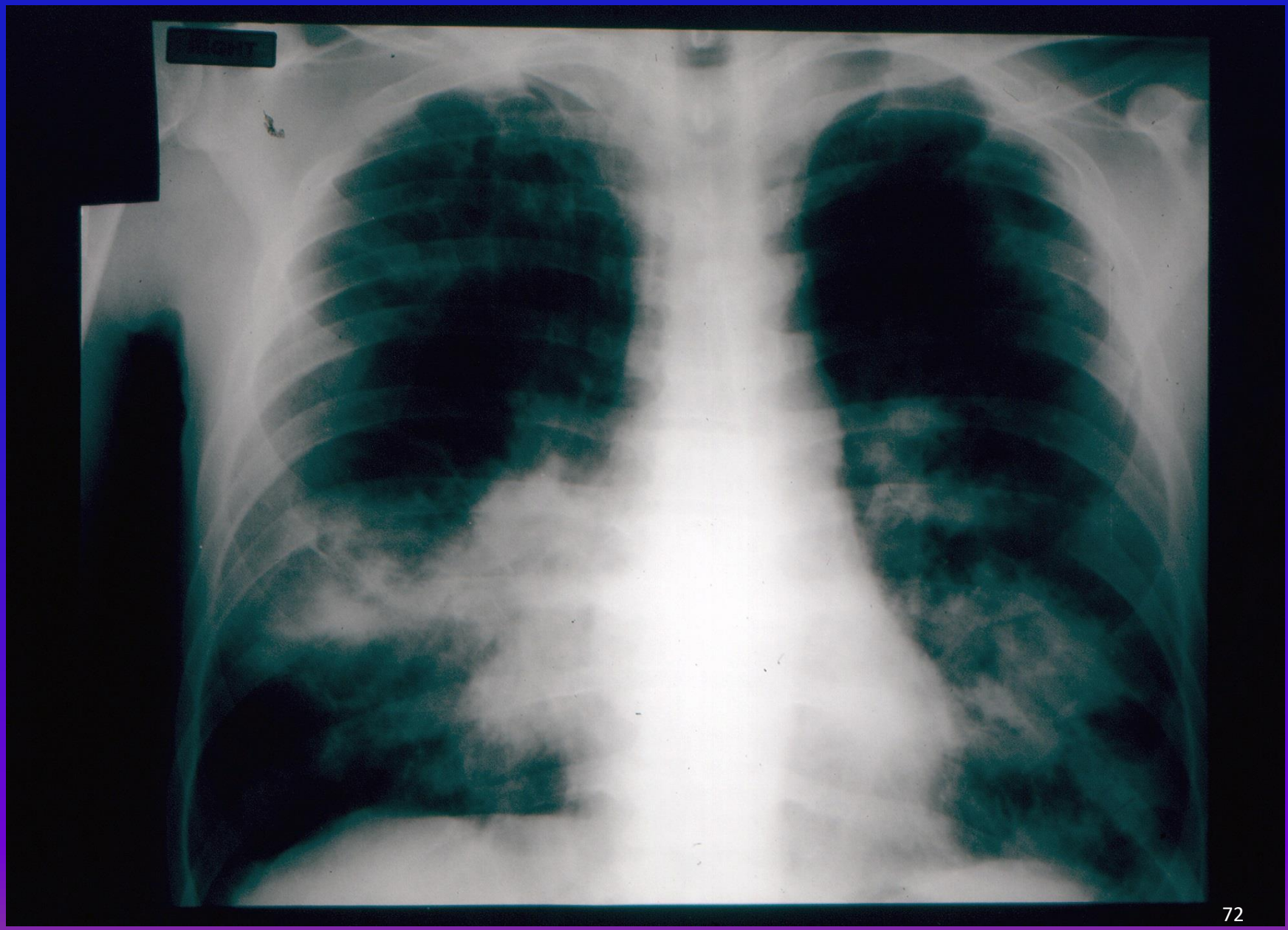
- Growth
- Natural history
- Complications
- Response to treatment
- Survival


LUNG CANCER
PROGNOSTIC FACTORS
EXTENT
METASTATIC SITES
PERFORMANCE STATUS
WEIGHT LOSS
CELL TYPE

Normal Chest X-ray

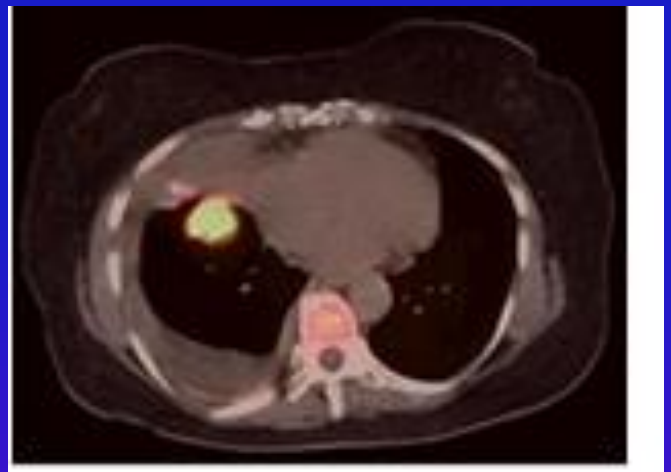




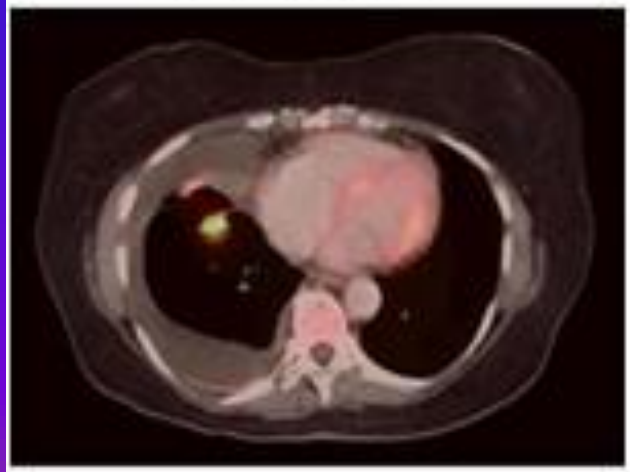

RIGHT

Chest CT Scan Showing Metastases

PET/CT scan
Positron Emission Tomography/Computer Tomography



Jan 3rd 2009



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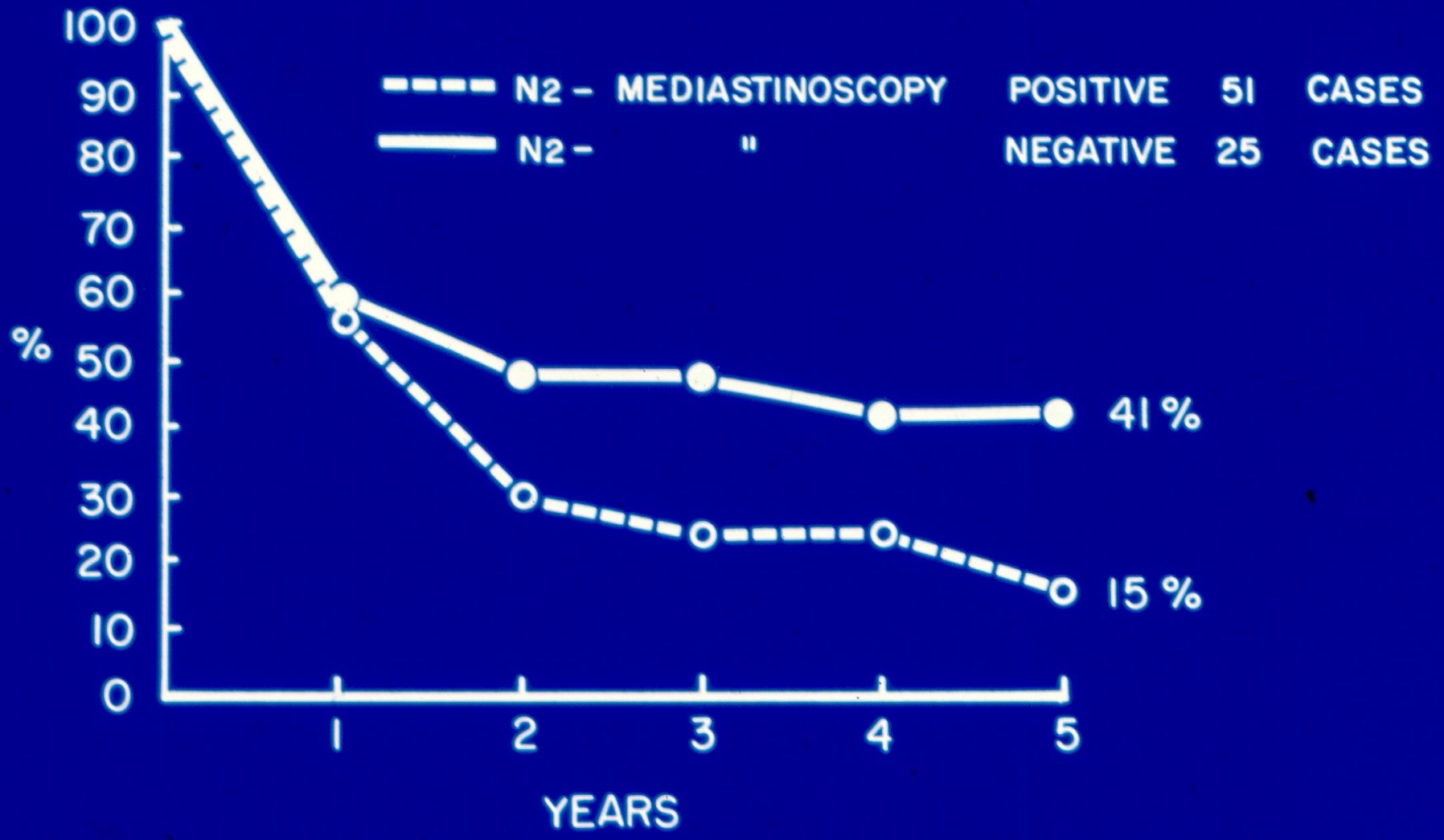

100
90
80
70
60
%
50
40
30
20
10
0
N2 – MEDIASTINOSCOPY POSITIVE 51 CASES
N2 – " NEGATIVE 25 CASES
41 %
15 %
1
2
3
4
5
YEARS

LUNG CANCER TREATMENT

Surgery for curative intent

Surgery for palliative intent

Radiation therapy

Systemic chemotherapy

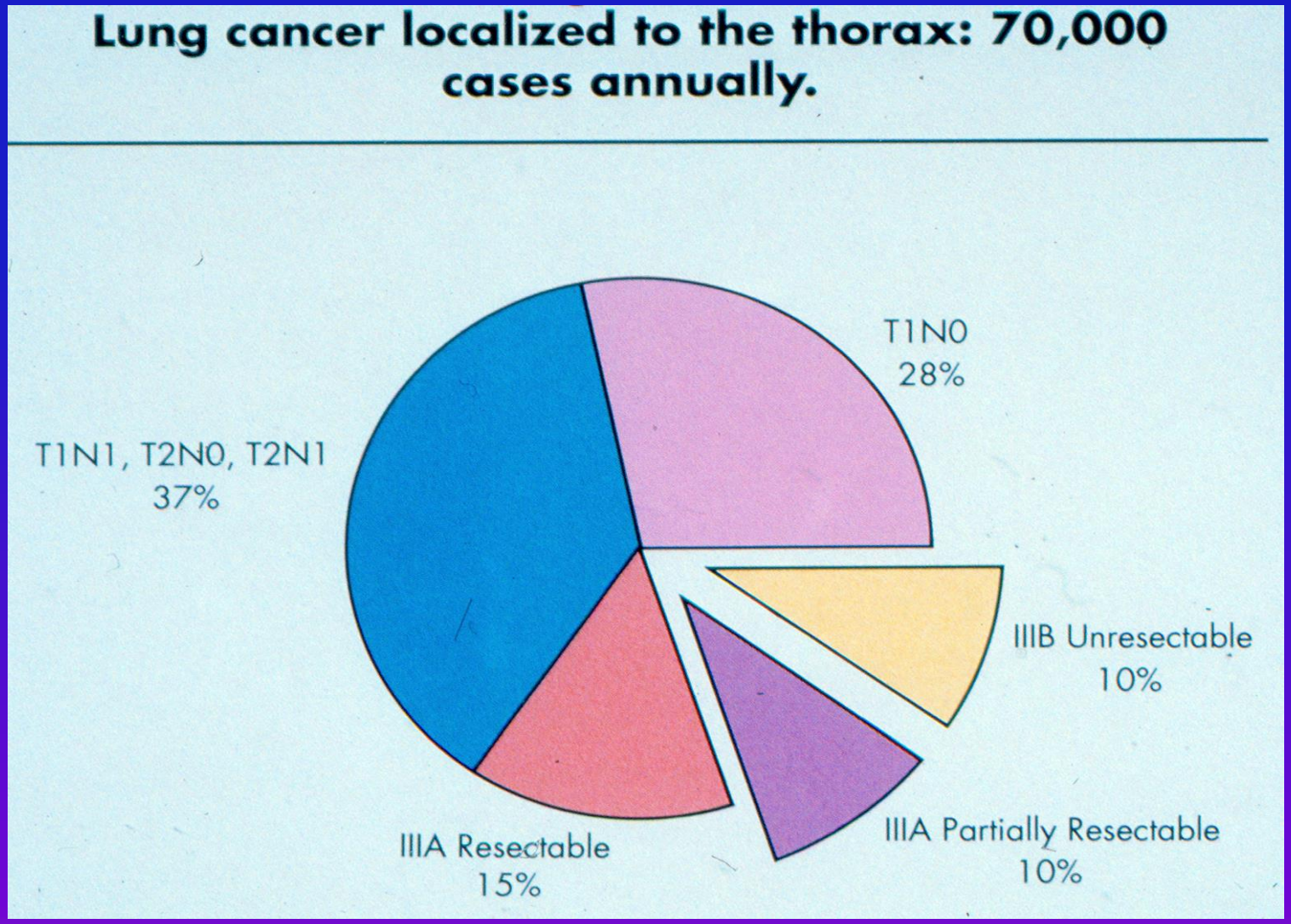
Intra-caviatry (intra-pleural) chemotherapy

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
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