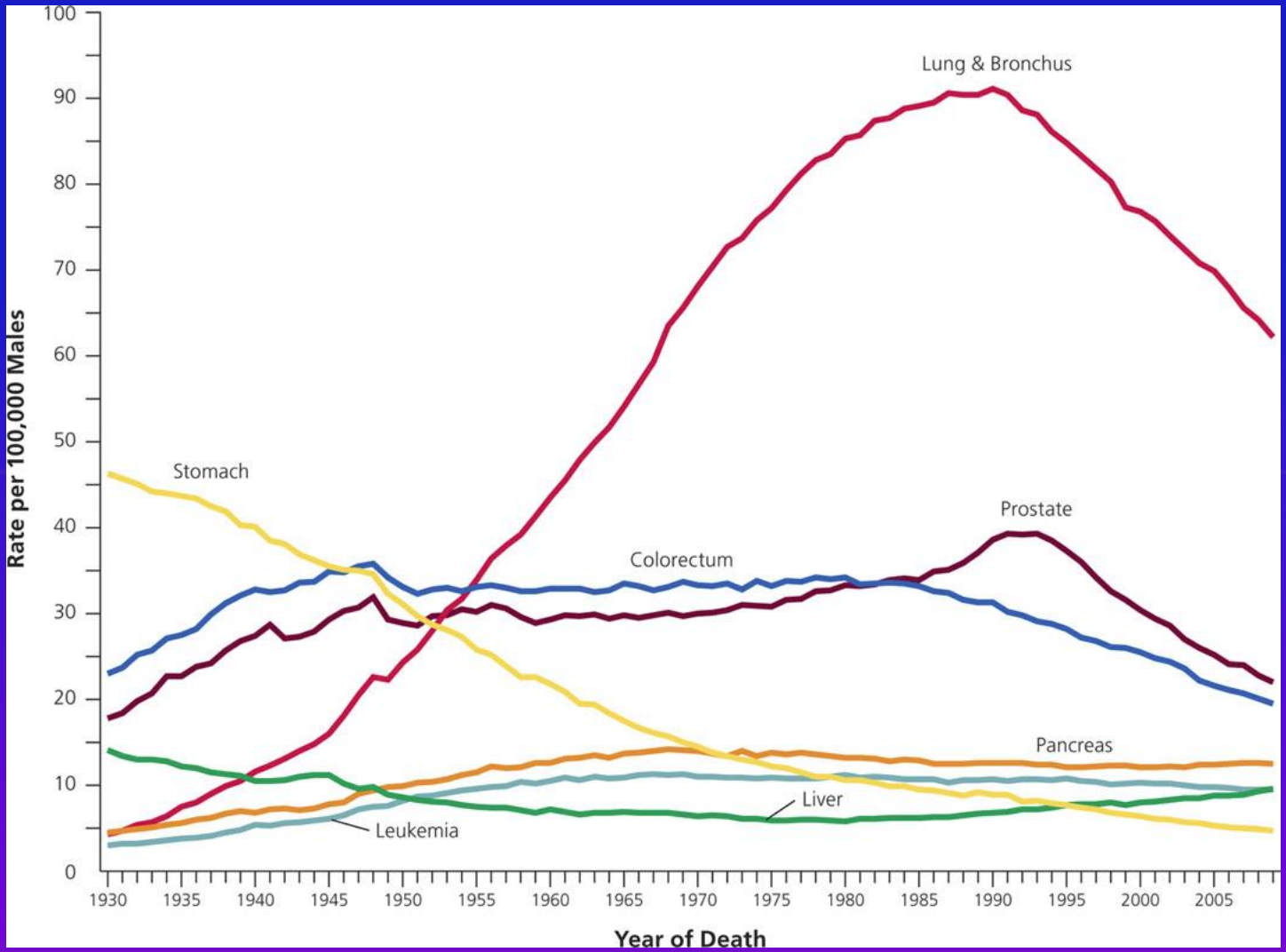
LECTURE #3

CANCER IN HUMANS

CANCER INCIDENCE IN USA - 2013



Cancer Statistics in USA – Est. 2016* and 2017**

	All sites	Lung	Breast (W)	Prostate	Colon
New cases	1,685,000	224,000	249,000	181,000	95,000
	1,689,000	222,000	255,000	161,000	96,000
Deaths	596,000	158,000	41,000	26,000	49,000
	601,000	156,000	41,000	27,000	50,000

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* Published 2016

** Published 2017

SEVEN WARNING SIGNS OF CANCER

Change in bowel or bladder habits

A sore that does not heal

Unusual bleeding or discharge

Thickening or lump in breast or elsewhere

Indigestion or difficulty in swallowing

Obvious change in a wart or mole

Nagging cough or hoarseness

EFFECTS OF TUMORS

DIRECT
- INVASION
- OBSTRUCTION
- NECROSIS
- INFECTION
- EFFUSIONS

INDIRECT = PARANEOPLASTIC SYNDROMES

WHEN AND IF ONE SUSPECTS CANCER

Personal history: Any previous cancer?

Constitutional symptoms? Cough?

Bleeding?

Family history: Any cancer cases?

Physical examination: Any enlarged lymph nodes

("glands") in the neck, axilla, groin?

Chest or abdominal fluid?

- Organ enlargement: Liver? Spleen?

Indirect methods (radiography, scintigraphy)

CANCER MANAGEMENT

1. Basic Medical Evaluation
2. Tumor Staging
3. Discuss with patient and family
    a. Second opinion (?)
    b. Cancer Conference (tumor board) (?)
1. Treatment
2. Rehabilitation
3. Follow-up

BASIC MEDICAL EVALUATION

History and Physical Examination

Constitutional Symptoms

Performance Status (E.C.O.G. PS)

Psychological Index

Constitutional Symptoms

Weakness, fatigue

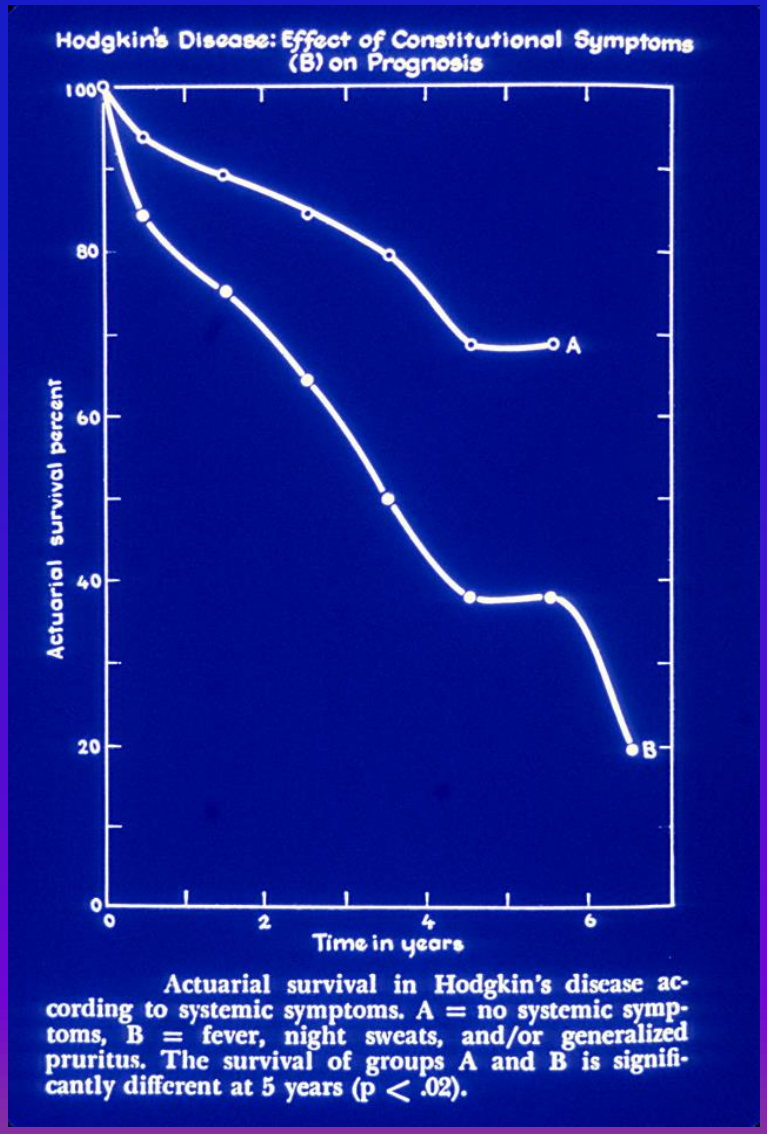
Anorexia, weight loss, cachexia

Unexplained fever

Diaphoresis, night sweats

Department o
Veterans Affa

Constitutional Symptoms and Survival



Actuarial survival in Hodgkin's disease according to systemic symptoms. A = no systemic symptoms, B = fever, night sweats, and/or generalized pruritus. The survival of groups A and B is significantly different at 5 years ($p < .02$).

ECOG PERFORMANCE STATUS

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1.	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about **more than 50% of waking hours**
3	Capable of only limited self-care, confined to bed or chair **more than 50% of waking hours**
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair

Interventional Methods of Diagnosis and Treatment

Needle aspiration and biopsies: Thoracentesis (Chest tap), Abdominal tap

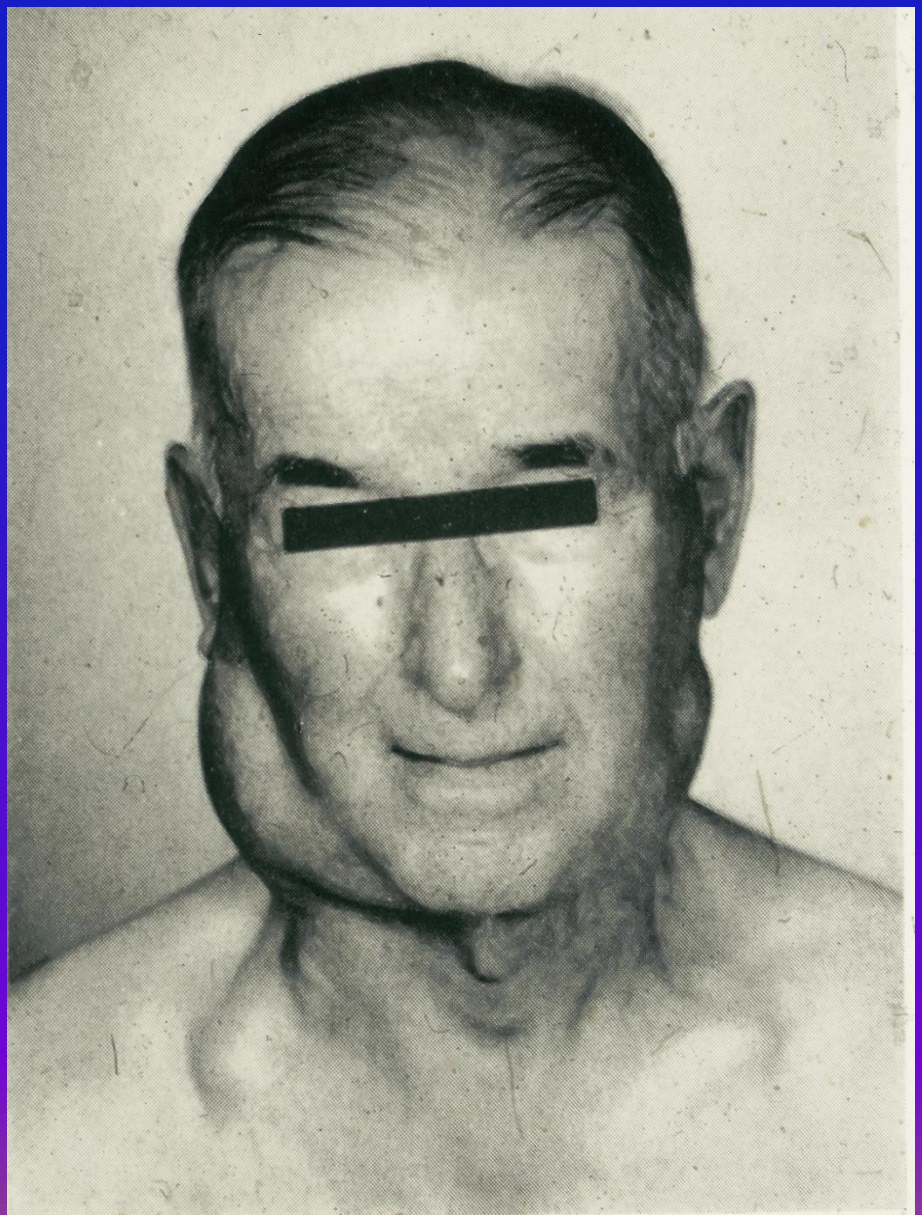
Biopsies: Diagnostic and excisional

Endoscopies: Bronchoscopy, UGI tract, Colonoscopy

Endoscopic Trans-Bronchial Ultrasound

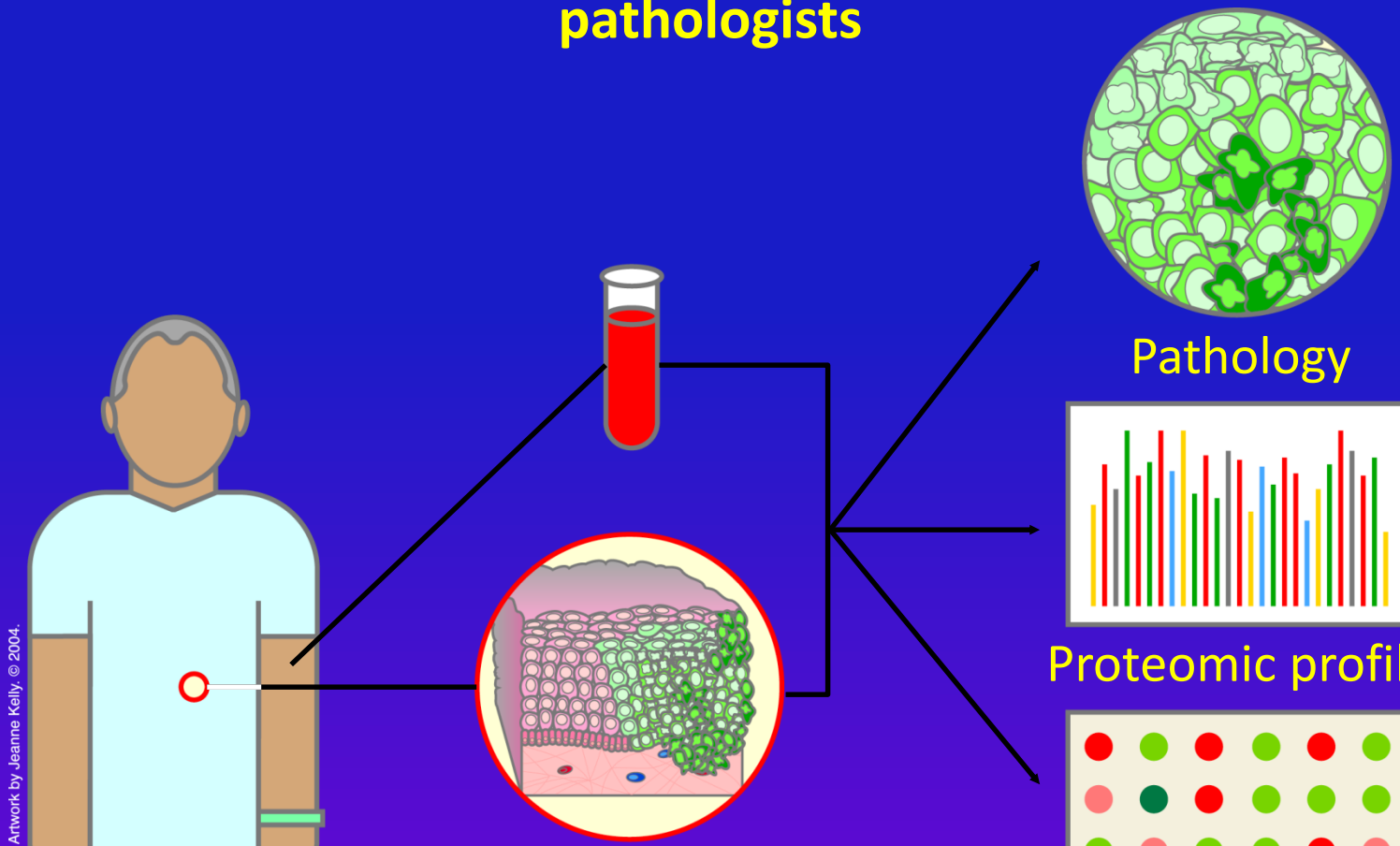
Thoracoscopy (looking into the pleural cavity)

Bilateral cervical and supraclavicular lymphadenopathy



CANCER DIAGNOSIS

Biopsy = Removal of a small piece of tissue to be examined by pathologists



Methods of Cancer Diagnosis and Staging, Evaluating the Response to Treatment, and Follow-up

Radiography: Conventional and with contrast

Ultrasound: External and endoscopic

Nuclear medicine scanning (scintigraphy)

Computed tomography (CT)

Magnetic resonance imaging (MRI and MRA)

PET-CT scanning

T = Primary tumor size

N = Lymph node involvement

M = Distant metastases

PURPOSE OF STAGING

To aid in determining prognosis

To facilitate selection of most effective treatments

To facilitate meaningful comparison of reported results from different sources

To evaluate cancer control measures

STAGING

THE MEASUREMENT OF THE EXTENT OF A CANCER:

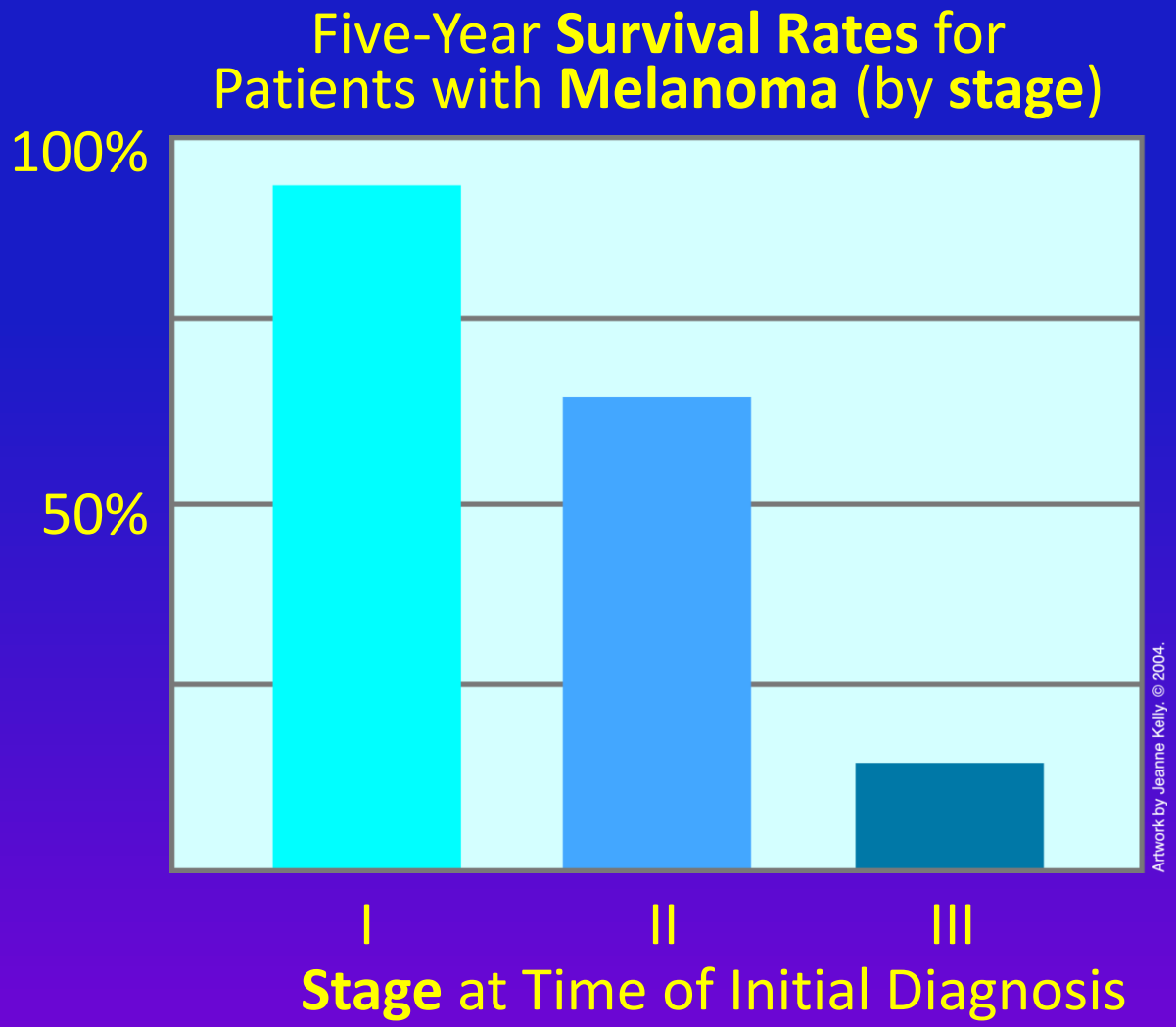
The classification of patients with cancer into groups with similar extent

TNM STAGING OF CANCER

CORRELATION BETWEEN TUMOR, LYMPH NODES, AND METASTASES

1. In all sites, there is good correlation between the size of the **tumor** and its local penetration (T), the involvement of **lymph nodes** (N), and the spread of the cancer to **remote sites** (metastases) (M)
2. Staging dictates the best treatment
3. Staging weighs heavily on prognosis

Tumor Staging



TUMOR MARKERS

1. Substances (mostly proteins) found in blood, urine, tissue, or body fluids.
2. Gene expression or DNA changes found in tumor tissue.

<u>They may:</u>

- Help in the diagnosis of cancer
- Reflect on the extent of the disease
- Predict the response to treatment
- Assess the response to treatment
- Determine recurrence

TUMOR MARKERS

Alfa-fetoprotein – Liver and testicular cancer

Beta-hCG - Testicular cancer

CA-125 – Ovarian cancer

CEA – Colon, breast, lung cancer

EGFR – Lung cancer

ER and PR – Breast cancer

HER2/neu – Breast, stomach, esophagus

PSA – Prostate cancer

DRAWBACKS OF THE TUMOR MARKERS

Small amounts are present in the in normal body (CEA, PSA)

Large amounts may be present in diseases other than cancer (CEA in ulcerative colitis, PSA in BPH)

Sensitivity = ability to identify the cancer

Specificity = ability to identify those without the disease

DIAGNOSIS of LUNG CANCER

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**

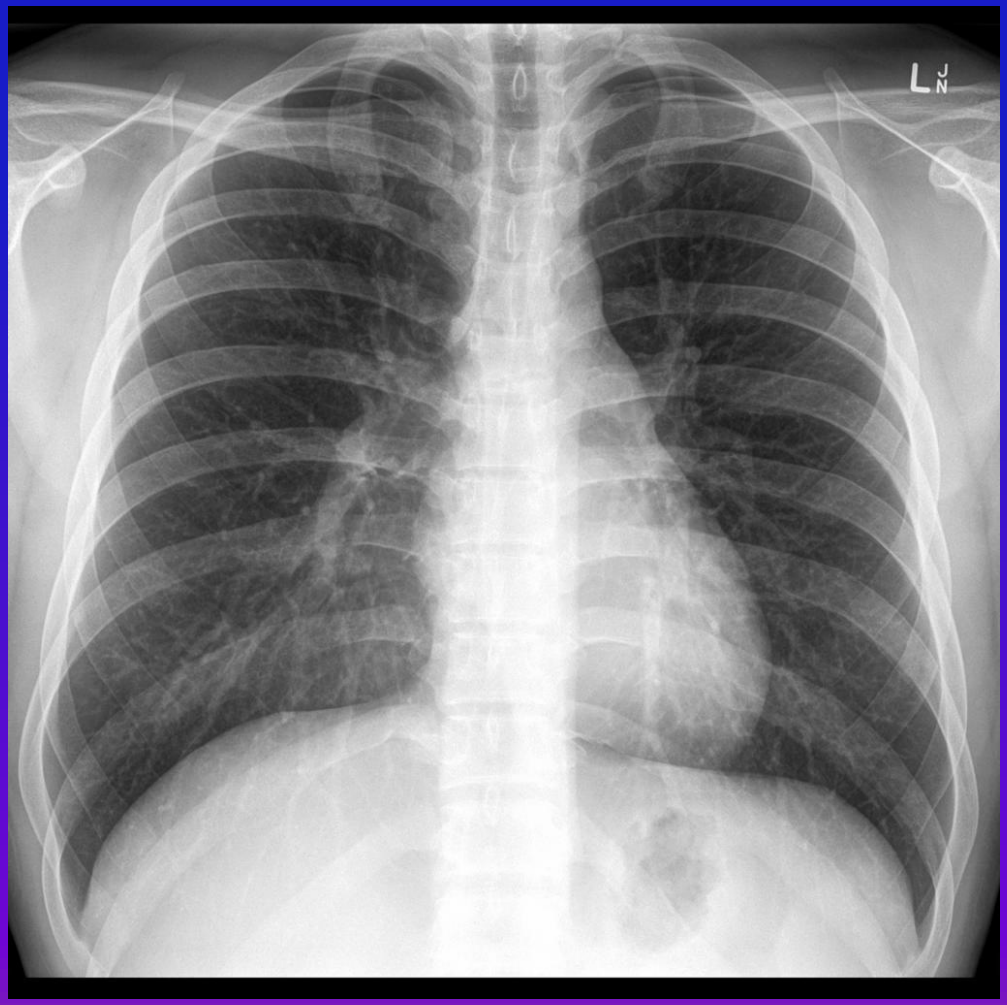
LUNG CANCER

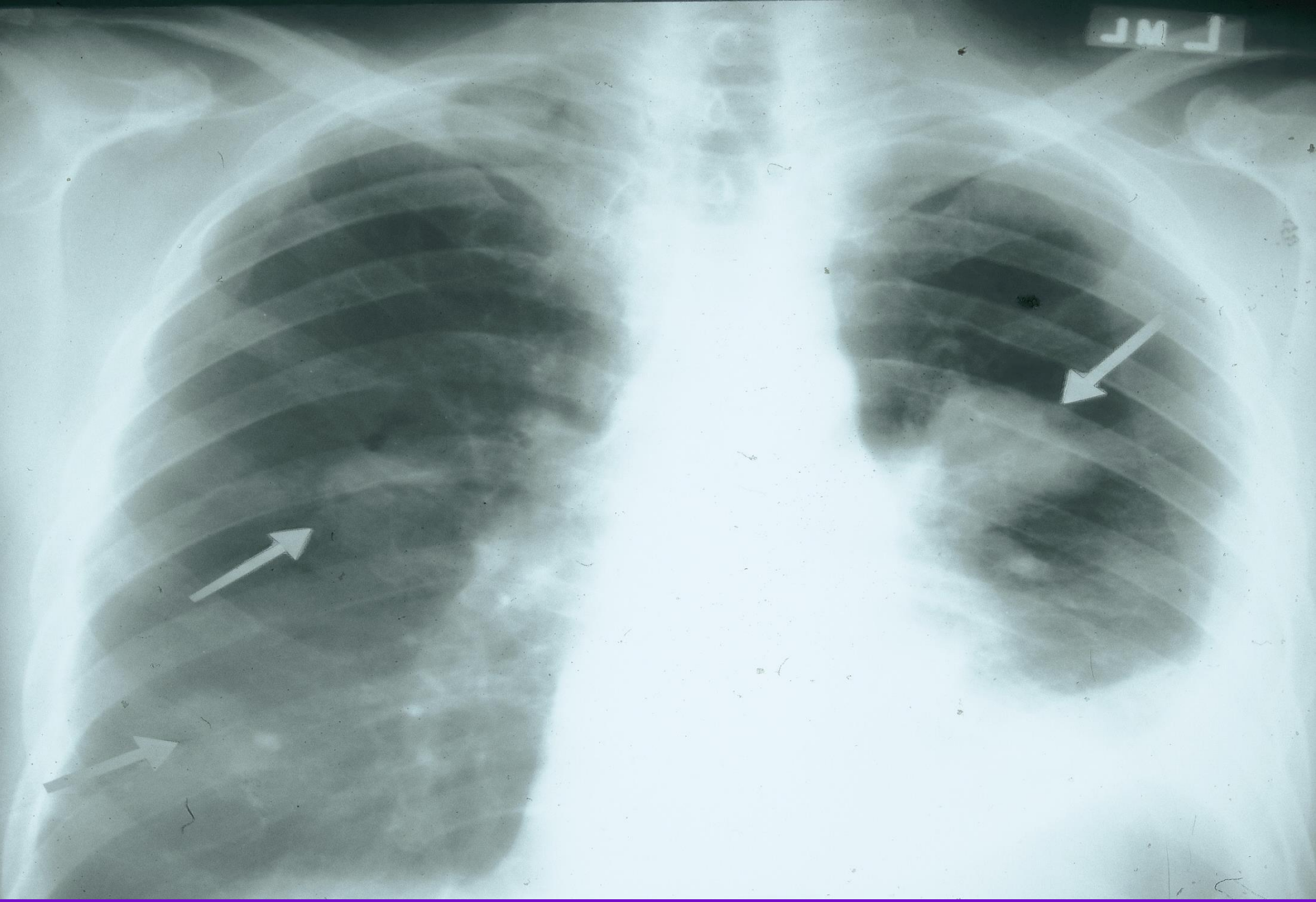
SYMPTOMS DURING COURSE OF DISEASE

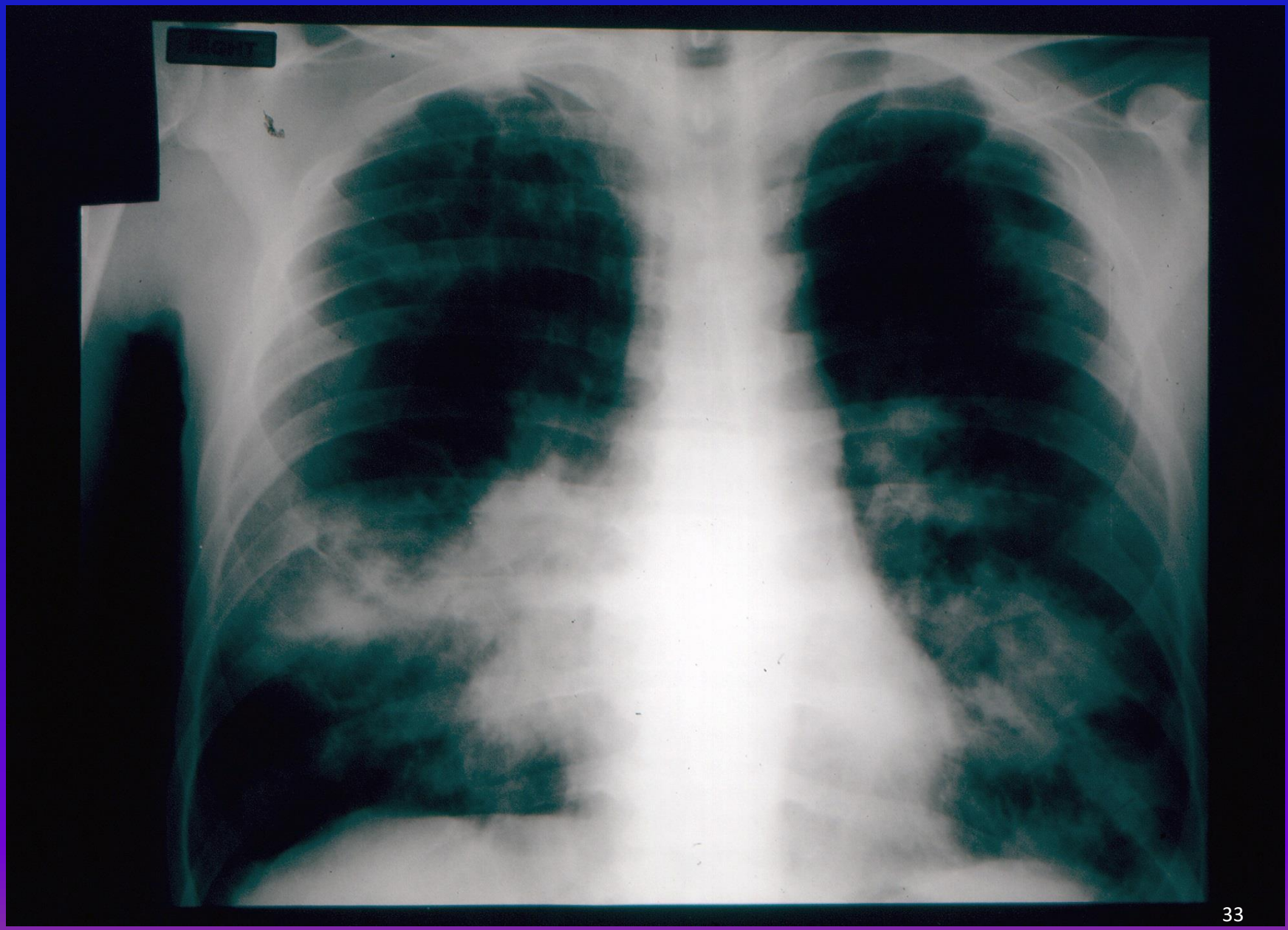
	% INCIDENCE*
COUGH	48-71
CHEST PAIN	28-50
DYSPNEA	23-42
HEMOPTYSIS	9-63
WEIGHT LOSS	31-49

*Data culled from 3 series (2404 patients)

Normal Chest X-ray

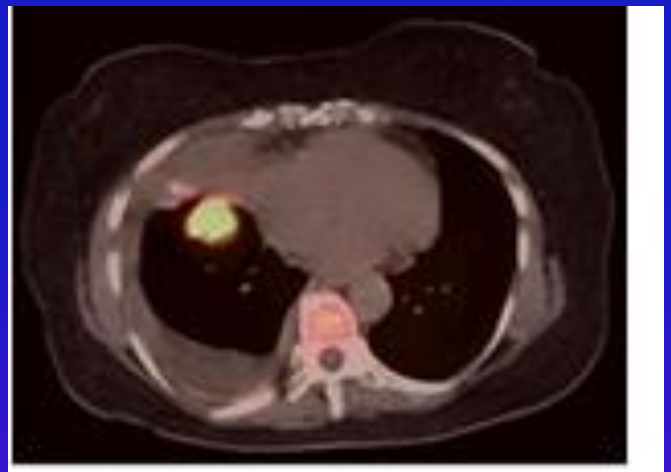




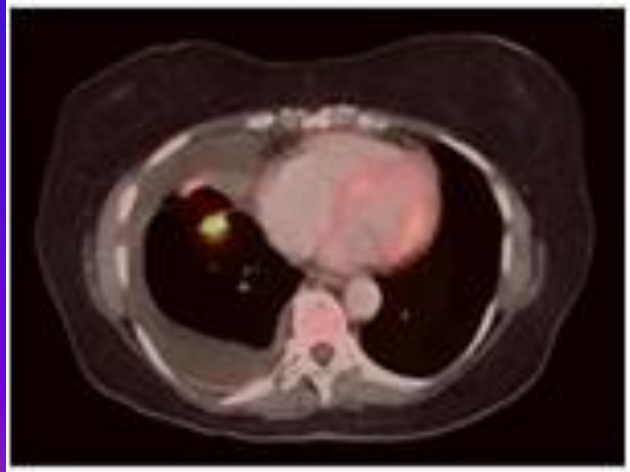

RIGHT

Chest CT Scan Showing Metastases

PET/CT scan
Positron Emission Tomography/Computer Tomography

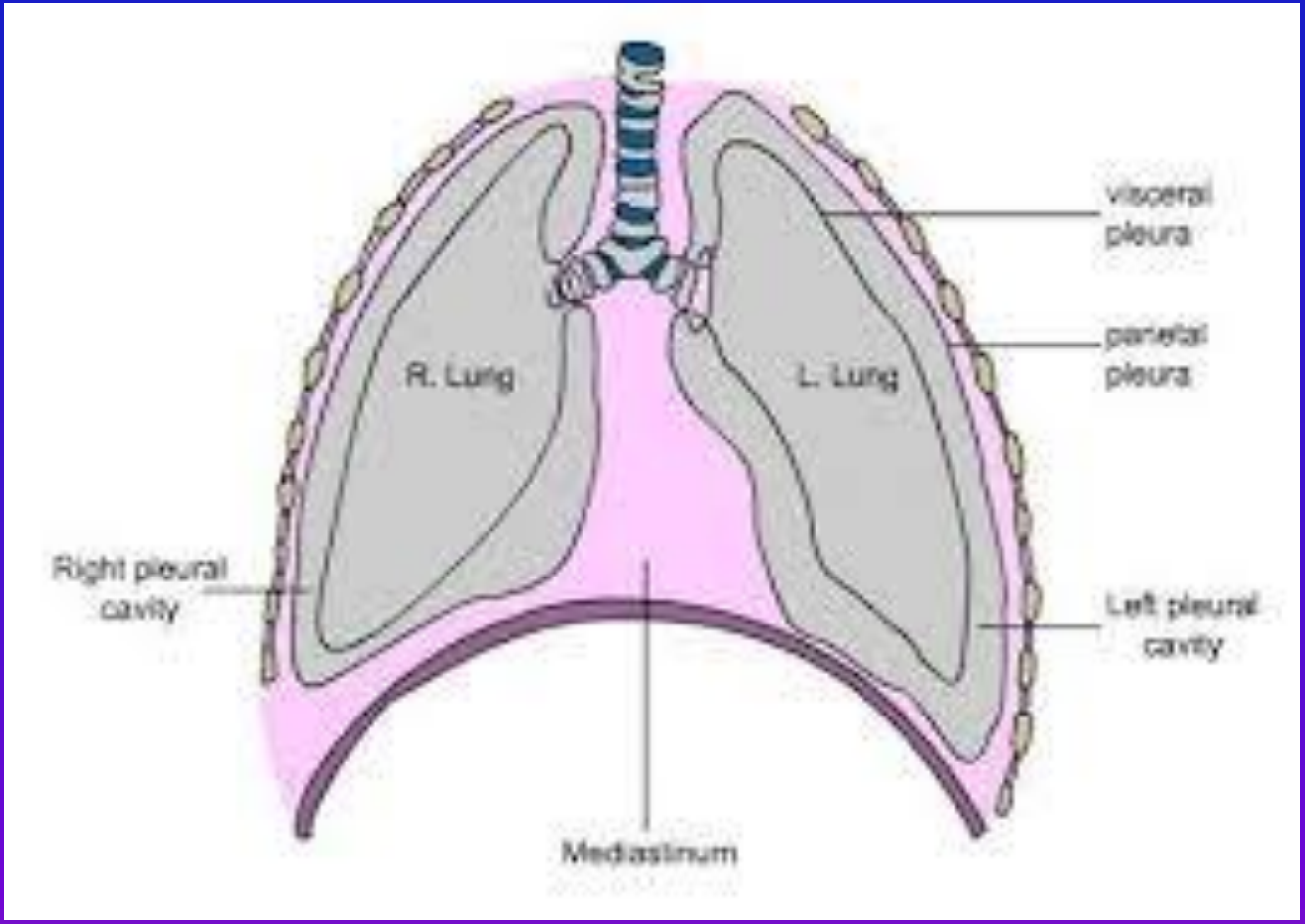


Jan 3rd 2009

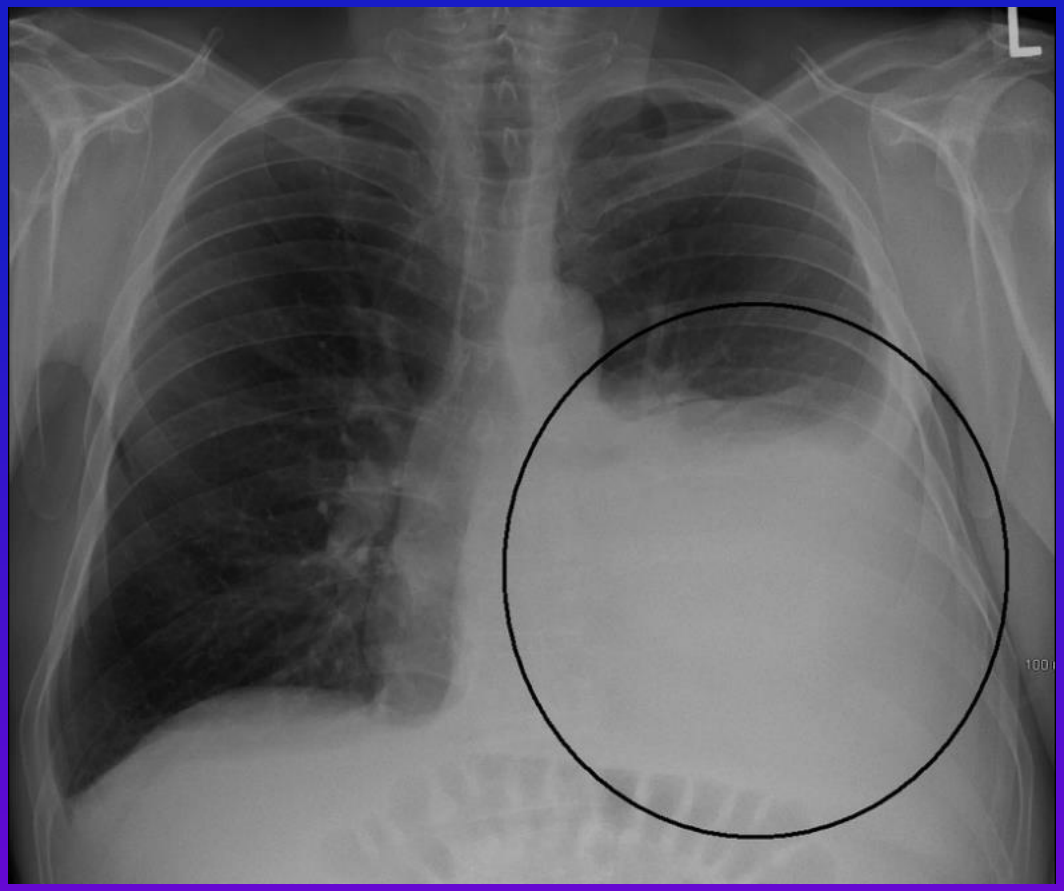


Jan 31st 2009

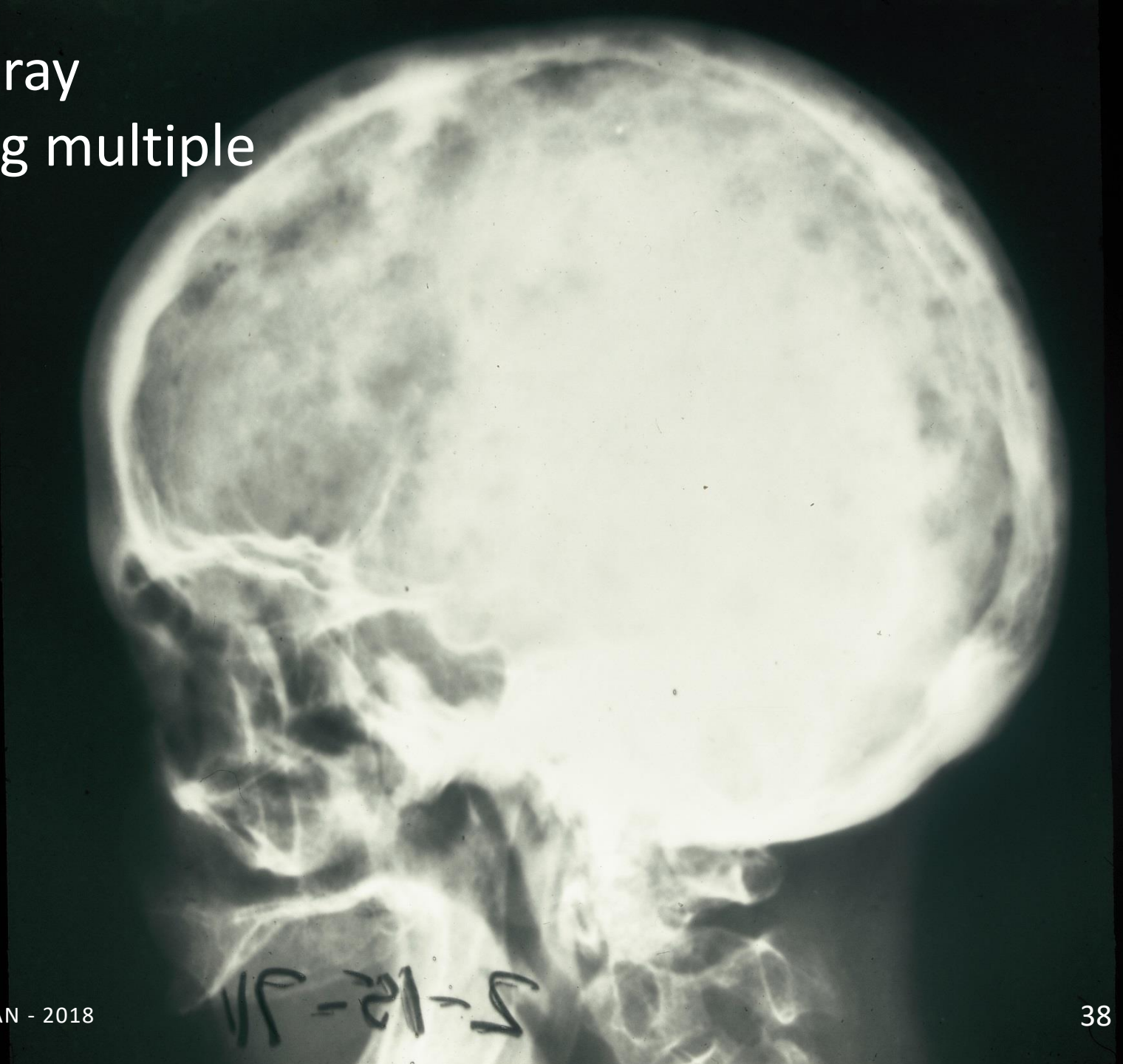
PLEURA


visceral pleura
parietal pleura
R. Lung
L. Lung
Right pleural cavity
Left pleural cavity
Mediastinum

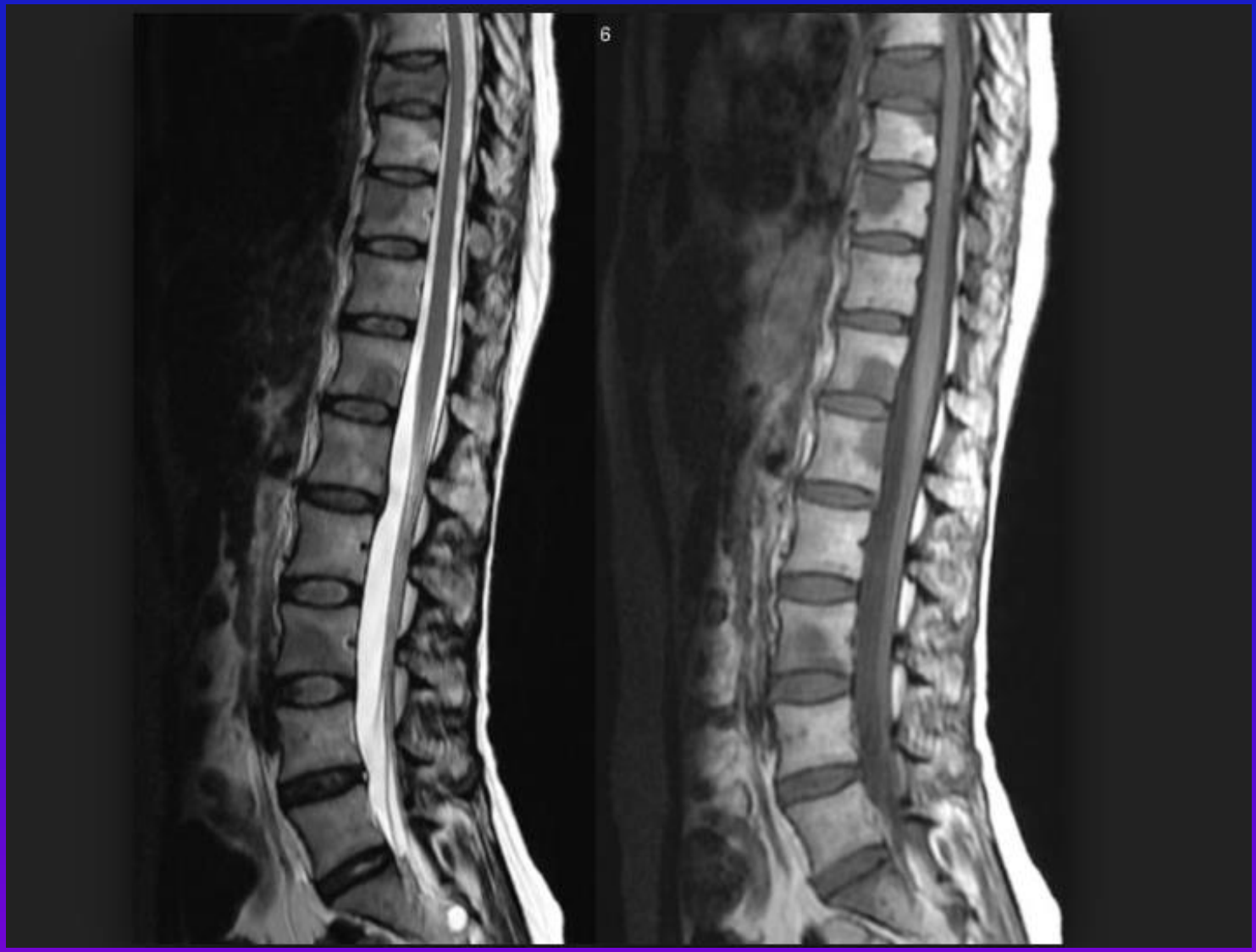
Left-sided pleural effusion



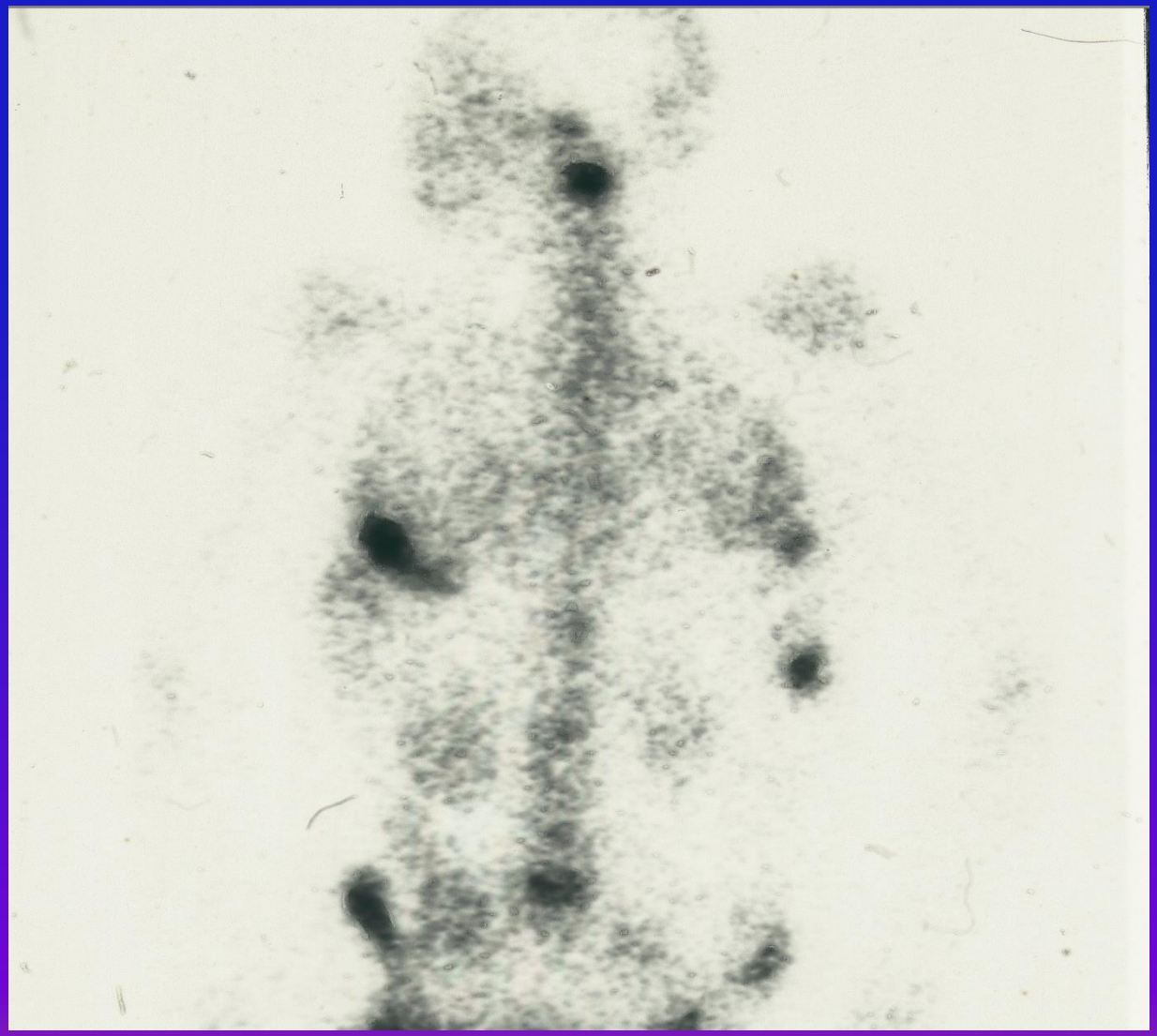
Skull X-ray showing multiple mets.



Spinal metastases



Bone scan showing areas of bone metastases



DIAGNOSIS OF BREAST CANCER

Breast Cancer

Some studies have shown an **association with meat consumption**

740 cases and 810 controls – Natl. Center Toxicology Research

Heterocycle amines (HAs) formed during **meat cooking** are **mammary carcinogens** in lab animals

Breast Cancer

Italian study - 1991-1994

2,569 cases and 2,588 controls

Risks: high alcohol intake (10.7%)

low β-carotene intake (15.0%)

BREAST CANCER

- Gender
- Age: 127/100,000 - in 40-44 y.o.
  229/100,000 - in 50-54 y.o
  348/100,000 - in 60-64 y.o.
  450/100,000 - in 70-74 y.o.

BREAST CANCER - Risk Factors (1)

- Previous breast cancer, atypical hyperplasia,
- Family history: 1st degree relative ⇨ x 2-3 fold
- Susceptibility genes: risk = 50%- 85%
- BRCA-1 occurs in 5% of women <70 y.o. w/ ovarian ca.
- Chromosome #17q = lifetime risk of 85% for breast ca.
  and 45% for ovarian cancer in families with
  multiple cases of cancer

BREAST CANCER – Risk Factors (2)

- Older age at pregnancy, nulliparity
- High socioeconomic status (Diet? Lifestyle?)
- History of high-dose radiation exposure
- Oral contraceptives, long-term estrogen Rx.
- Obesity, high-fat diet

PRESENTING SYMPTOMS

"LUMP" IN THE BREAST

(80% of cases). More than 90% of breast cancers discovered by women themselves.

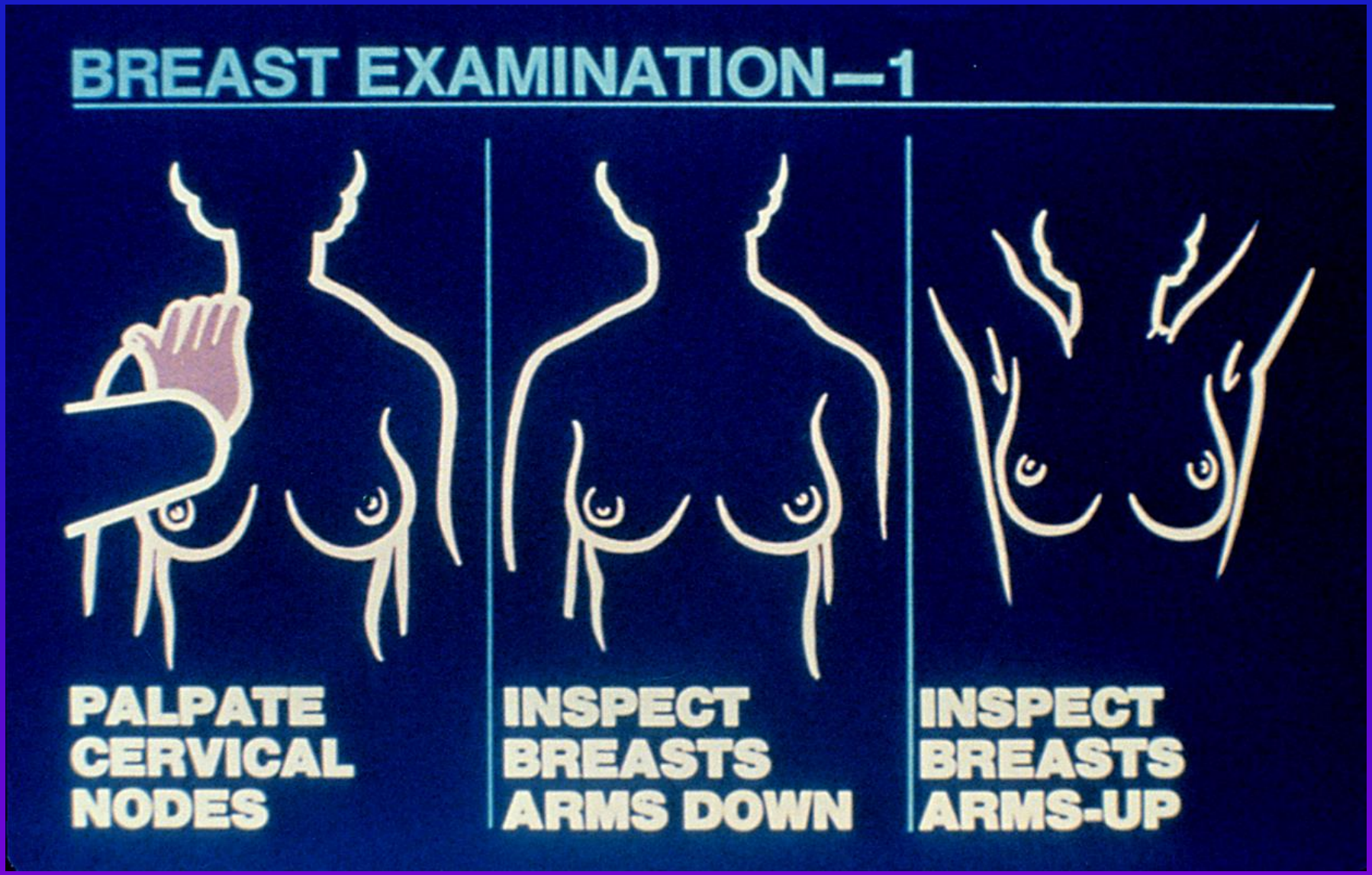
PAIN IN THE BREAST

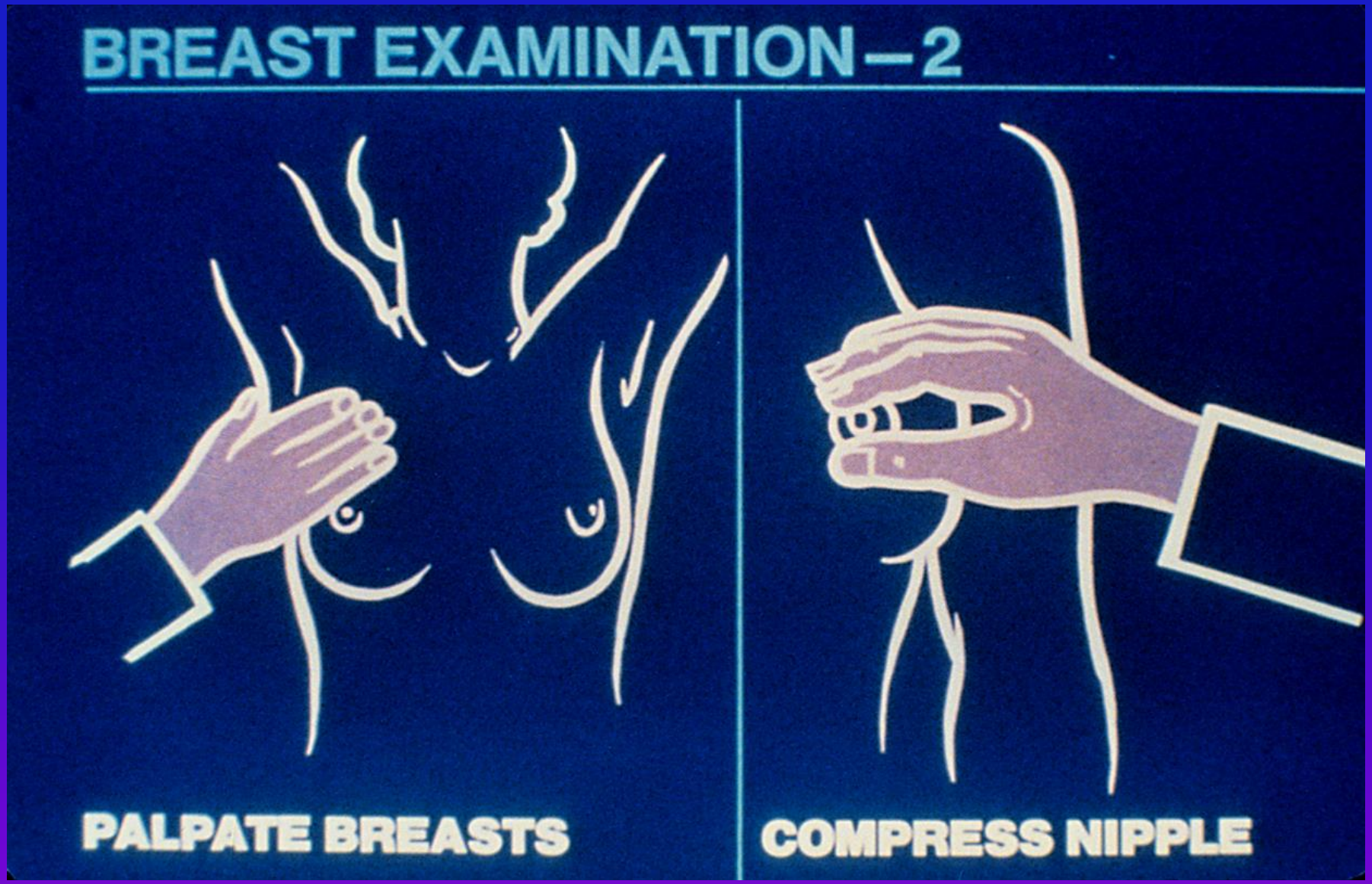
NIPPLE
- DISCHARGE
- EROSION
- RETRACTION
- ENLARGEMENT
- ITCHING

BREAST
- REDNESS
- HARDNESS
- ENLARGEMENT
- SHRINKING

RARE
- AXILLARY MASS
- ARM SWELLING
- BONE PAIN


'9 1 12 30


BREAST EXAMINATION—1
PALPATE CERVICAL NODES
INSPECT BREASTS ARMS DOWN
INSPECT BREASTS ARMS-UP

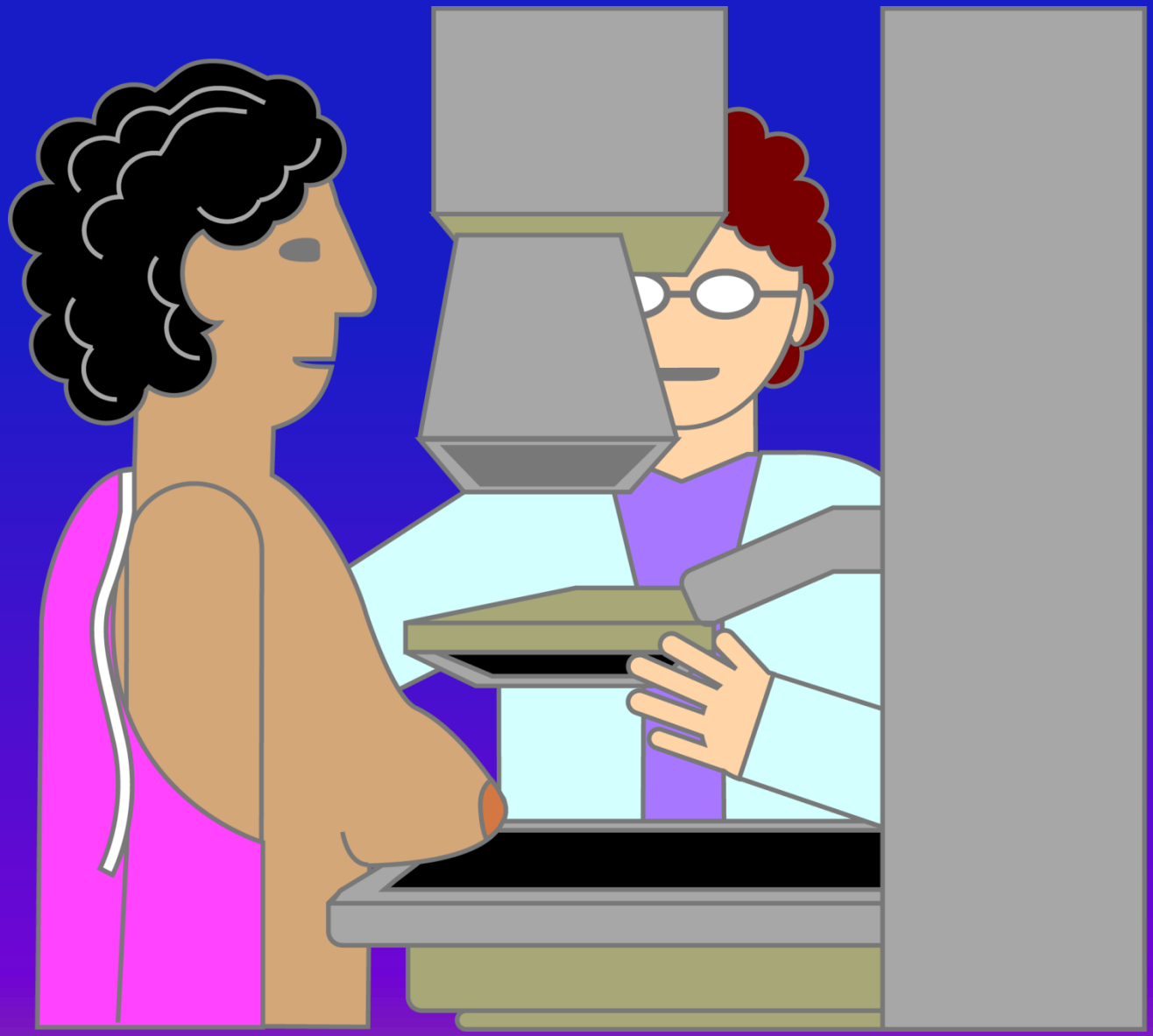

BREAST EXAMINATION—2
PALPATE BREASTS
COMPRESS NIPPLE

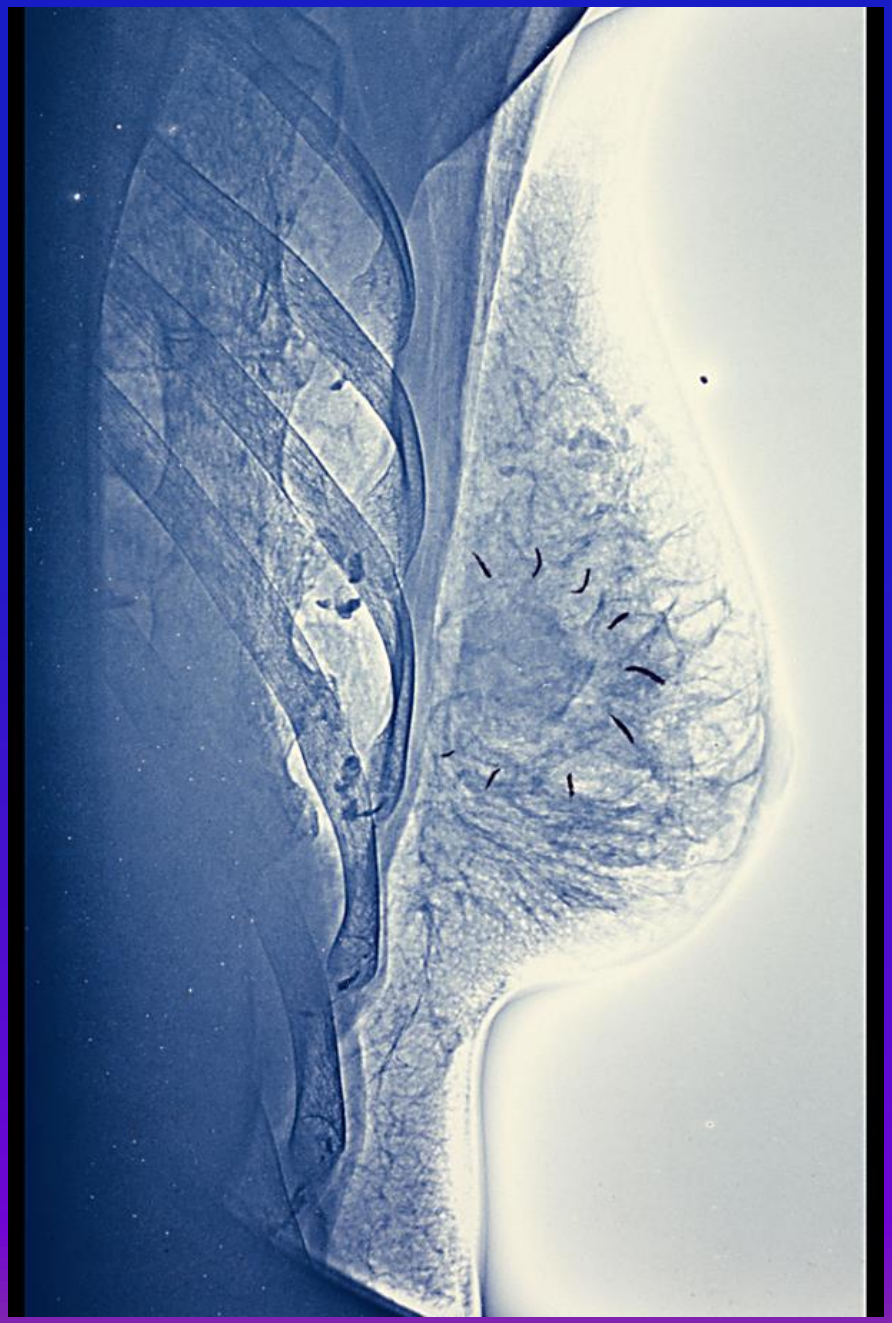
BREAST EXAMINATION—3

EXAMINE AXILLAE

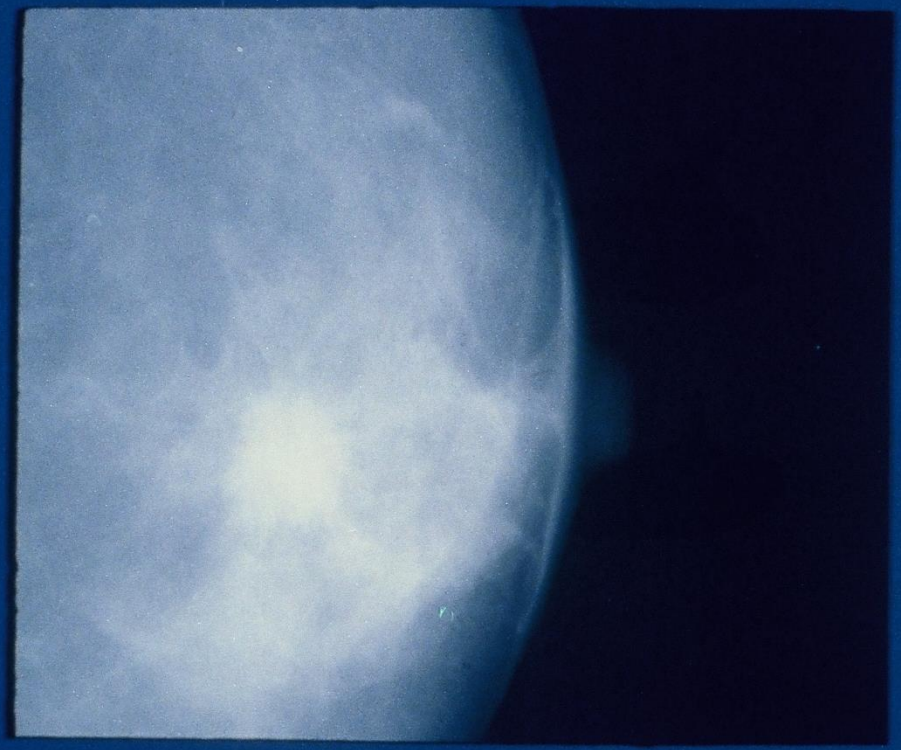
PALPATE BREASTS
PATIENT SUPINE

Mammography

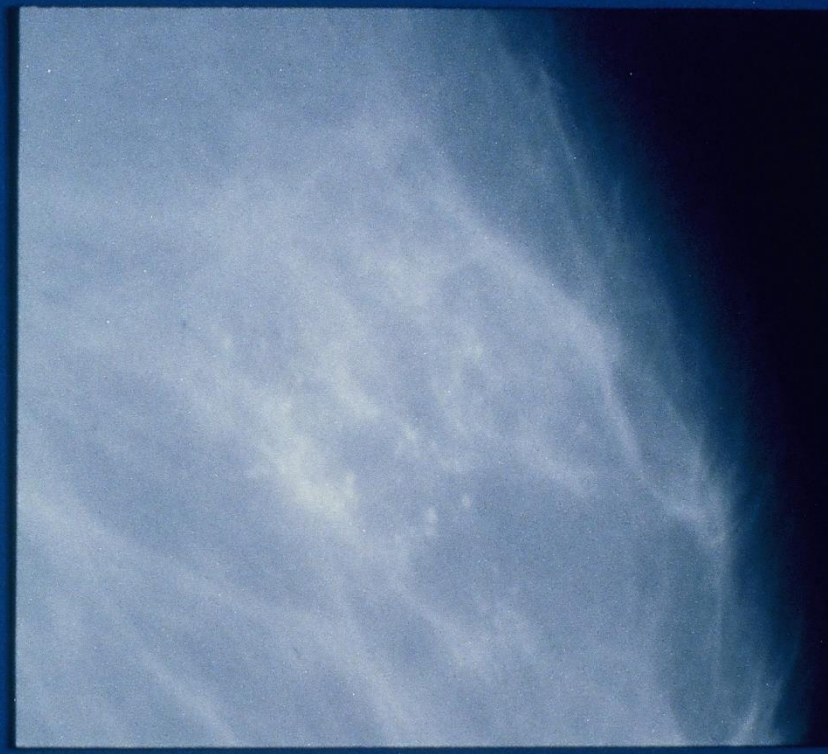




MAMMOGRAPHIC SIGNS OF CANCER

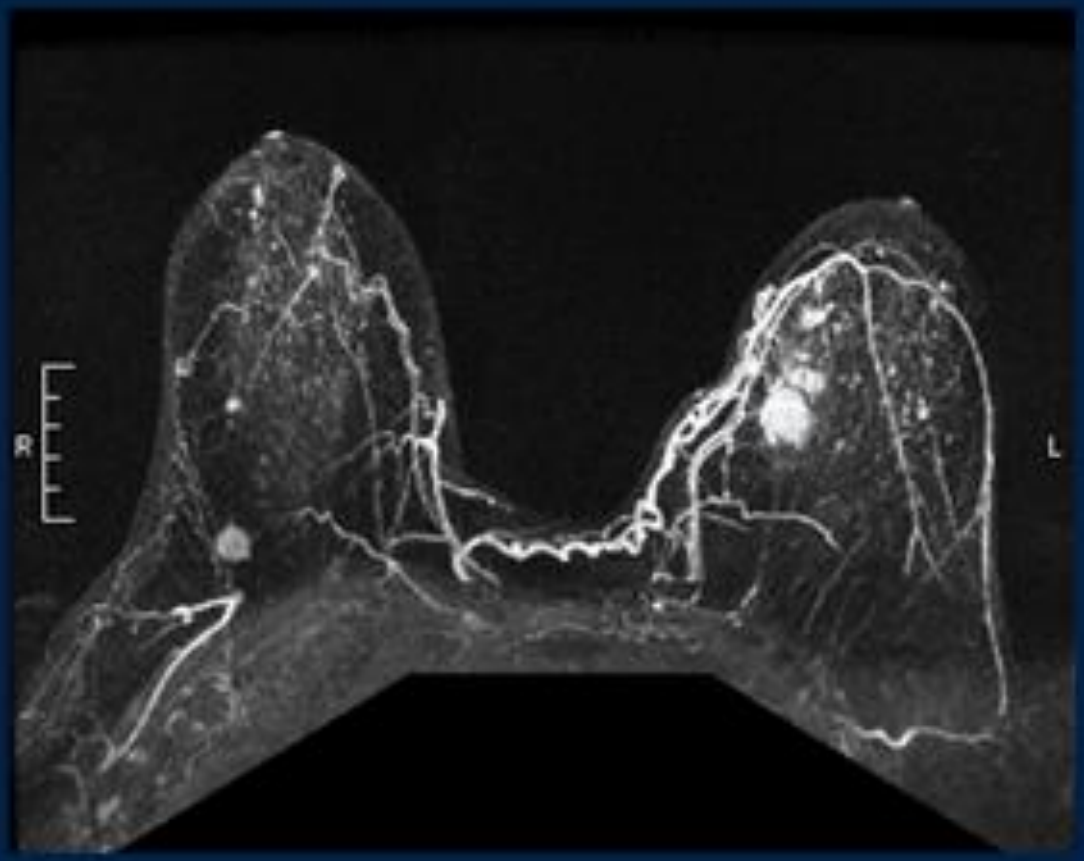


Irregular Mass



Microcalcifications

MRI as a Breast Cancer Screening Tool



- Left breast: Known cancer, low-grade papillary carcinoma
- Right breast: High-grade invasive ductal carcinoma only seen on MRI

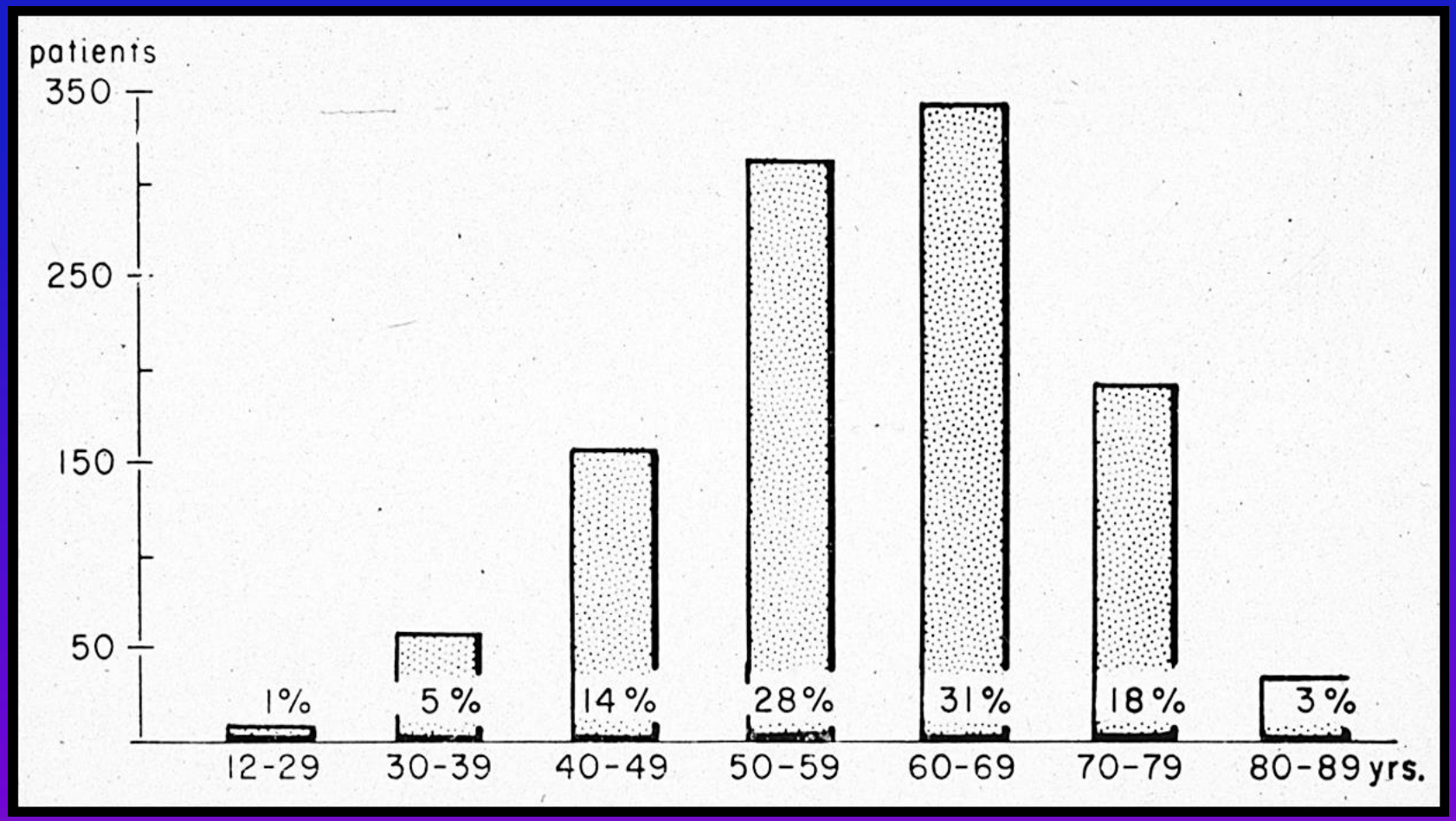
Courtesy E. Rosen

Metastatic breast cancer to the skull

INTERMISSION

DIAGNOSIS of COLON CANCER

COLON CANCER - INCIDENCE



Colorectal Cancer - Burden of Suffering

- 2016 - 96,000 new cases in U.S.
- 2016 - 50,000 deaths in U.S.
- Lifetime risk in U.S. = 2.6%
- 60% of cases are advanced at time of diagnosis
- 5-yr. survival
  - localized = 91%
  - regional = 60%
  - distant = 6%

Risk Factors for Colorectal Cancer

- Age > 50 years
- High fat; low fiber and vegetables
- Tobacco
- Alcohol, obesity
- Personal history of adenomas or cancer
- Family history of adenomas or cancer

Colon Cancer

Population-based study in No. California, Utah, and Minnesota, 1991 - 1994

1,993 cases and 2,410 controls

Western diet - increased risk of colon cancer in both genders

Colon Cancer

- Adventist Health Study - California,
  32,051 Non-Hispanic White
- Positive association with **total meat**
  intake (p=.01)
- Positive association with **red meat**
  intake (p=.02)
- Inverse association with legume intake

Colon Cancer

- Obesity increases risk of colon cancer
- Physical exercise decreases the risk
- Red meat increases the risk. Heterocycle amines?
- Other dietary fat does not increase the risk

Colorectal Cancer - Risk Factors

Familial syndromes (6% of cases):

- Hereditary polyposis
- Hereditary non-polyposis colorectal cancer

History of CRC in first-degree relative

Personal history of:

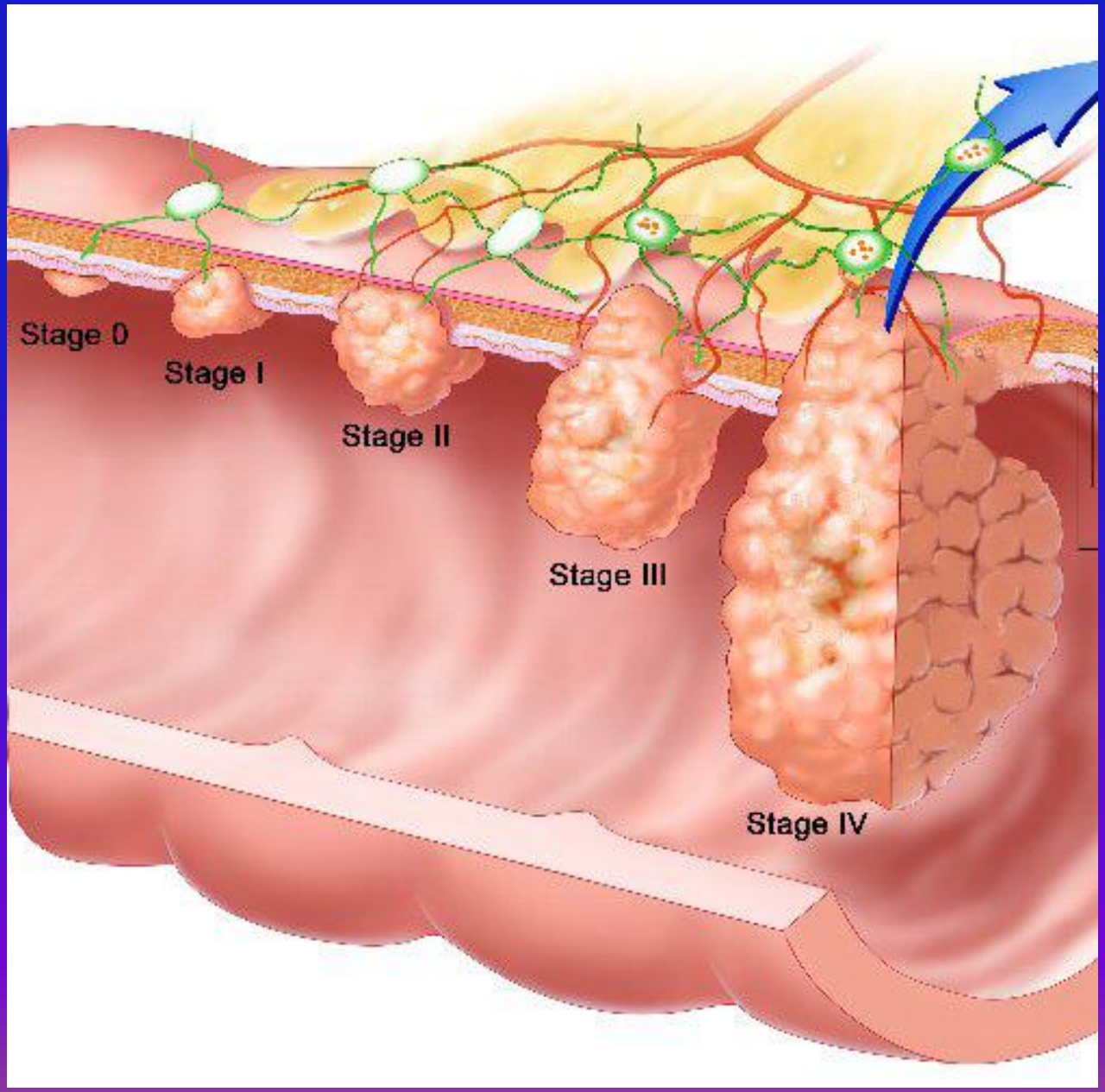
- Ulcerative colitis
- Colorectal cancer
- Adenomatous polyps

Colon Cancer – Risk Diet

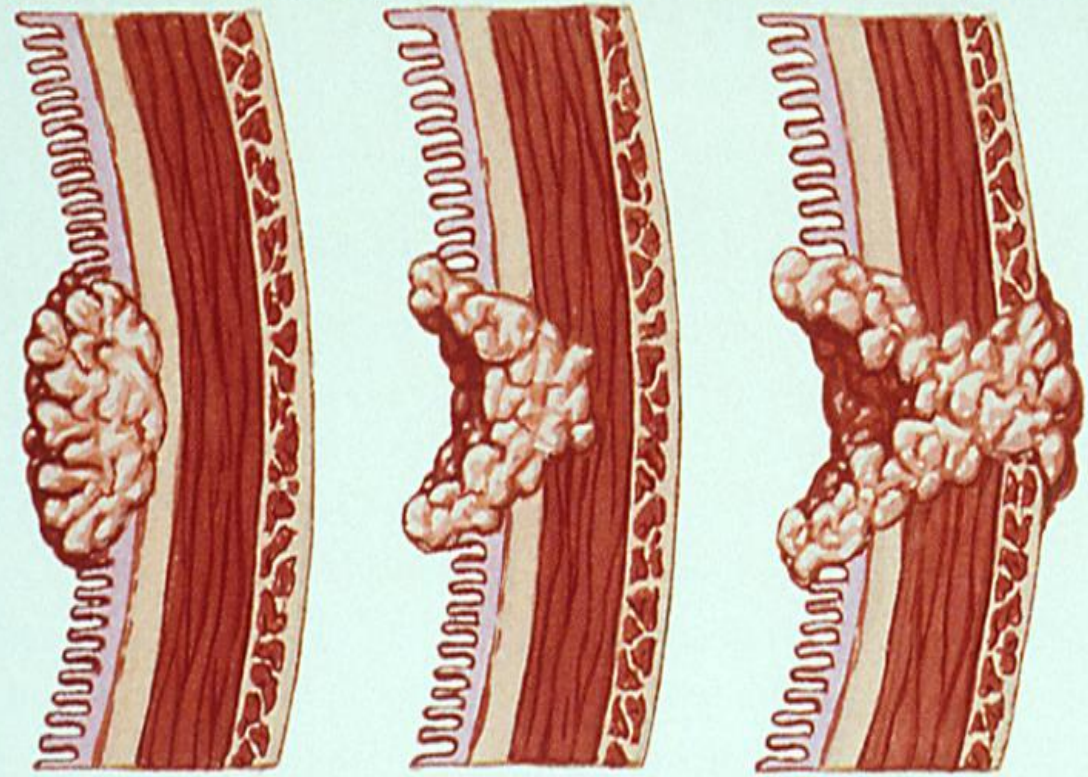
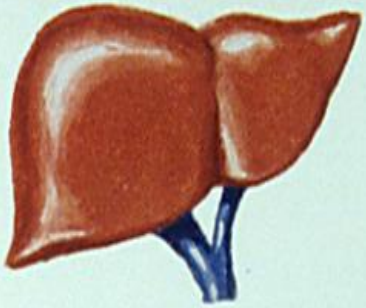
- **Adventist Health Study**

  - California, 1976-1982
- 32,051 Non-Hispanic White
- Positive association with total meat intake (p=.01)
- Positive association with red meat intake (p=.02)
- Inverse association with legume intake

Stages in colon cancer development

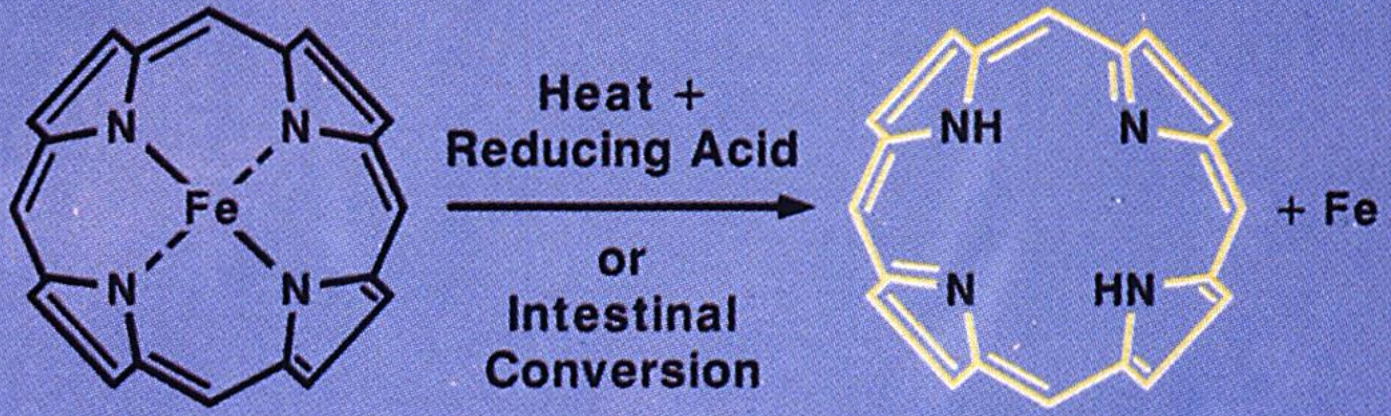


Prognostic Indicators in Colorectal Cancer

Tumor status	Node status	Systemic status
 Limited to mucosa and submucosa (T_1); Invasion into, but not beyond, muscularis propria (T_2); Penetration of full thickness of bowel wall (T_3)	 Lymph nodes normal (N_0)  Lymph node metastasis (N_1)	 No distant metastasis (M_0)  Distant metastasis (M_1)

Tumor staging assesses depth of invasion (T) into or through bowel wall, presence or absence of lymph node (N) and distant organ metastasis (M)

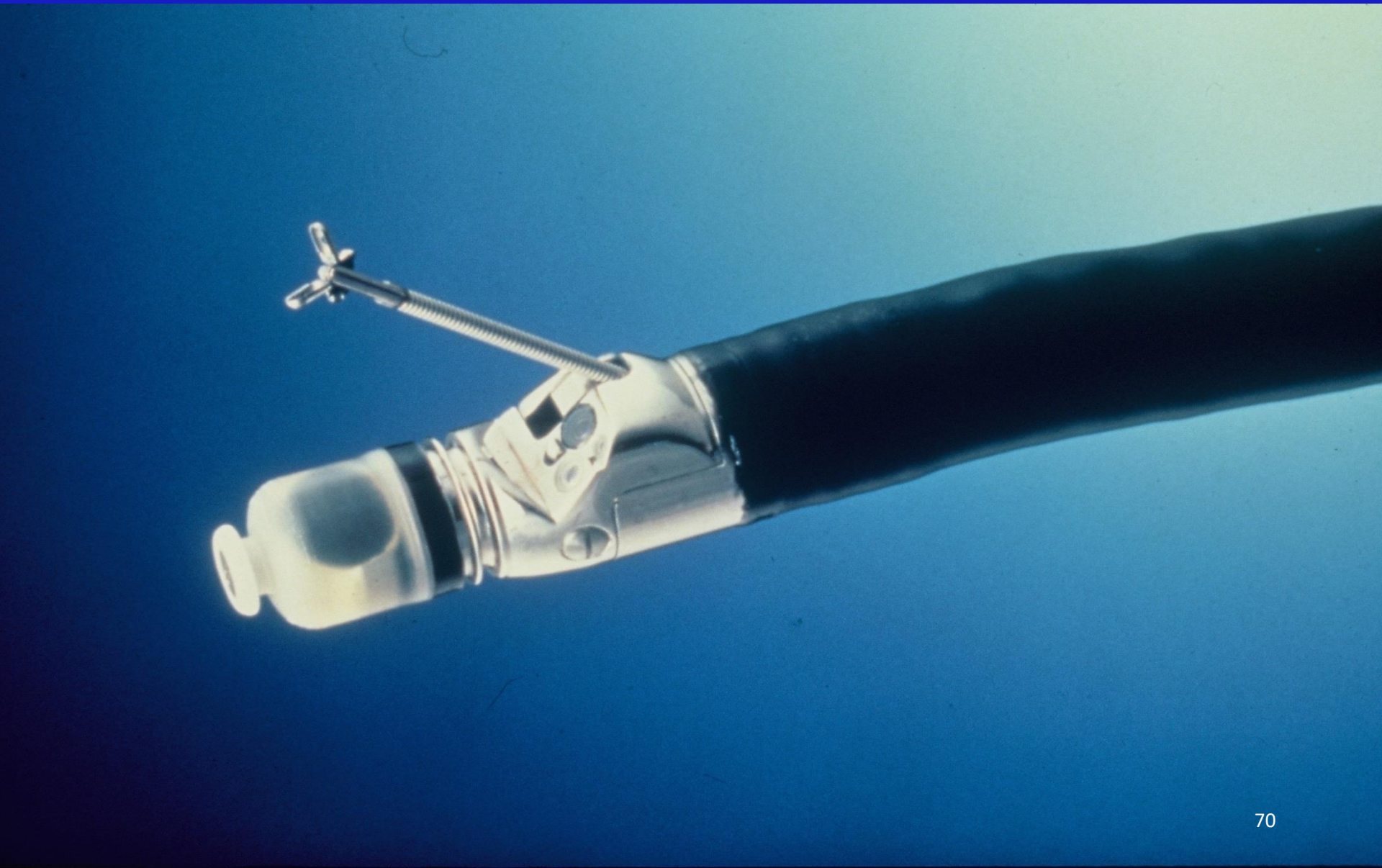
HEMOQUANT TEST



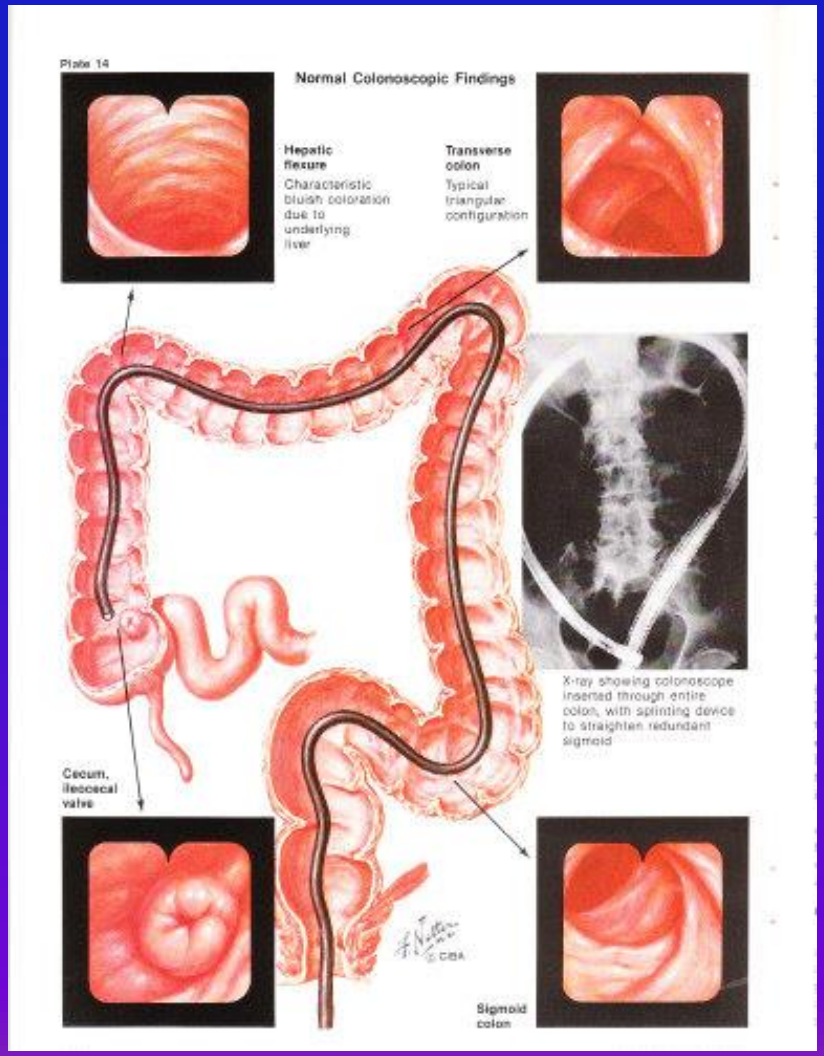
HEME
(Non-Fluorescent)

PORPHYRIN
(Fluorescent)

FIBERSCOPE

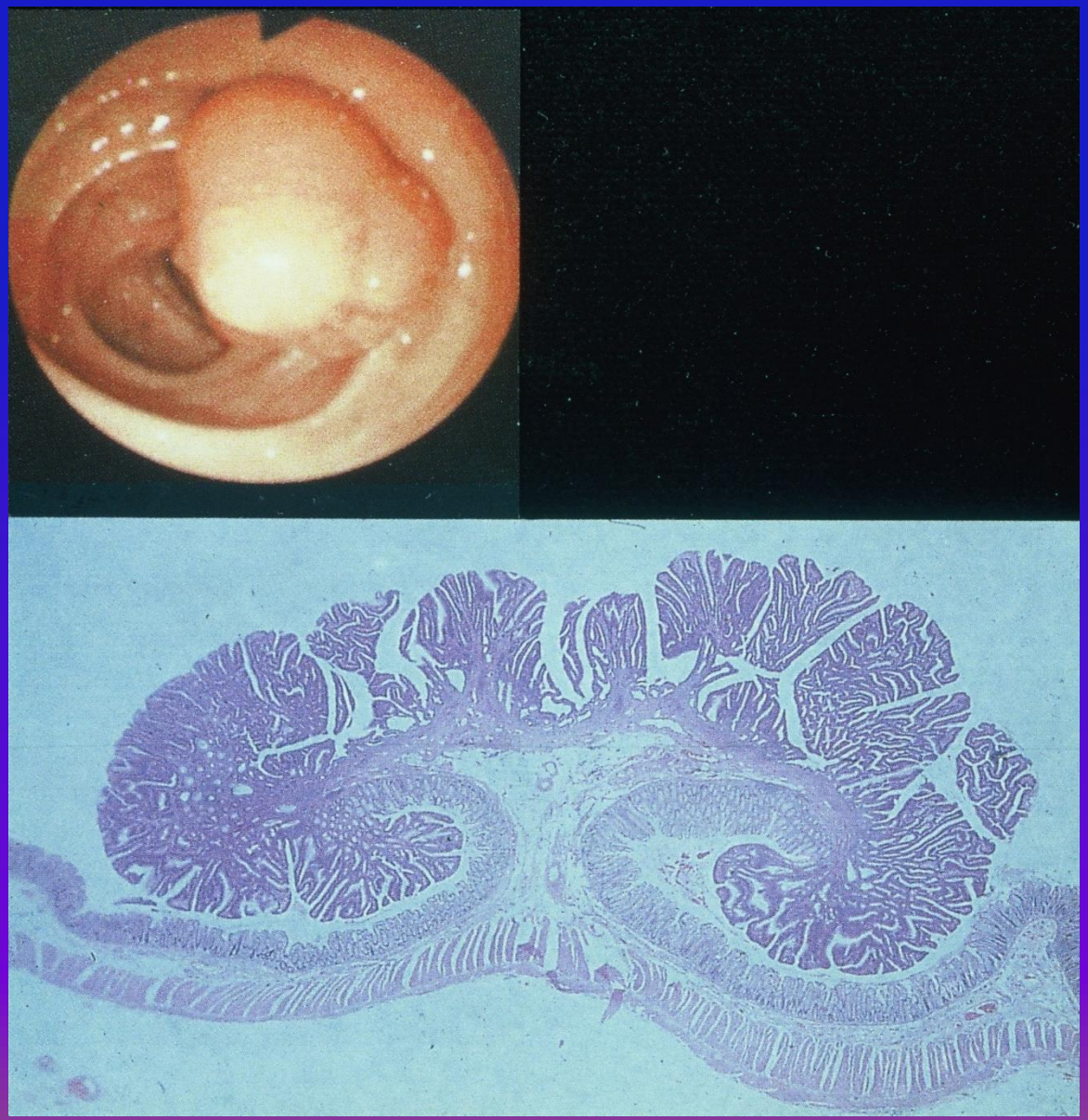


COLONOSCOPY

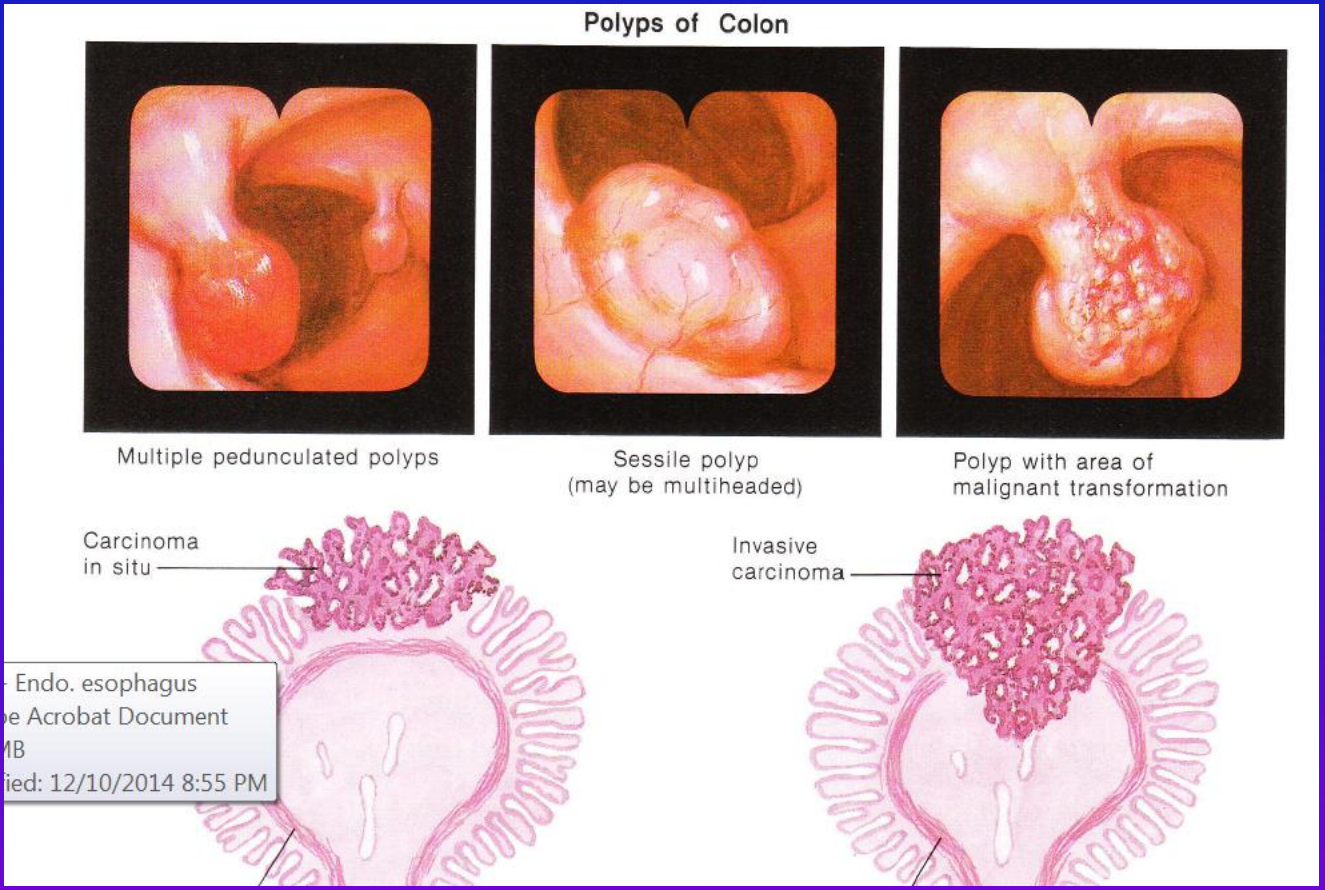


Familial Adenomatous Polyposis

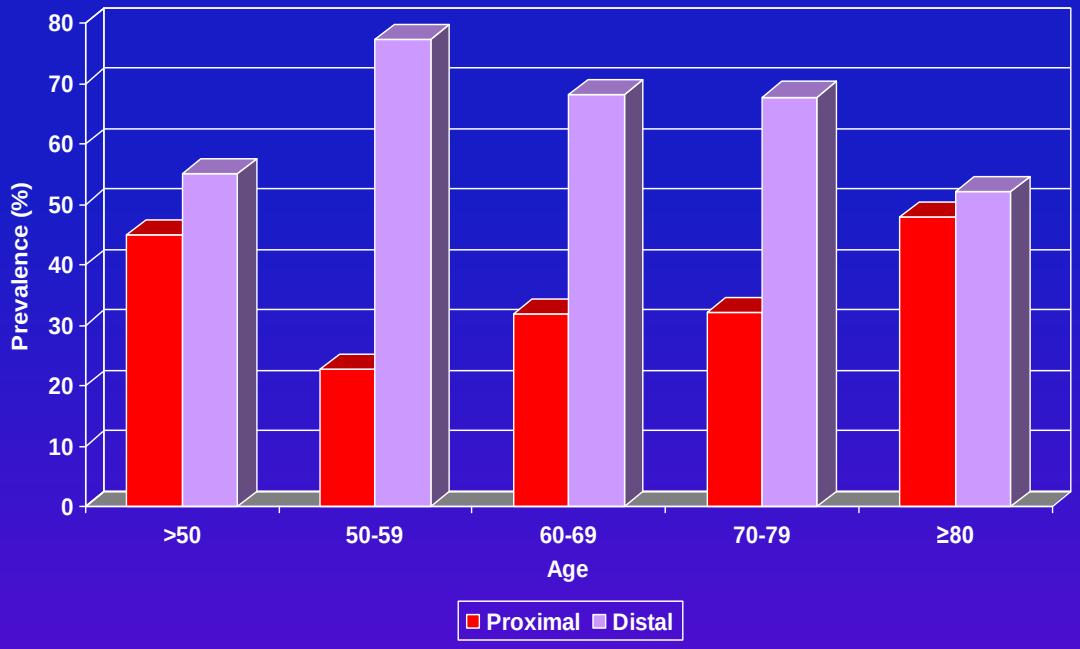
Fibroscopic and Microscopic Views of a Colon Polyp



Colonoscopy – Colon Polyps



PREVALENCE OF PROXIMAL VS. DISTAL COLON CANCER BY AGE GROUP



Mantel-Haenszel Chi-Square Test
p = 0.0481

DIAGNOSIS OF PROSTATE CANCER

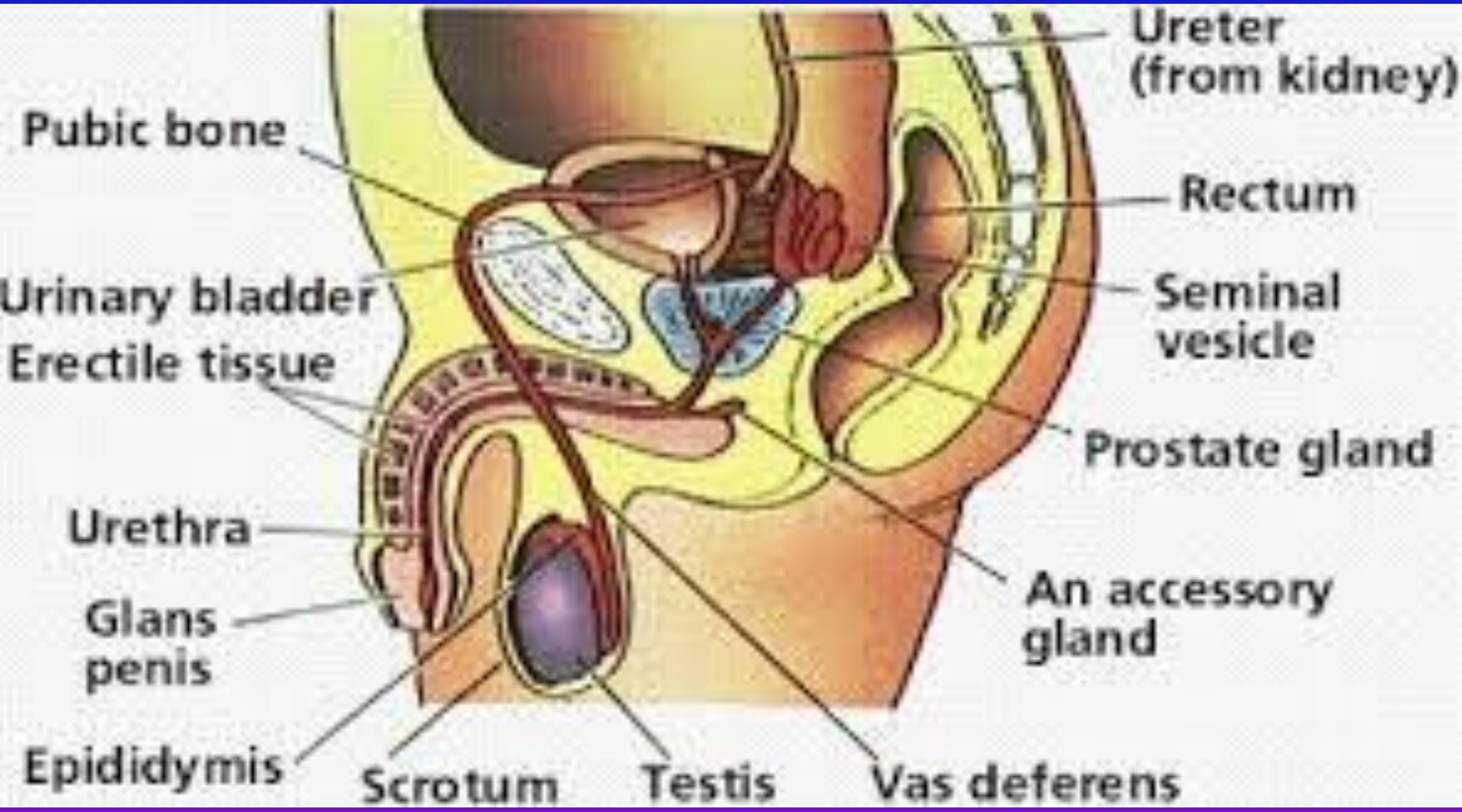
PROSTATE CANCER

- Data from 59 countries
- Mortality **inversely associated** with
  - consumption of cereals (p=.001)
  - nuts and oilseeds (p=.003)
  - fish (p=.001)
- Protective effect of soy products (p=.0001)

PROSTATE CANCER - Burden of Suffering

- 2017 – 161,000 new cases in U.S.
- 2017 - 27,000 deaths in U.S.
- Risk increases with age after 50 yrs.
- Risk is higher in African American men.
- Lifetime risk in U.S. men = ~10% - High morbidity
- 10-yr. survival: confined = 75%
  regional = 55%
  distant = 15%
-

MALE GENITAL APPARATUS

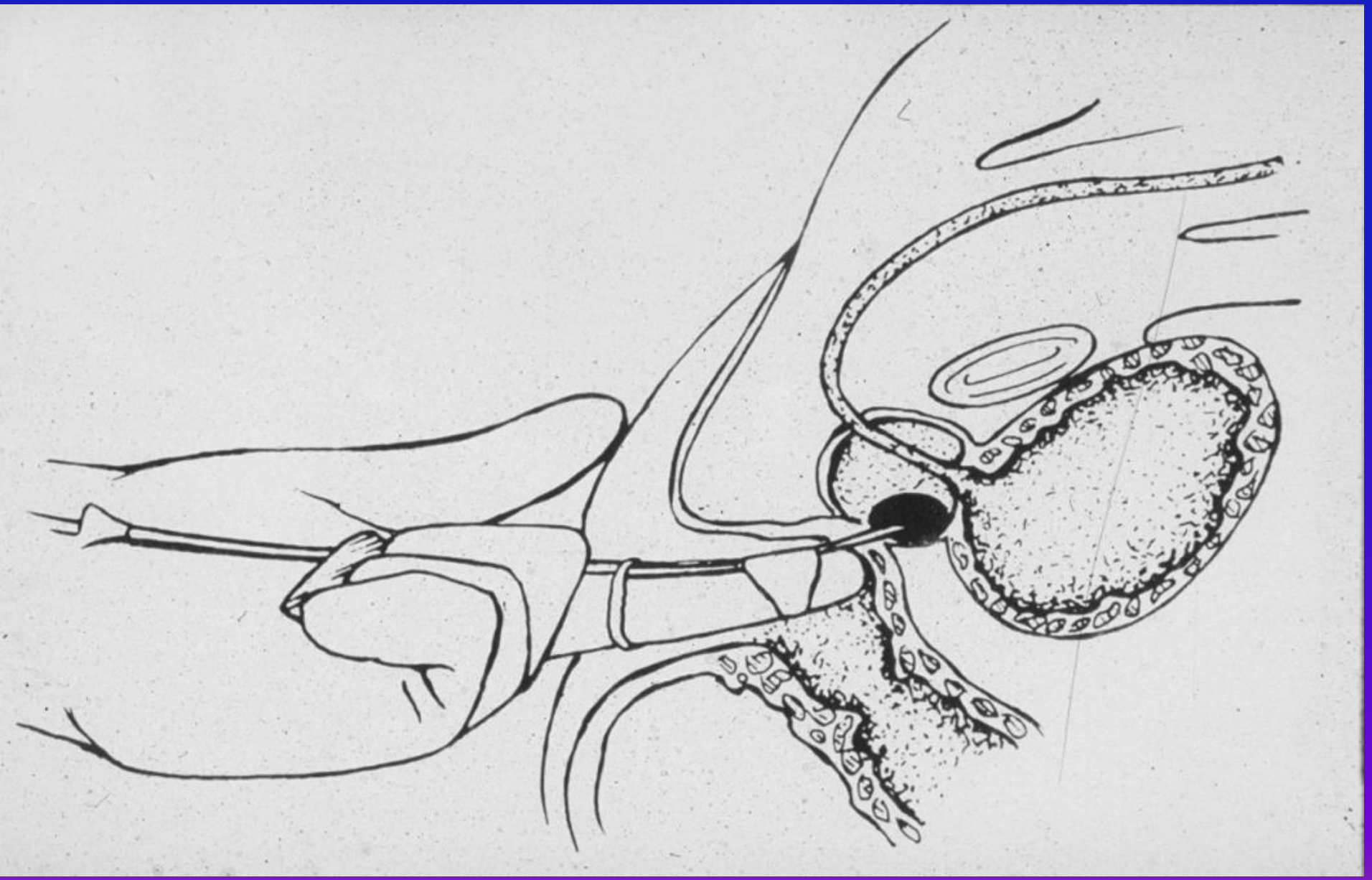


Pretreatment PSA as Staging – Prognosis Marker to Dictate Treatment

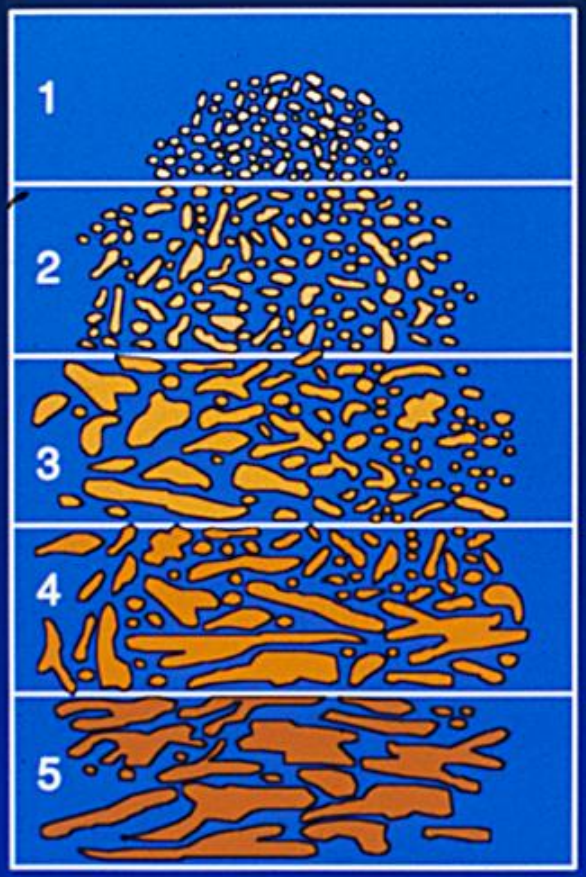
PSA Value	Comment
≤ 4.0 ("Normal")	High probability of localized disease
4-1 - 10.0	Very low risk of metastases (limited radiographic staging needed)
> 10.0 - 20.0	Low risk of metastases
> 20.0	Risk of metastases

PROSTATE SPECIFIC ANTIGEN (PSA)

- Produced by benign and malignant prostate epithelium
- Screening value
- Sensitivity = 73%
- Specificity = 91%
- Lead time = 5.5 yrs.



Gleason Grading of Prostate Cancer



	Primary & secondary pattern summed for Gleason score sum	
Well differentiated	1+1=2 2+1=3 2+2=4	"Good"
Moderately differentiated	3+2=5 3+3=6	"Intermediate"
Moderately-poorly differentiated	3+4=7 4+3=7	"Intermediate"/ "Bad"
Poorly differentiated	4+4=8 5+4=9 5+5=10	"Bad"

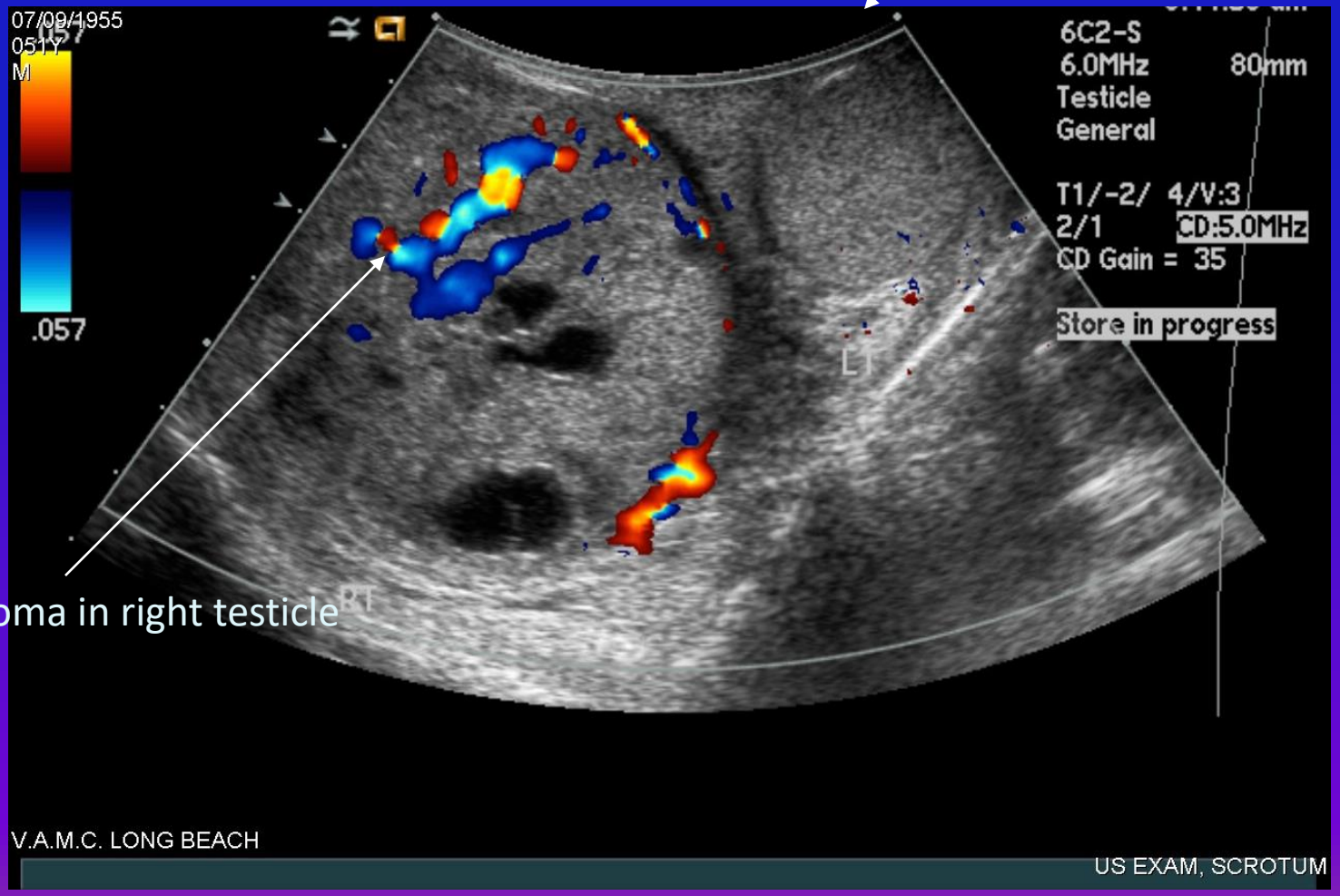
PROSTATE CANCER
Occult Lymphnode Metastases *vs.* Tumor Stage and Grade

Clinical Stage (Localized Dis.)	**Tumor Grade** (Gleason) Well (2-4) %	Intermediate (5-7) %	Poor (8-10) %
T1, N0, M0	5	23	50
T2, N0, M0	5-28	20-27	27-38
T3, N0, M0	18	42	68

DIAGNOSIS of TESTICULAR CANCER

Ultrasound of the Scrotum: Right Testicle Cancer

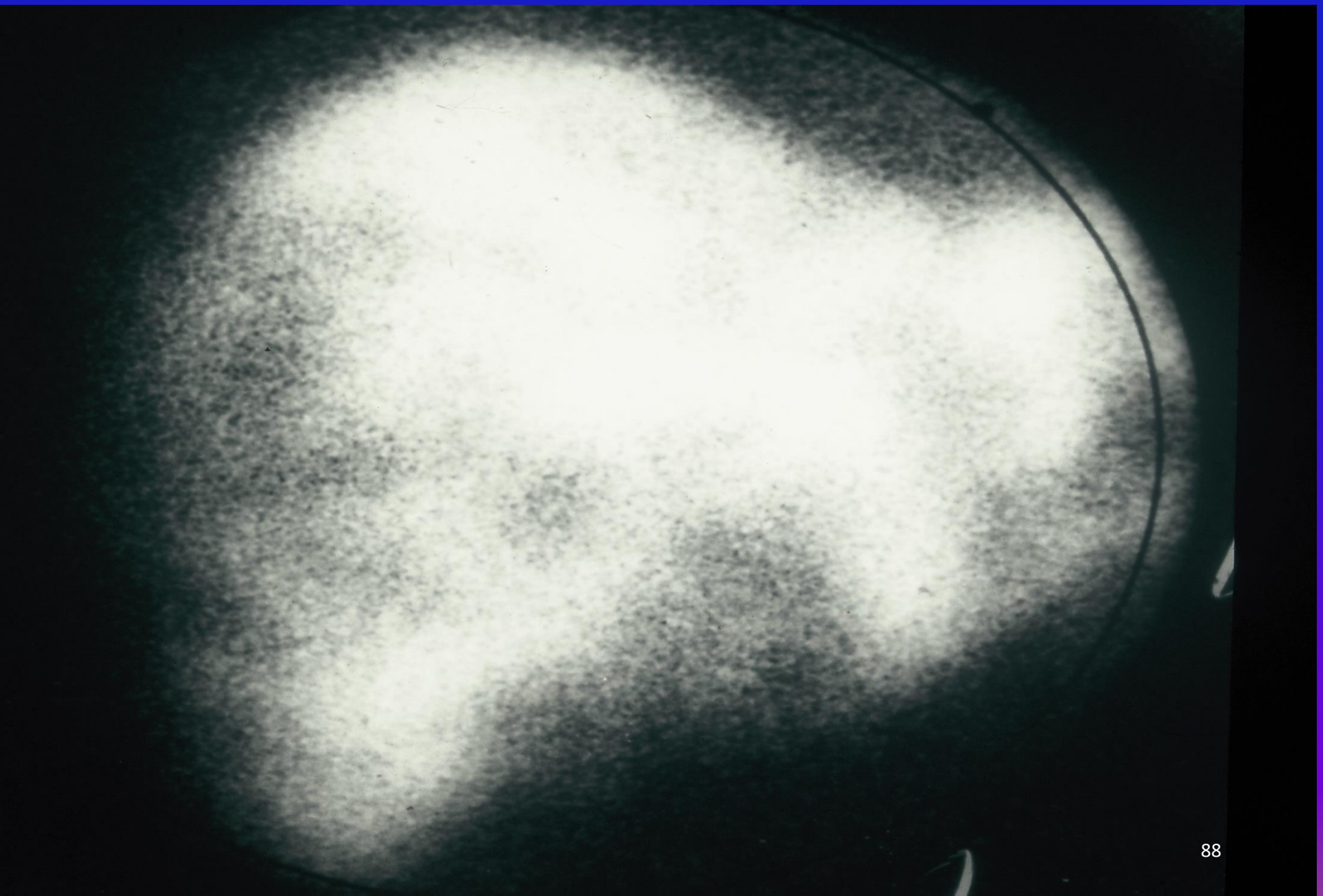
Normal left testicle



Seminoma in right testicle

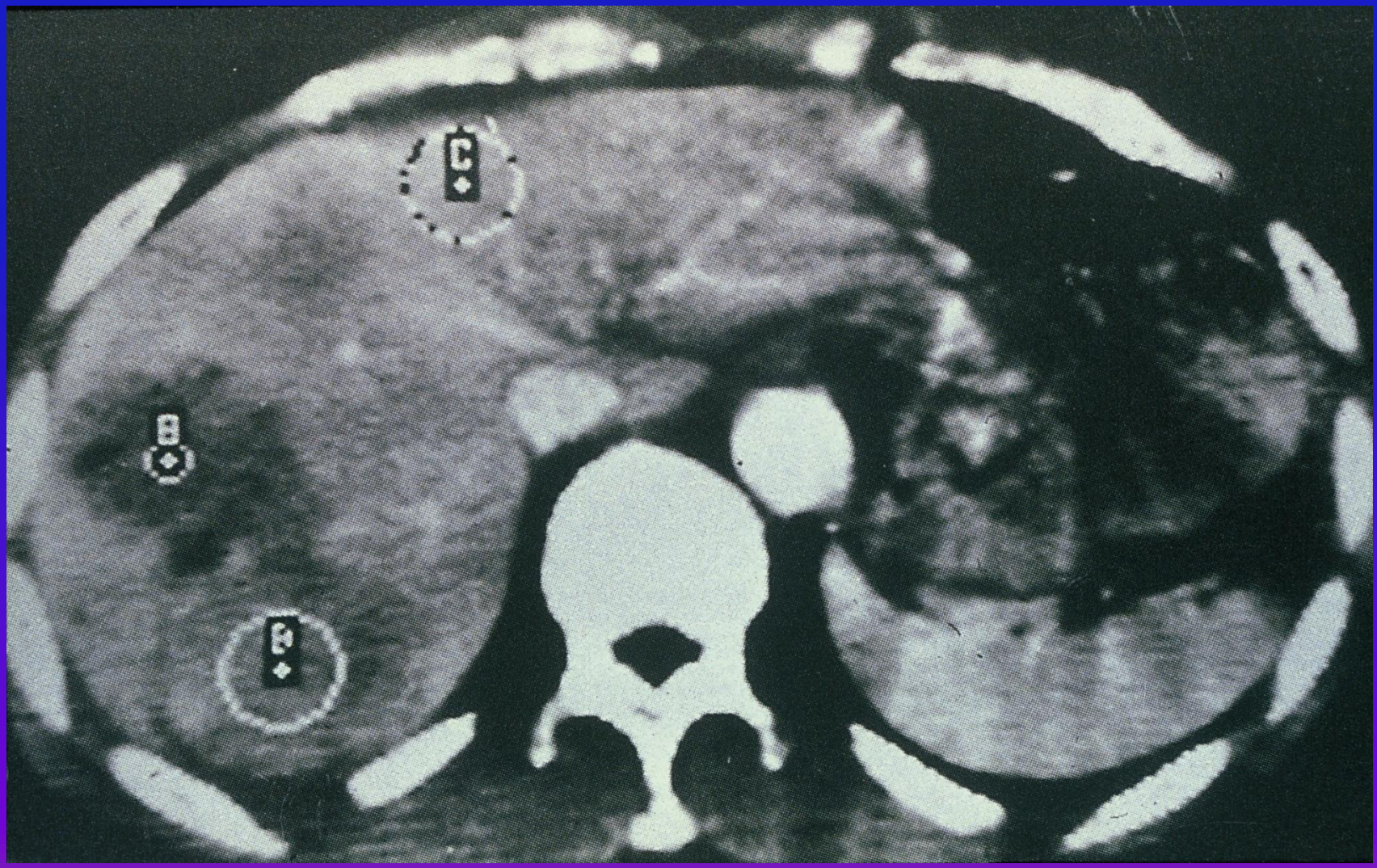
LIVER, SPLEEN, and ABDOMEN

LIVER SCAN SHOWING DEFECTS

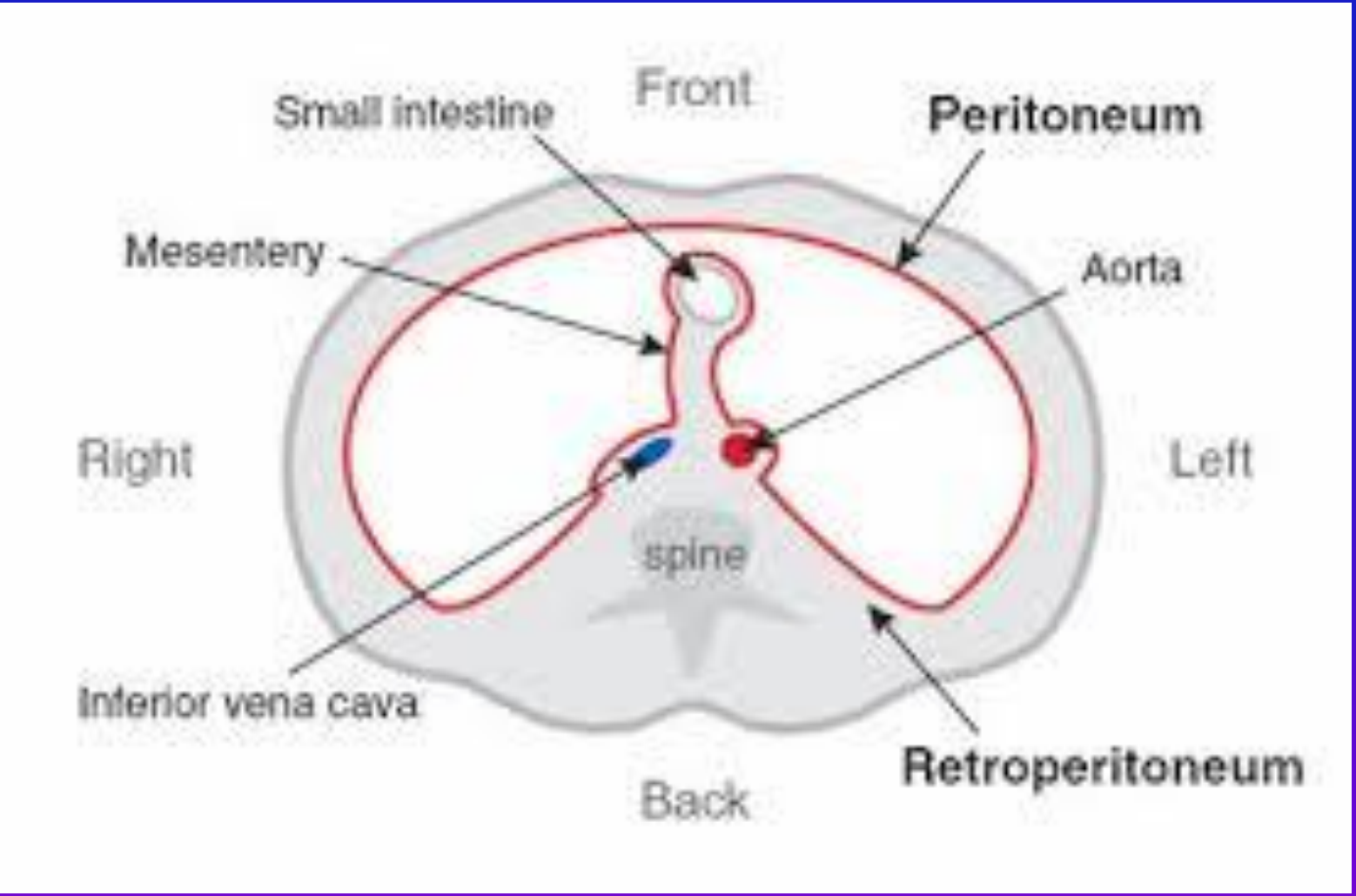


Metastatic Cancer in the Liver

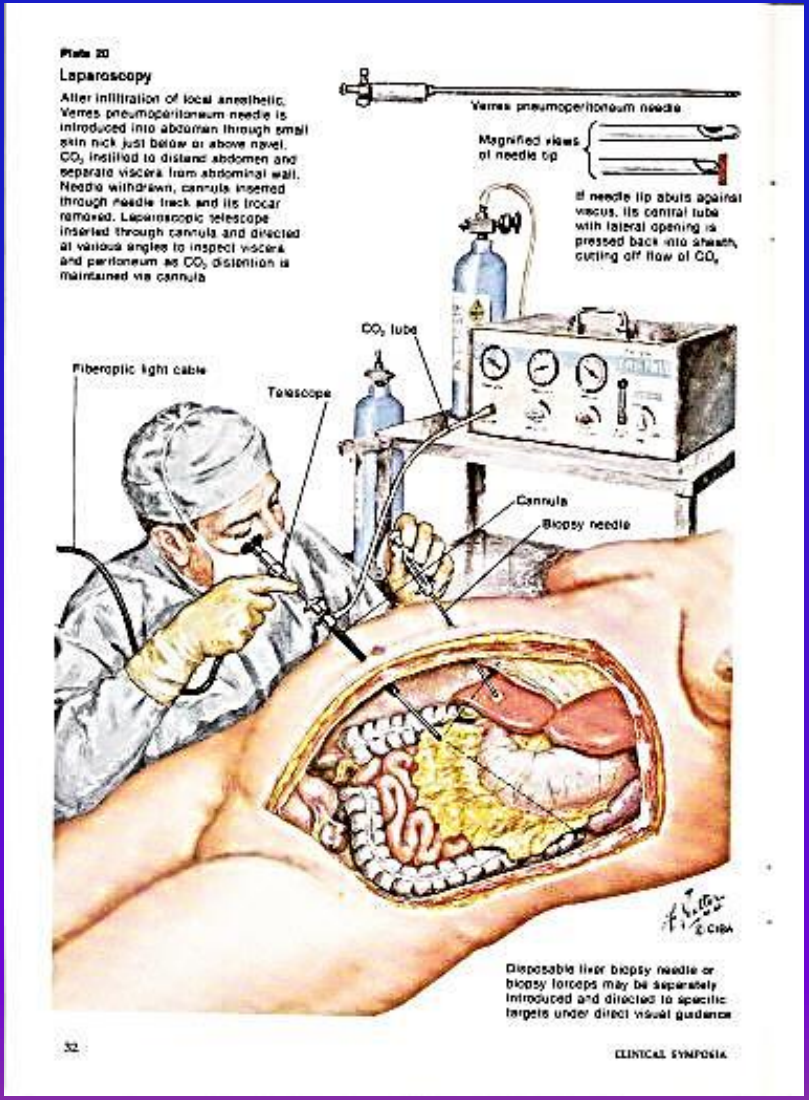
CT Scan - Metastatic cancer to the liver



PERITONEUM - SCHEMA



LAPARASCOPY (Looking into the Abdominal Space)



END OF LECTURE #3