

LECTURE #5

BMI FORMULA

USA **BMI=** $703 \times \frac{\text{weight (lb)}}{\text{height}^2 (\text{in}^2)}$

METRIC **BMI=** $\frac{\text{weight (kg)}}{\text{height}^2 (\text{m}^2)}$

OBESITY

Body Mass Index (BMI)

$$\text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 \text{ (m)}}$$

<u>BMI</u>	<u>NIH Classification</u>
<18.5	Underweight
18.5-24.9	Normal Weight
25-29.9	Overweight
30-34.9	Obesity I
35-39.9	Obesity II
>40	Extreme Obesity

OBESITY AND CANCER

NEW FINDINGS

- ~30% of adults are obese (**BMI > 30**)
- ~35% of adults are overweight (BMI 25 - 30)

- Women: Uterine cancer 6-fold
Kidney cancer 5-fold

- Men: Liver cancer 6-fold
Colorectal cancer ~1.75-fold

Cancer Death Rates of Obese Compared to that of Individuals with Normal Body Weight (BMI < 25)



CANCER TREATMENT

Is cancer

a curable disease?

Cancer is no longer **the most lethal** of chronic diseases

Cancer is now the **most chronic** of lethal diseases

CHEMOTHERAPY OF ADVANCED CANCER

CURABLE

Choriocarcinoma

A.L.L. in Children

Hodgkin's Disease

Histiocytic Lymphoma

Mixed Lymphoma

Burkitt's Lymphoma

A.M.L.

Testicular Cancer

Ovarian Carcinoma

Wilms' Tumor

Embryonal Rhabdomyosarcoma

Ewing's Sarcoma

CHEMOTHERAPY OF ADVANCED CANCER

IMPROVED SURVIVAL

Breast Carcinoma

C.M.L.

P. Vera

C.L.L.

Lymphocytic Lymphoma

Multiple Myeloma

Small Cell Lung Ca

Prostatic Carcinoma

Soft Tissue Sarcomas

CONTINUUM OF CANCER CARE

PREVENTION

SCREENING

DIAGNOSIS

STAGING

TREATMENT

REHABILITATION

FOLLOW-UP

CANCER TREATMENT PRINCIPLES

Localized – Adjuvant ChemoRx. + Surgery +/- RT

Regional (N+) – Surgery + Adjuvant RT + CT +/-
ImmunoRx.

Metastatic (spread +) – ChemoRx, Biologicals,
Immunotherapy +/- **Surgery for “debulking”** +
ChemoRx. +/- Radiation

Cancer Prognosis and Survival

Patient's general condition, co-morbidities

Performance status

Psychological index

Tumor histology, grade of aggressiveness

Tumor stage (T, N, and M)

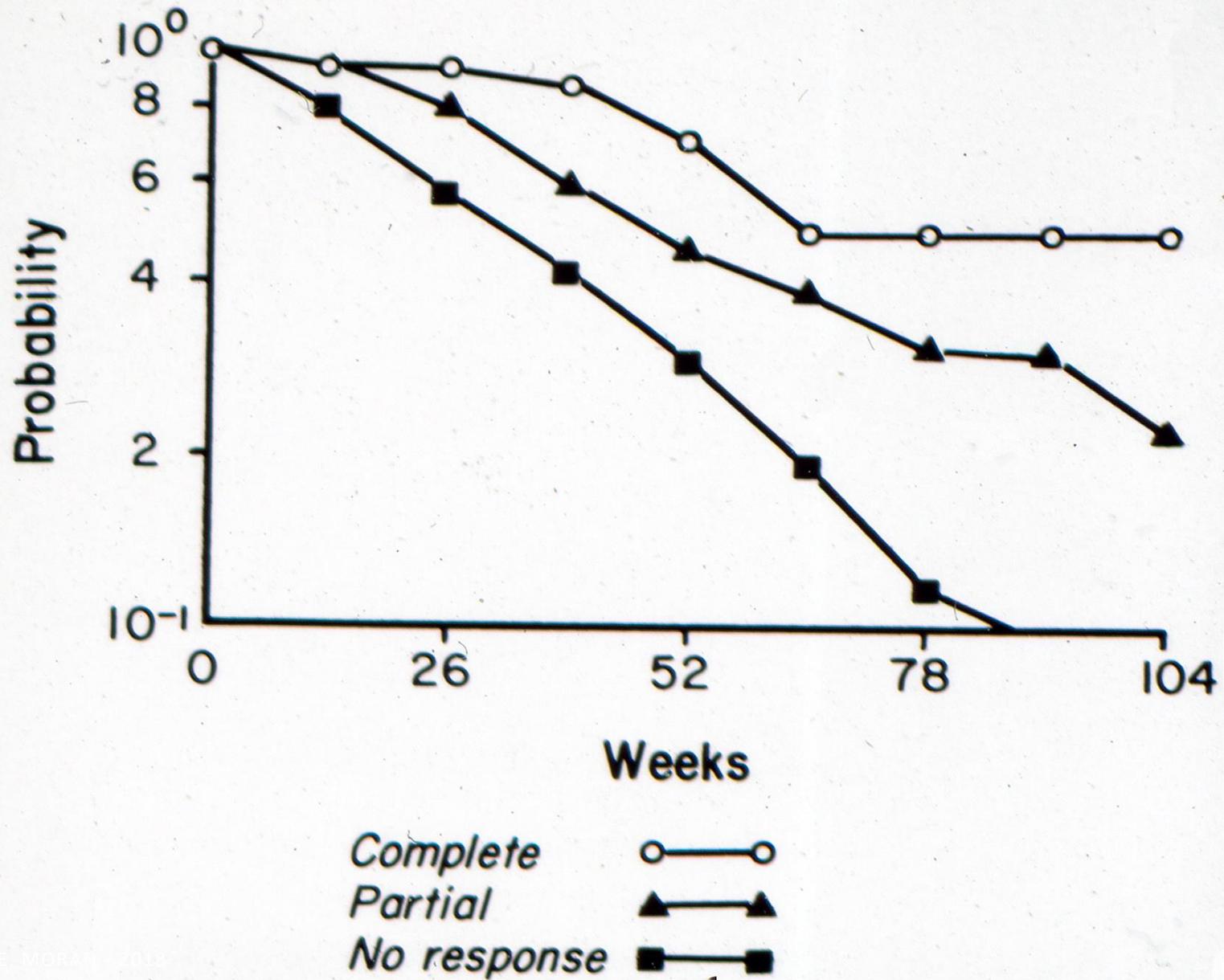
Treatment modality available

Responsiveness to treatment

Cancer is **no longer the most lethal** of chronic diseases.

Cancer is now **the most chronic** of lethal diseases.

RESPONSE



SURGERY

What should we know?

- Disease control - rates?
- Side effects?
- Indicated for the particular patient?
- Quality of life?

Radical prostatectomy with removal of seminal vesicles

- Retropubic prostatectomy
- Perineal prostatectomy
- Laparoscopic/robotic prostatectomy

(Nerve-sparing technique and Pelvic lymph node sampling are necessary)

NEW SURGICAL TREATMENTS

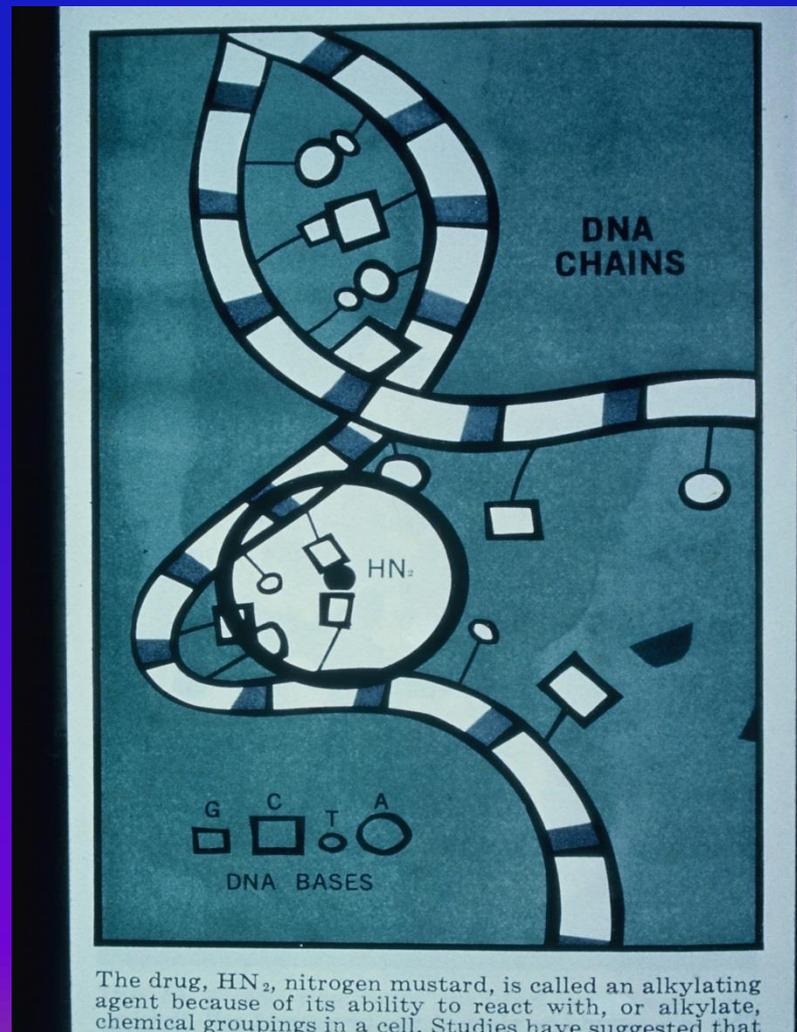
Debulking the tumor mass

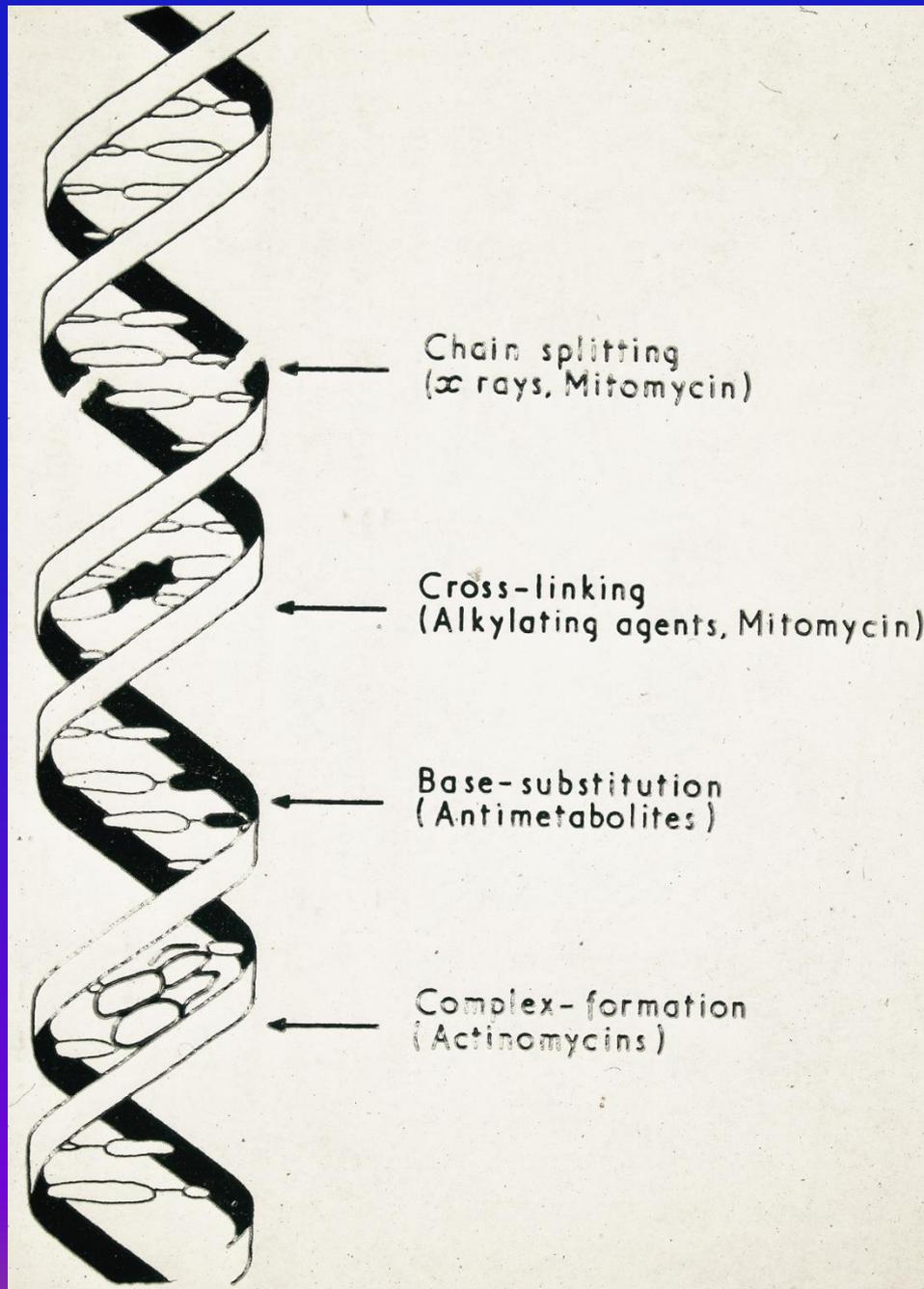
Removal of the primary tumor in presence of
metastases

Removal of metastases in liver, lungs, brain

CANCER CHEMOTHERAPY

FIRST FINDINGS





Principles of Combination Chemotherapy

1. Each drug should be active when used alone against the tumor.
2. The drugs should have different mechanisms of action.
3. The toxic effects of the drugs should not overlap, so that each can be administered at or near its maximum tolerated dose.

ADJUVANT CHEMOTHERAPY

ADJUVANT CHEMOTHERAPY

EFFECTIVENESS

Breast Cancer	- CMF - TMX (?)
Head and Neck	- preop + RT
Bone & Soft Tissue Sarcomas	- preop + RT
Small Cell Lung	- postop
Colon	- postop
Brain	- postop

CELL-MEDIATED IMMUNITY

T-lymphocytes identify aggressors and try to destroy them through the production of **lymphokines** (synthesized proteins)

- Killer T-cells
- Helper T-cells
- Suppressor cells

HUMORAL IMMUNITY

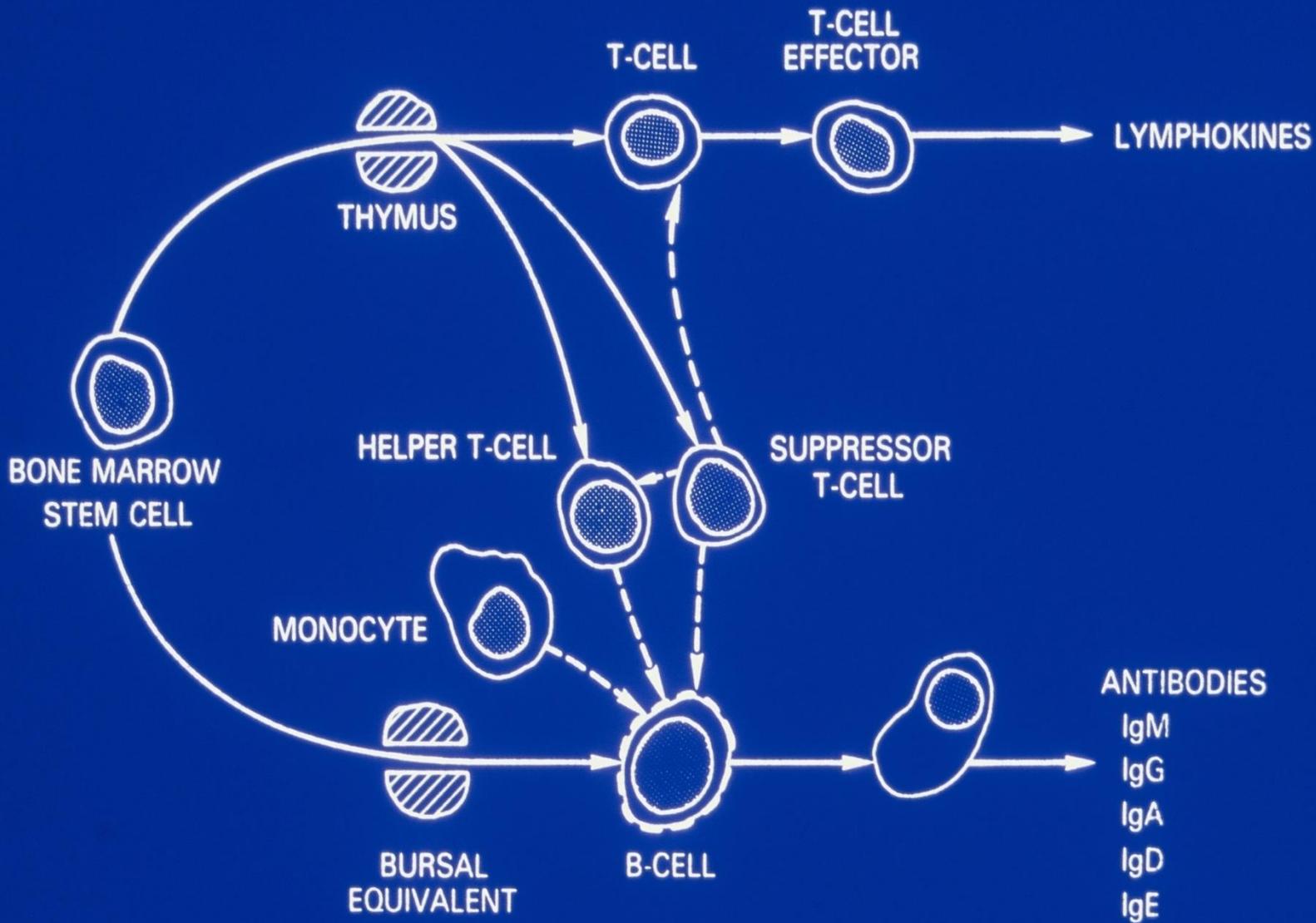
B-lymphocytes synthesize immunoglobulins which function as **antibodies** combining with foreign **antigens** (bacteria and viruses):

IgG – major immunoglobulin (80%)

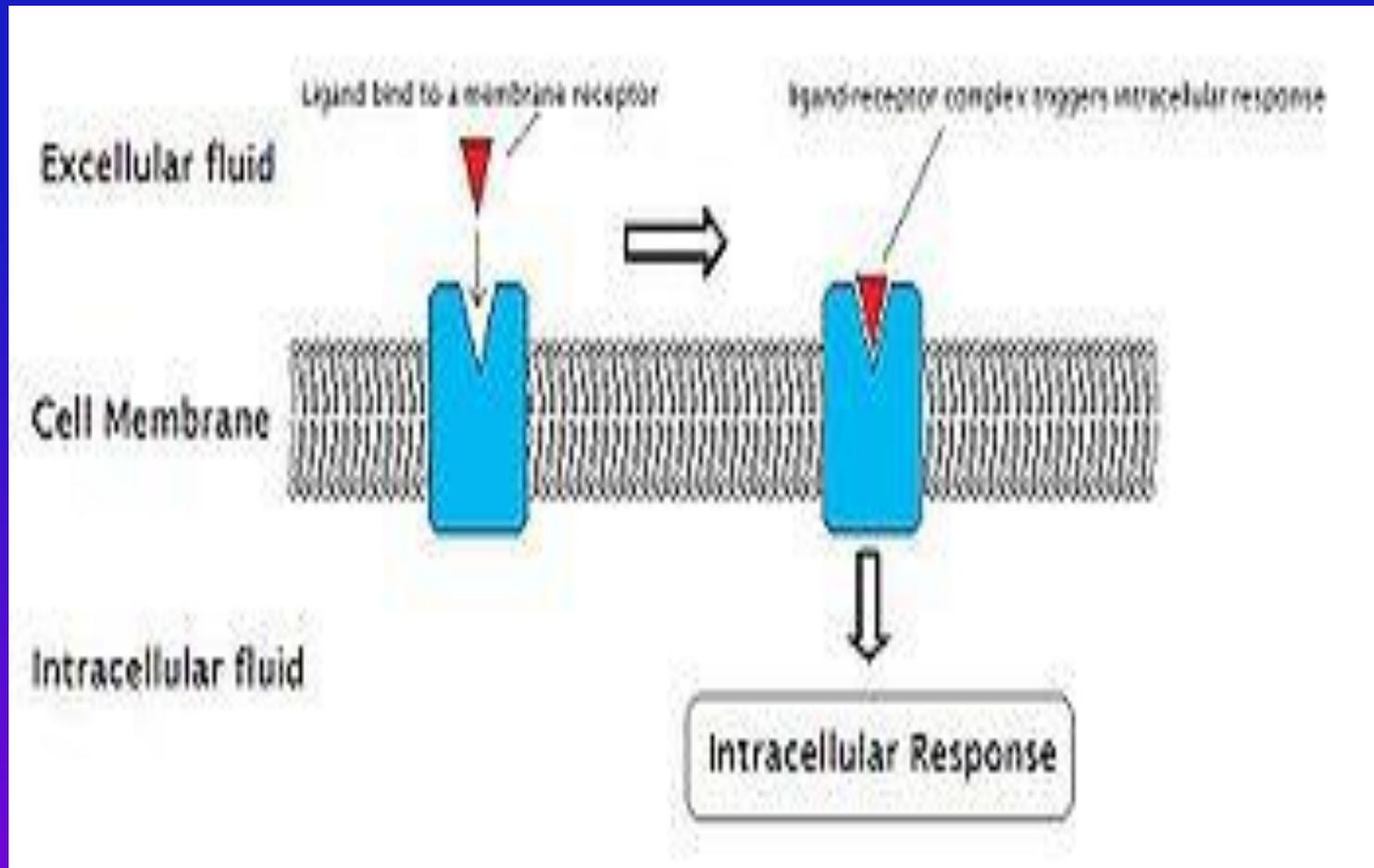
IgM – mostly intravascular

IgA – in body secretions, GI and respiratory tract

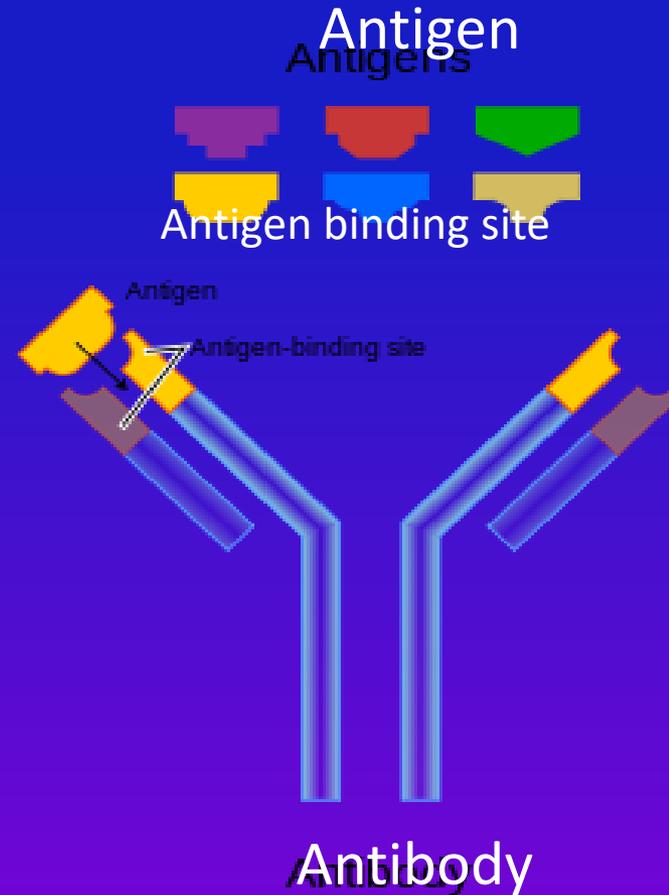
IgE – active in hypersensitivity (allergy)



CELL MEMBRANE RECEPTORS



Immunoglobulin Molecule, Antigen, and Antibody



IMMUNOTHERAPY OF CANCER (1)

Active immunotherapy:

Non-specific: BCG

Levamisole

Interferon

Interleukin 2

Specific: Tumor antigen vaccines

Immunotherapy of Cancer (2)

Passive immunotherapy

Antibodies: Monoclonal or Polyclonal Antibodies

Conjugated with toxins

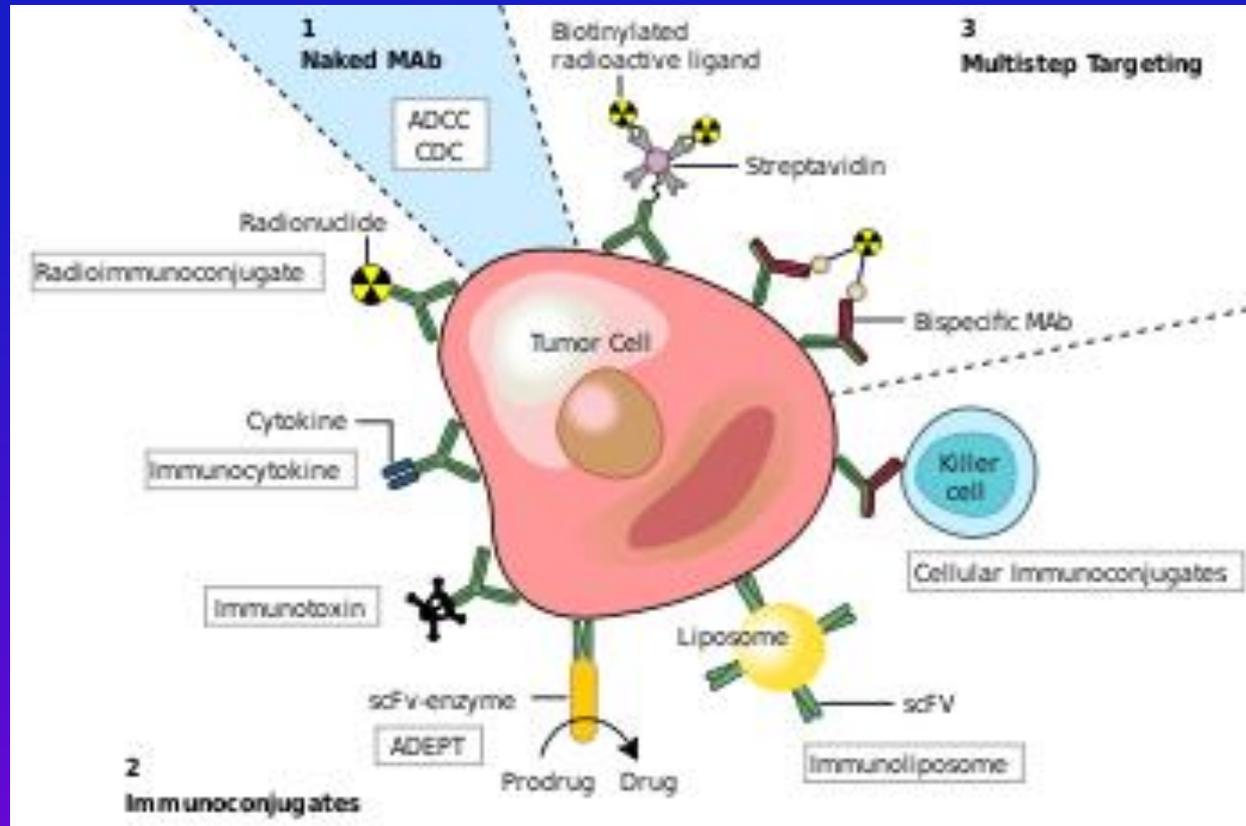
Radiolabeled

Cells: Tumor-infiltrating lymphocytes

Response to Cancer Immunotherapy

	<u>%</u>
Urinary bladder	60-70
Kidney cancer	15-20
Malignant melanoma	10-15
Cutaneous T-cell lymphoma	80
Lymphoma	40-50
Multiple myeloma	50

Monoclonal Antibodies to Cancer Cell



Development of a Malignant Tumor

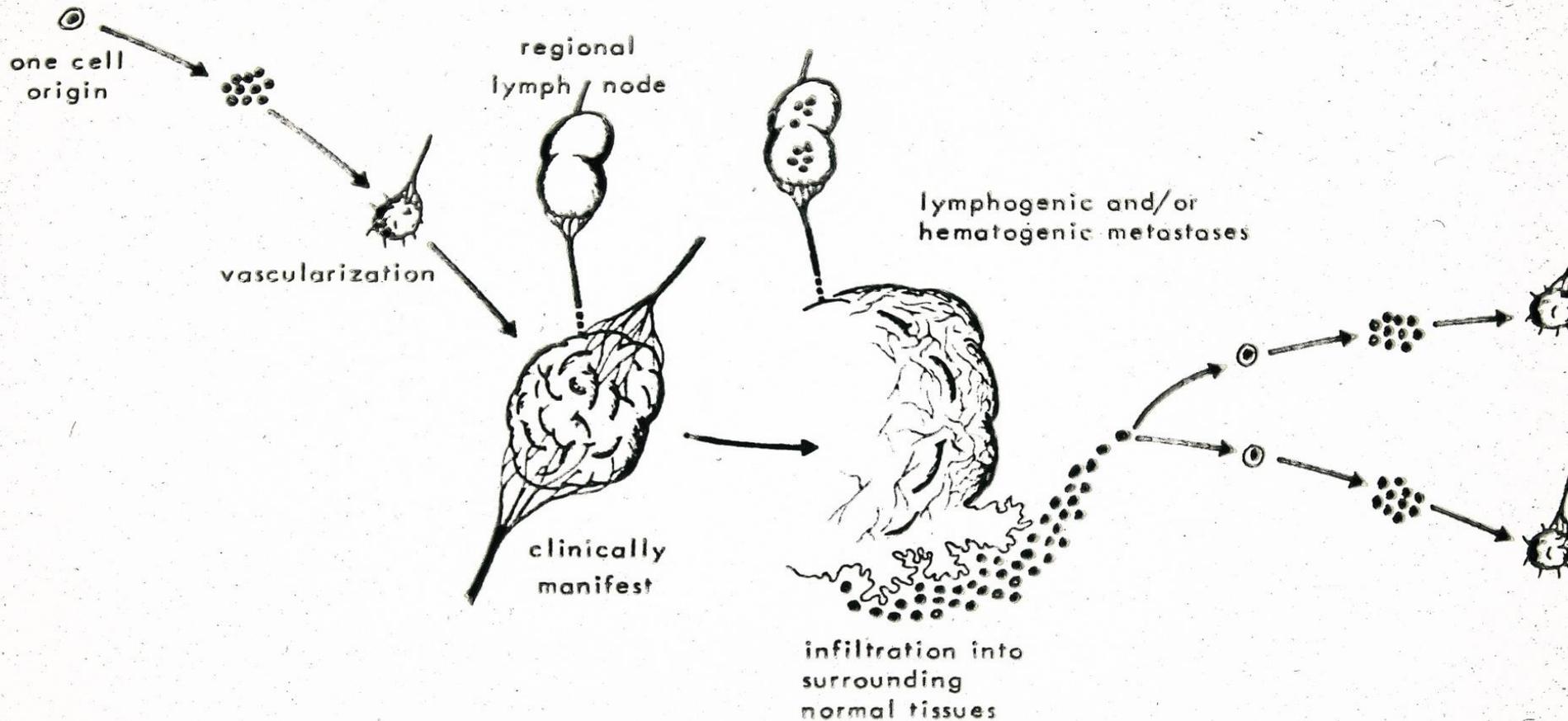
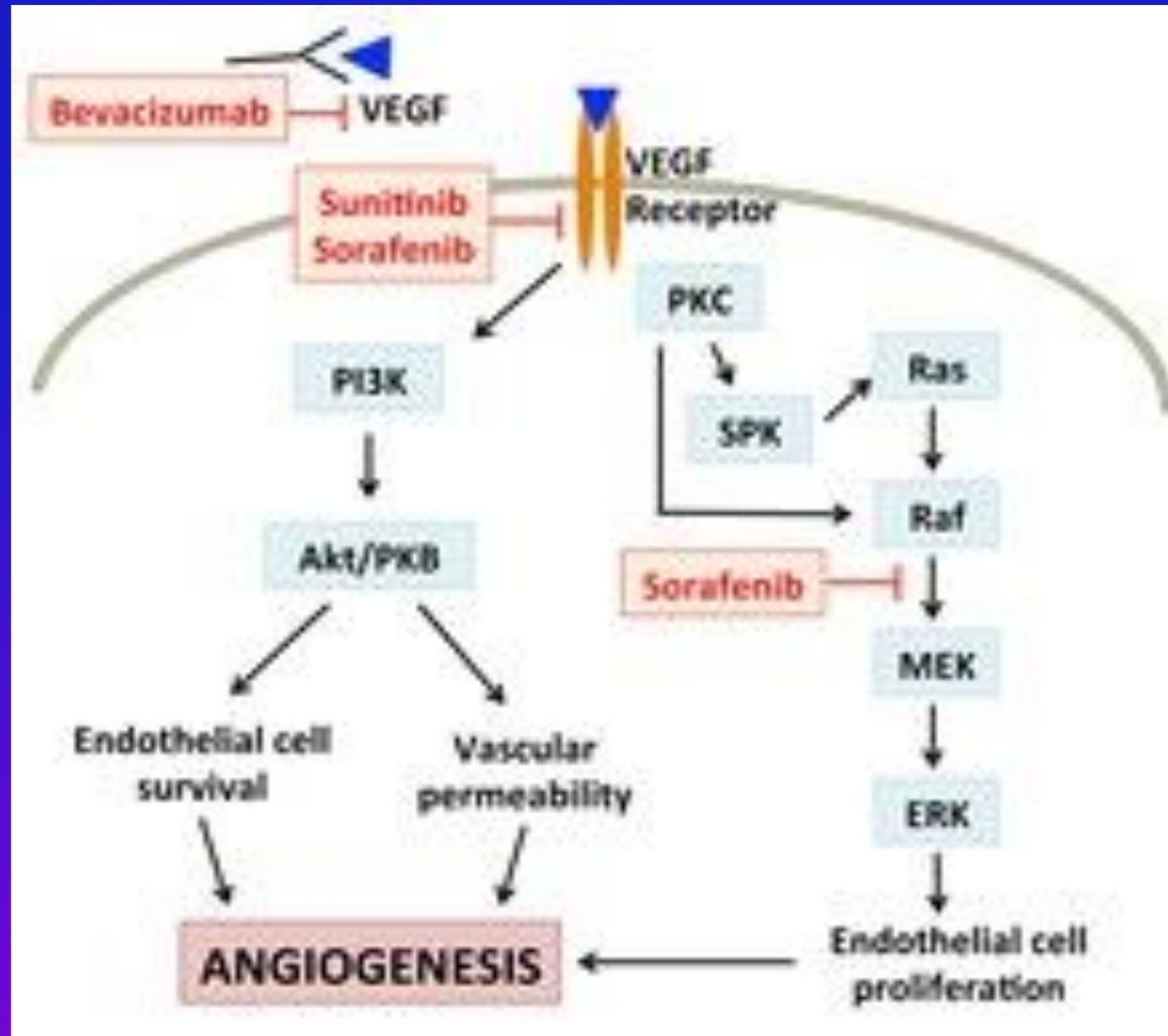


Figure 1. Development of a tumor.

Anti-angiogenesis



TREATMENT OF FEMALE BREAST CANCER

BREAST CANCER - Risk Factors (1)

- Previous breast cancer, atypical hyperplasia.
- Family history: 1st degree relative \Rightarrow 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 treatment
- Obesity, high-fat diet

BREAST CANCER - Early Detection

- 2-view mammography \pm Clinical Breast Examination
→ **Mortality \downarrow 20-30% in 50-69 y.o. women**
- In women 40-49 y.o. = no significant benefit (?)
- Yearly CBE only vs. no screening = no data.

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

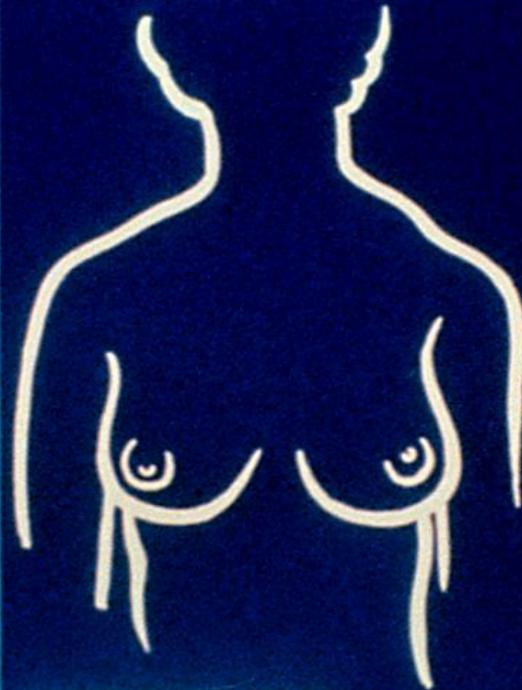
AXILLARY MASS
ARM SWELLING
BONE PAIN



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**

TREATMENT OF BREAST CANCER

Surgery

Radiation therapy

Hormonal therapy (anti-estrogens):

Tamoxifen

Aromatase inhibitors

Biologicals:

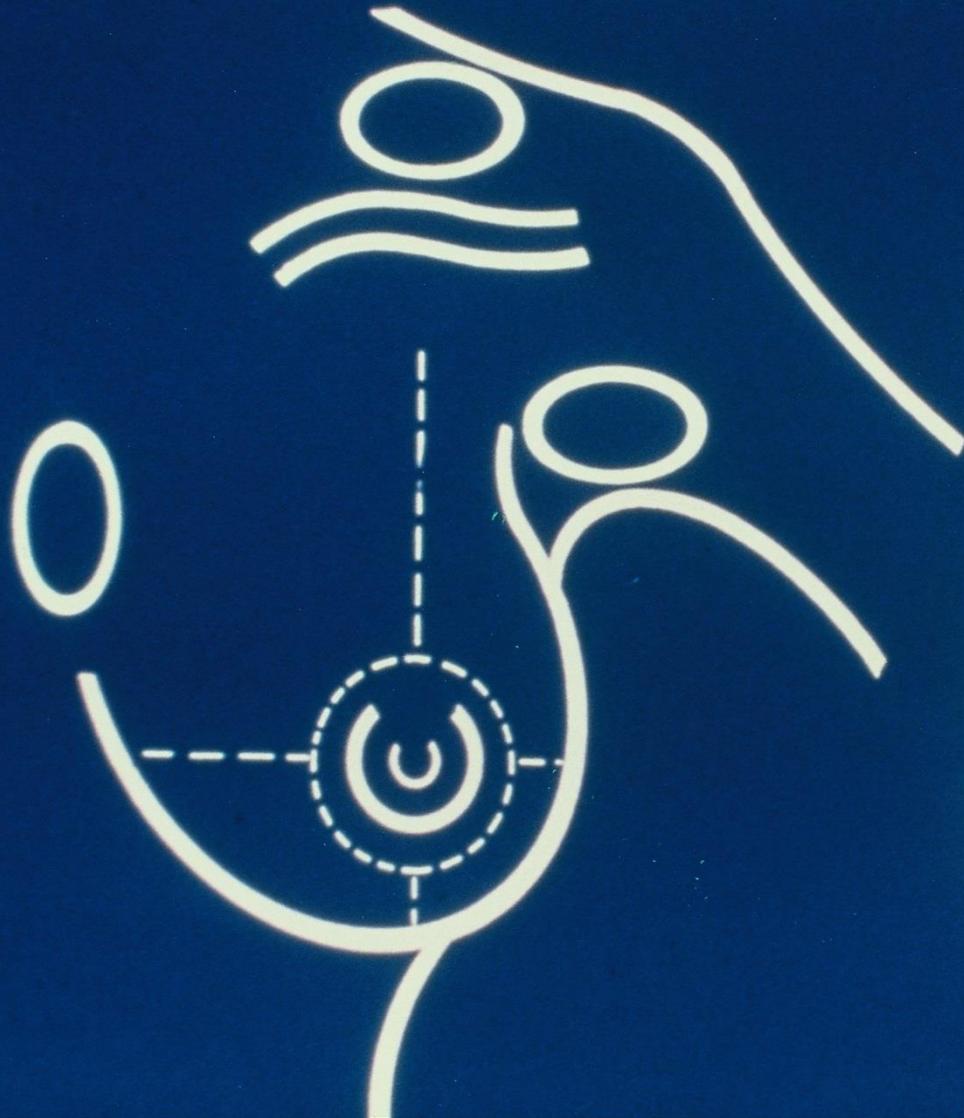
Monoclonal antibodies

Tyrosine kinase inhibitors

Chemotherapy

BREAST CANCER

REGIONAL SPREAD



LYMPHATIC
AXILLARY
SUPRACLAVICULAR
INTERNAL MAMMARY
SKIN
SUBCUTANEOUS TISSUES
NIPPLE
CHEST WALL

Surgery of the Breast

Halsted, 1894 – Radical mastectomy (removal of breast, pectoral muscles, lymph nodes)

Handley, 1954 – Int. mammary lymph nodes involvement

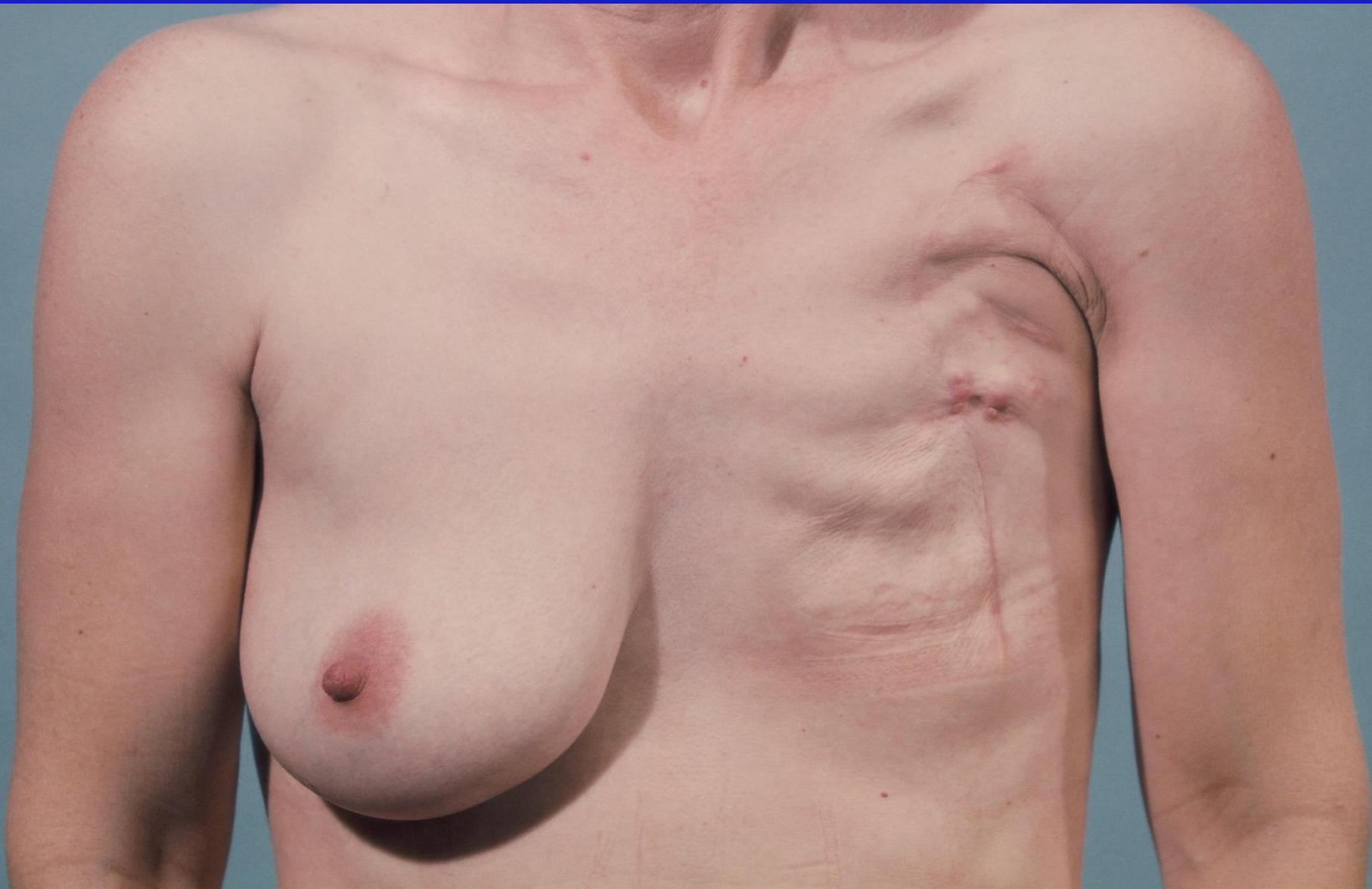
Urban, 1964 – Extended radical mastectomy

Modified radical mastectomy – Preservation of pectoral muscles

Simple mastectomy – Removal of breast and axil. LN's

“Lumpectomy”, sentinel LN's + Radiation

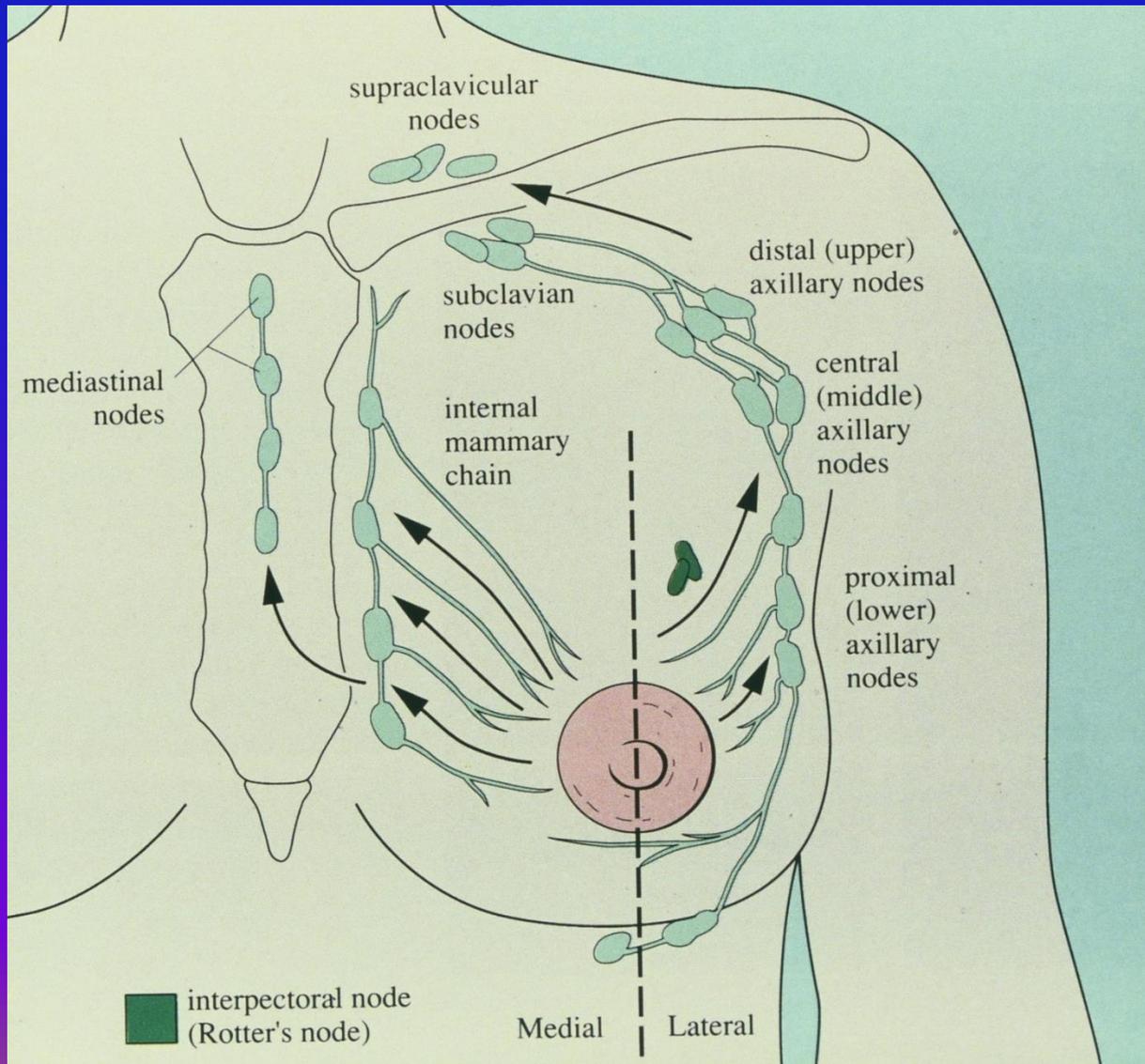
State after Left Total Mastectomy



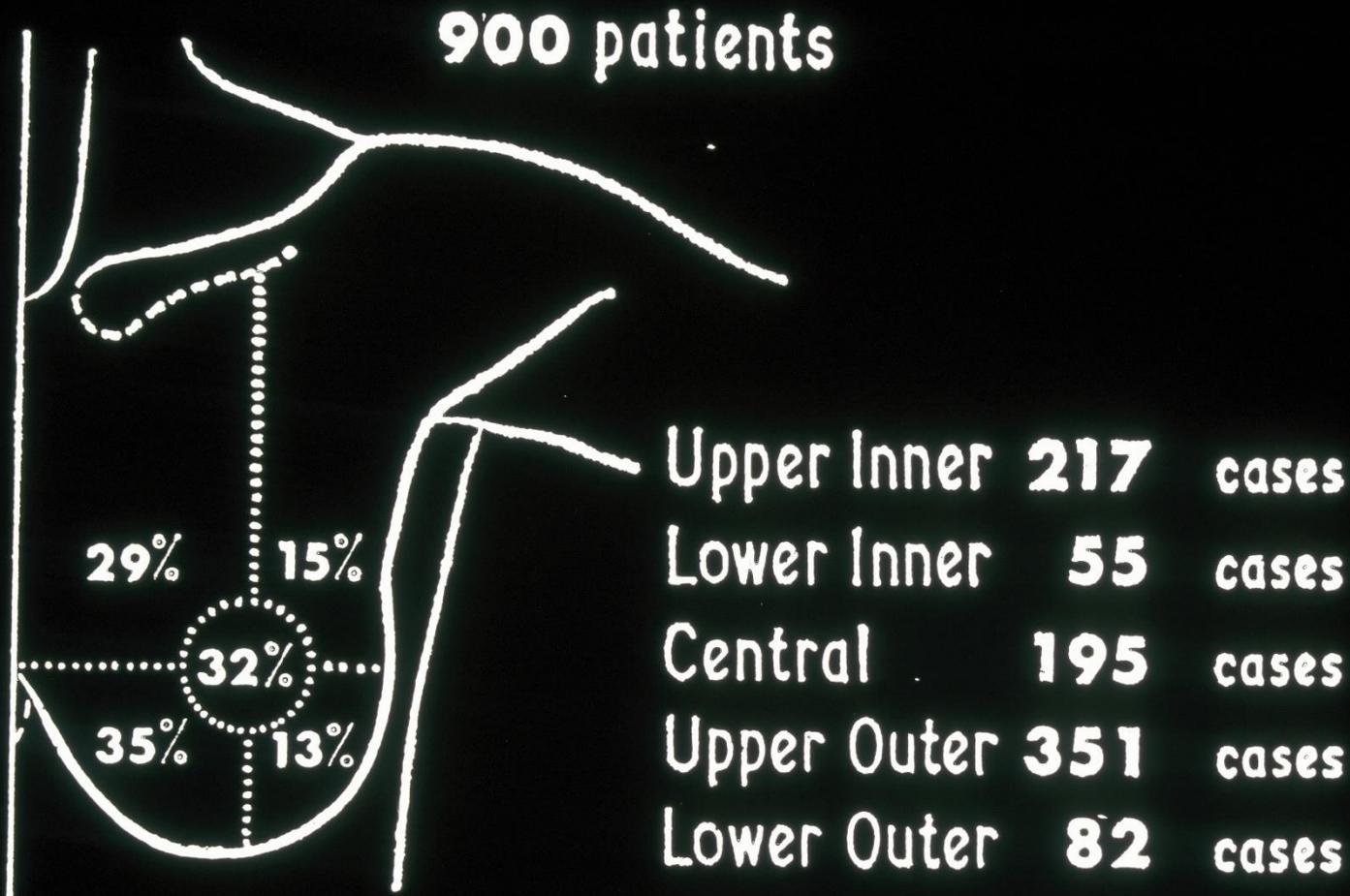
Lymphedema of the Arm after Radical Mastectomy



Lymphatic Spread of Breast Cancer



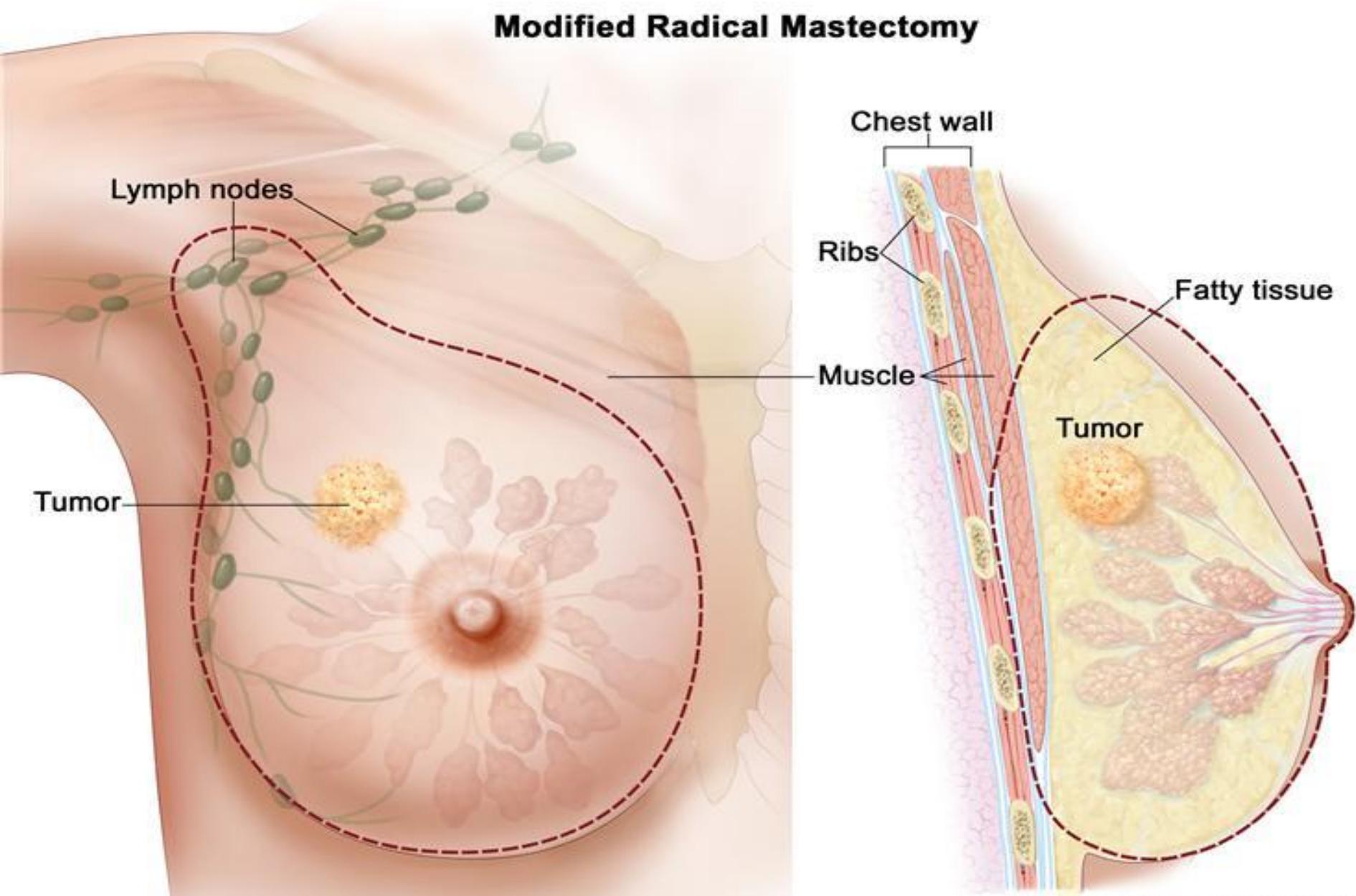
Internal Mammary Lymph Nodes Metastases



Frequency of internal mammary metastases in the different zones of the breast in 900 patients

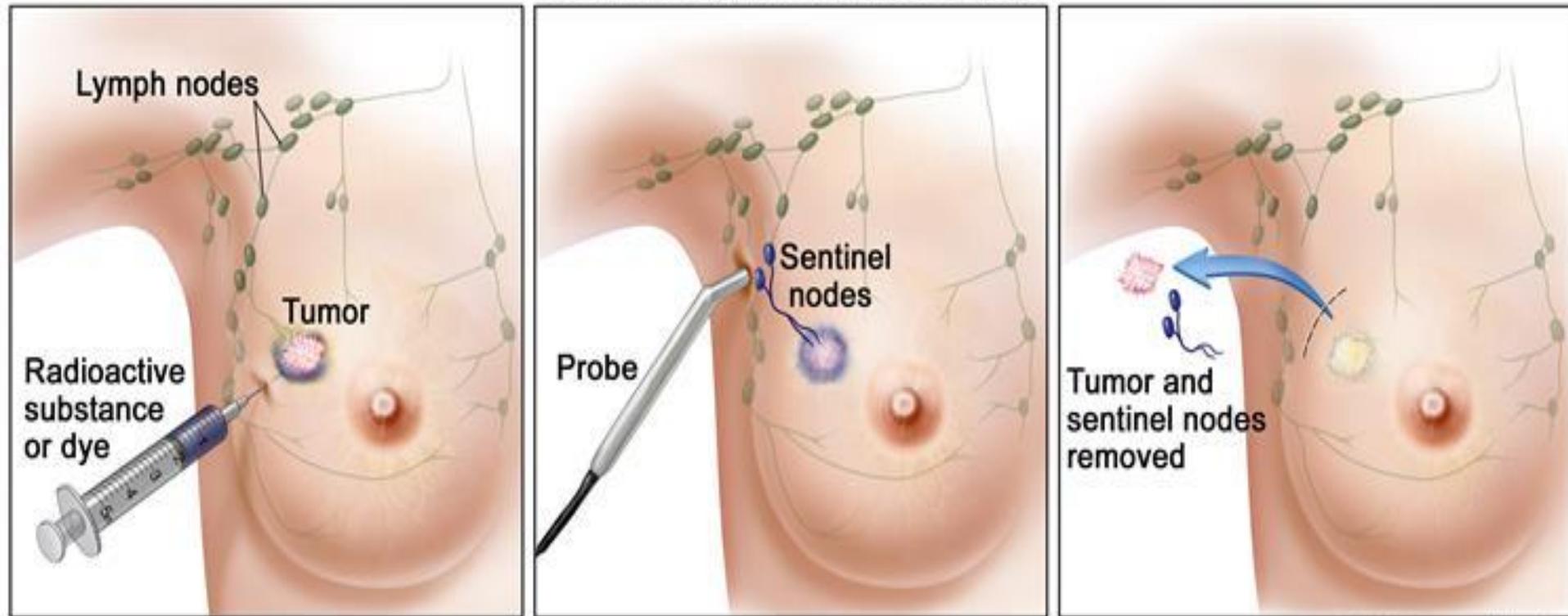
Modified Radical Mastectomy

Modified Radical Mastectomy



Sentinel Lymph Node Biopsy

Sentinel Lymph Node Biopsy

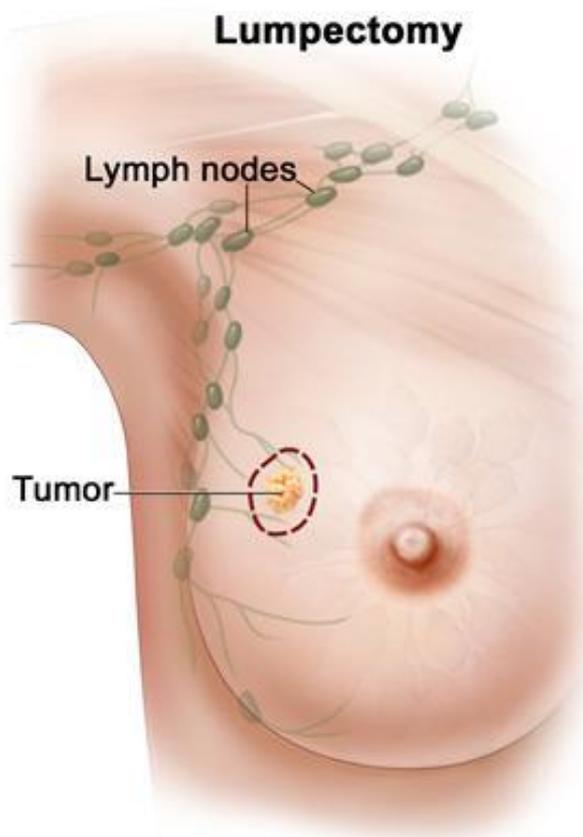


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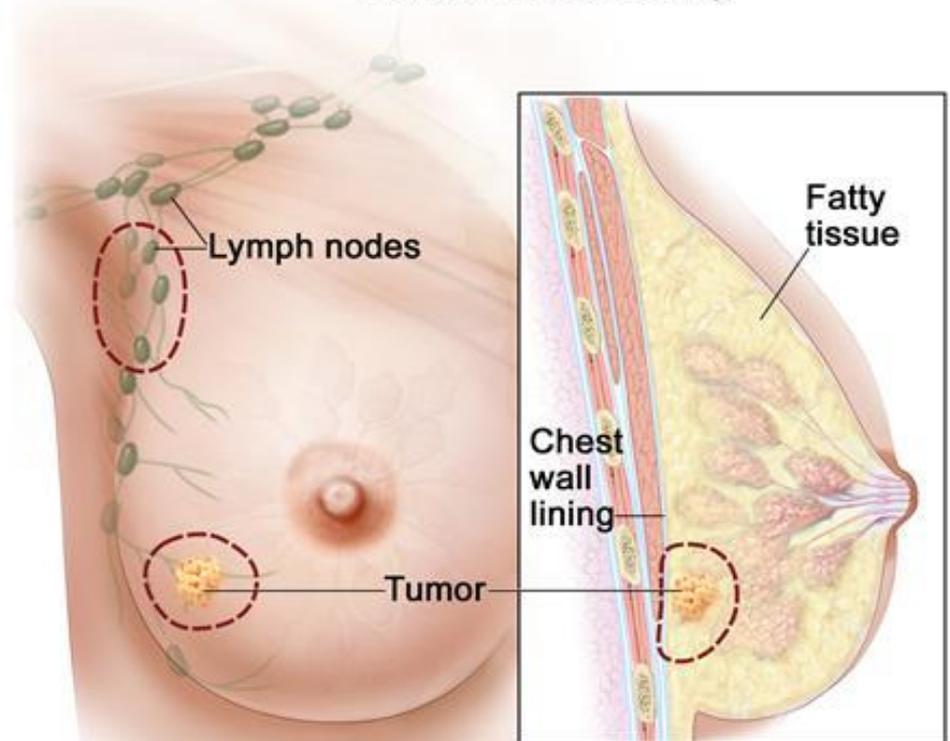
Treatment of Breast Cancer

Breast-conserving Surgery

Lumpectomy



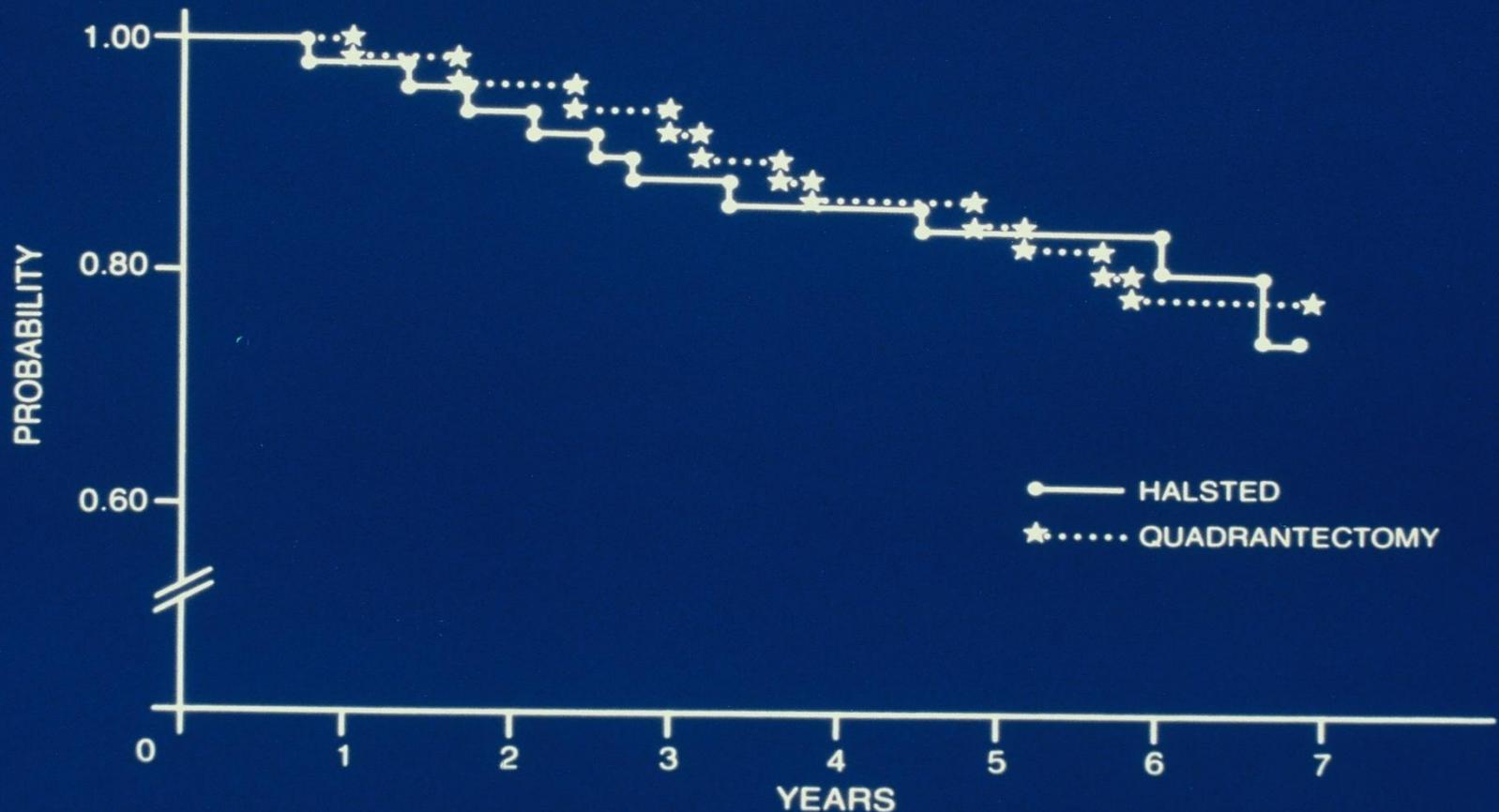
Partial Mastectomy



BREAST CANCER - LIMITED DISEASE

LIMITED SURGERY WITH RADIATION THERAPY VS. RADICAL MASTECTOMY

Actuarial Disease-Free Survival

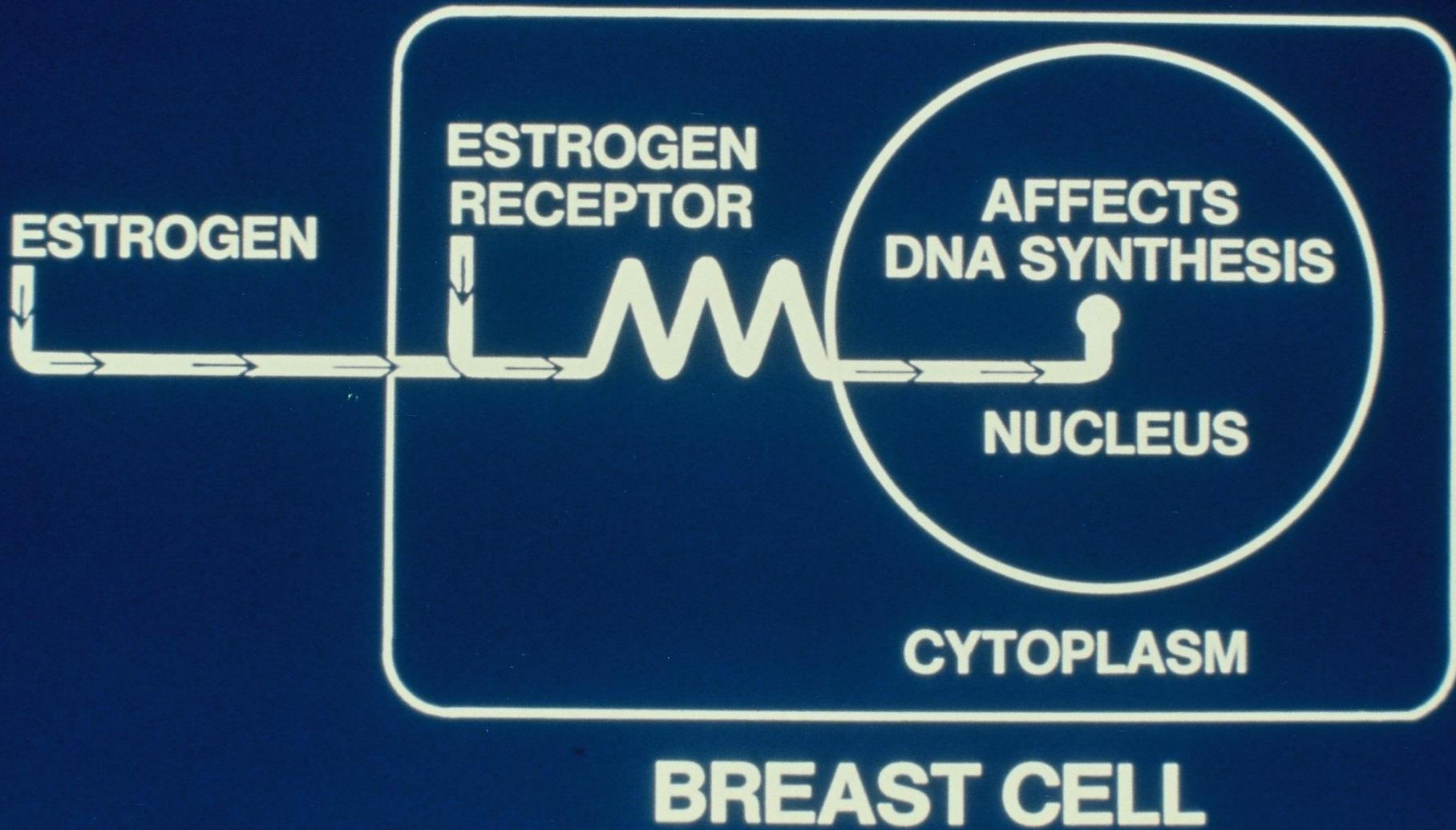


BREAST CANCER

HORMONAL DEPENDENCY

- Urinary estrogen excretion
- Urinary 11-deoxy-17-oxysteroids
- Urinary 17-hydroxycorticosteroids
- Steroid hormones in breast cancer tissue
- Hormone receptors in breast tissue

ESTROGEN RECEPTORS



Estrogen and Progesterone Receptors in Breast Cancer Tissue

Progesterone Receptor +

Responsive to Endocrine Therapy

ER—

0%

5%

ER+

54%

55%

HERCEPTIN

- Recombinant DNA-derived monoclonal antibody.
- **Binds selectively to Human Epidermal Growth Factor Receptor 2 protein (HER2).**
- Effective mostly in tumors overexpressing the HER2 protein.
- Cardiac toxicity (cardiomyopathy).

BREAST CANCER ADJUVANT SYSTEMIC TREATMENT

NODE POSITIVE

PREMONOPAUSAL - CHEMOTHERAPY

**POSTMENOPAUSAL - HORMONAL THERAPY
(TAMOXIFEN)**

BREAST CANCER ADJUVANT SYSTEMIC TREATMENT

NODE NEGATIVE

CHEMOTHERAPY - HIGH RISK PATIENTS (?)

- T > 3 cm.
- Neg. steroid receptors
- Grade 3
- High proliferative activity

TAMOXIFEN - HIGH E.R. LEVEL

BREAST CANCER

INDICATIONS FOR IRRADIATION

- **Breast mass < 5 cm**
- **Fixation of tumor to pectoral fascia**
- **Skin fixation, edema**
- **Multiple foci of invasive tumor**
- **Vascular or lymphatic invasion**
- **20% or more positive axillary nodes**

BREAST CANCER CHEMOTHERAPY

Various combinations of drugs.

The duration depends on extent of tumor and response.

1. **Neoadjuvant ChemoRx:** To shrink the tumor for easier surgical removal.
2. **Adjuvant ChemoRx:** To remove any cancer not seen but thought of remaining after surgery.
3. **For Advanced Cancer:** To treat metastases.

PROSTATE CANCER

Prostate Cancer Warning Signs

Difficulty to urinate
Blood in the urine

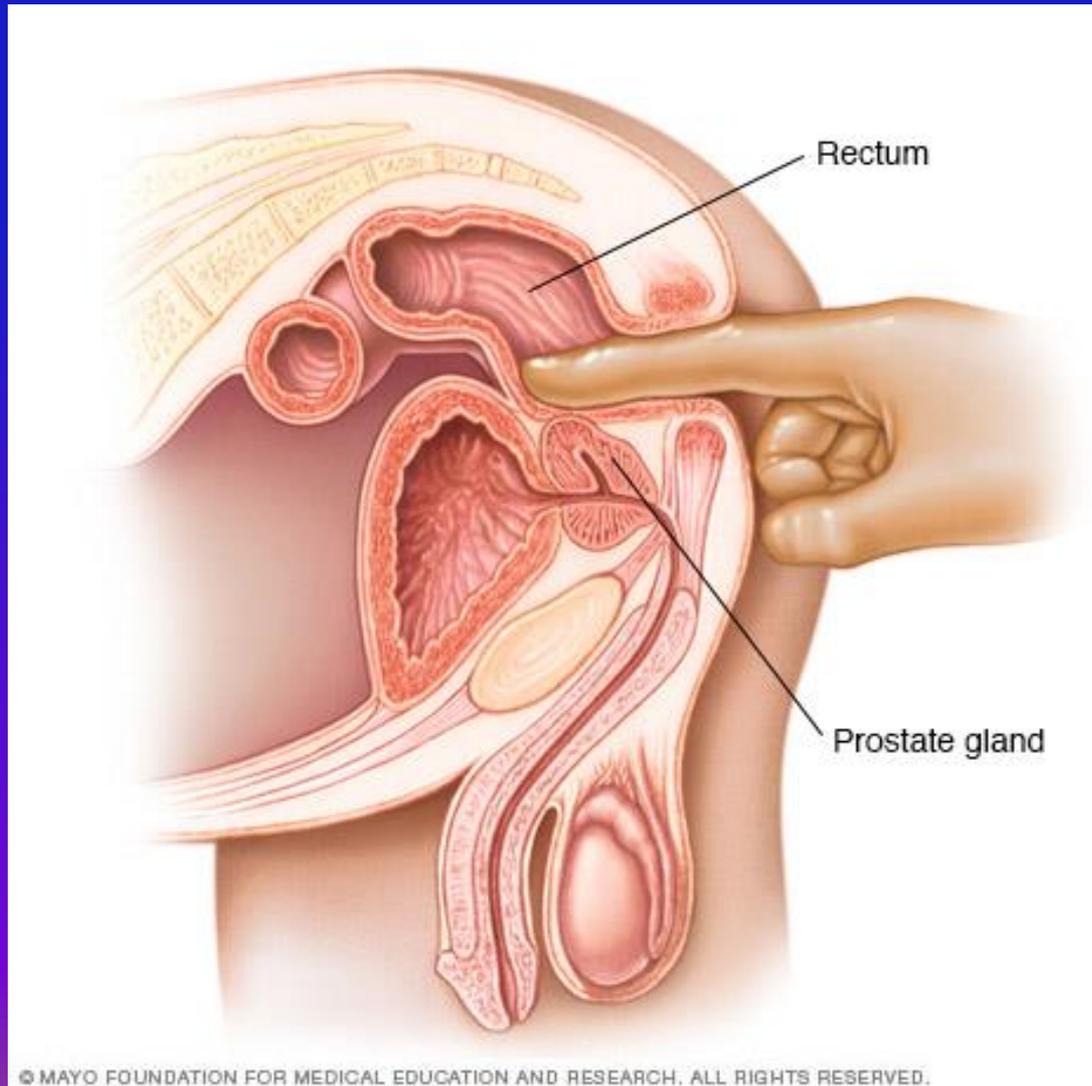
Urinary difficulties
are similar with
those of BPH

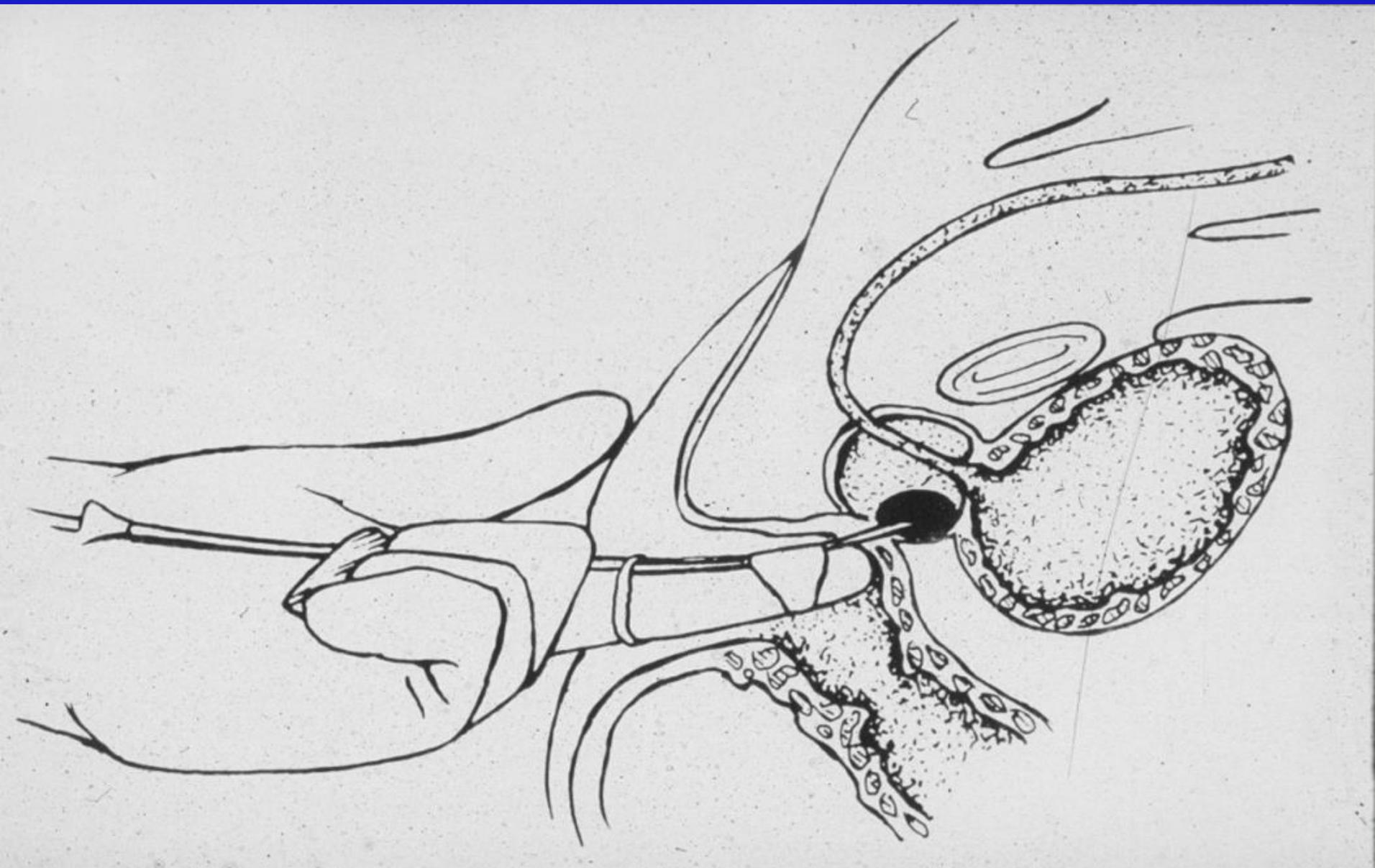
Impotence

Bone pain in hips, spine, ribs

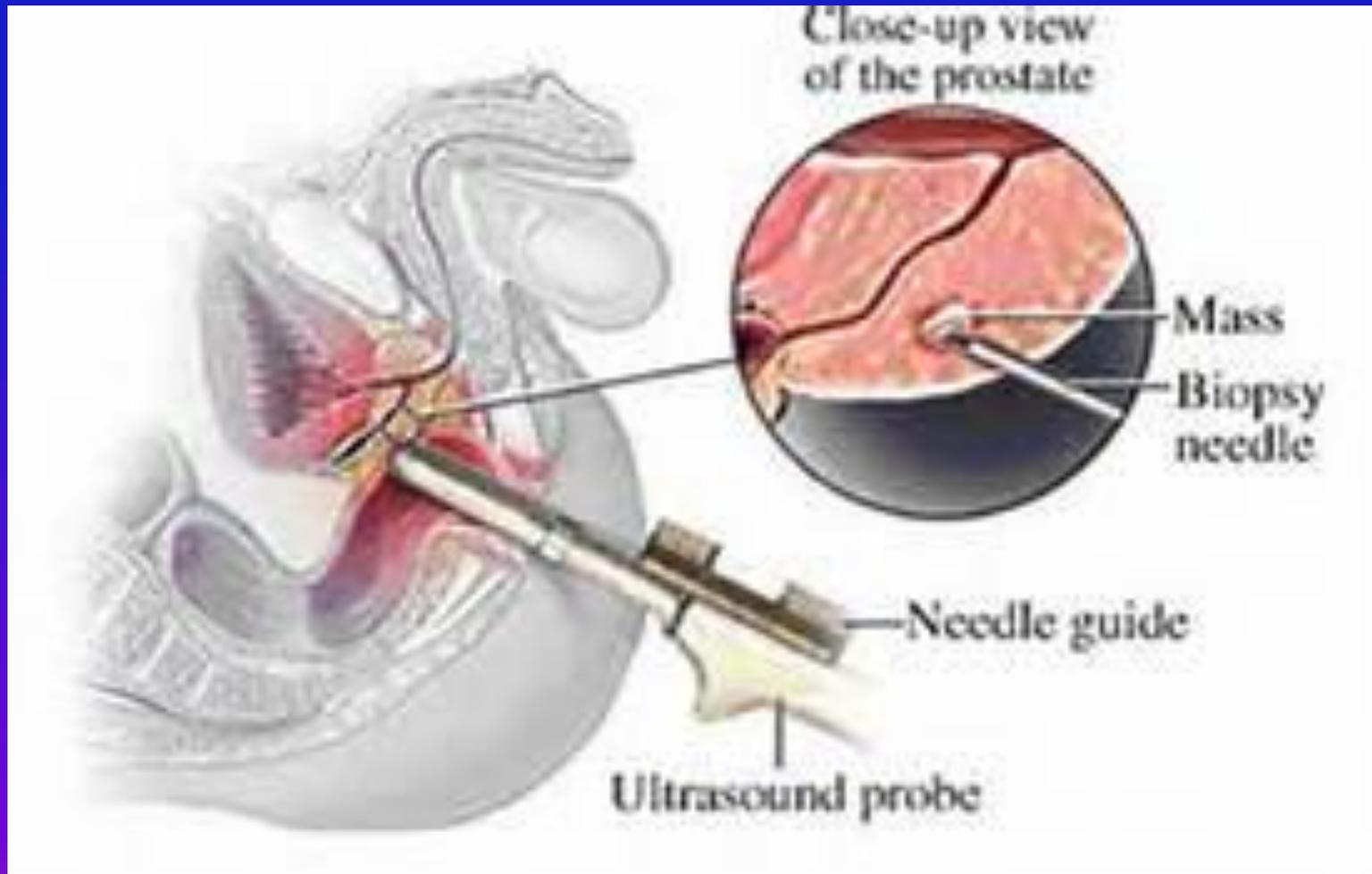
Nerve pain in legs

Digital Rectal Examination (DRE)





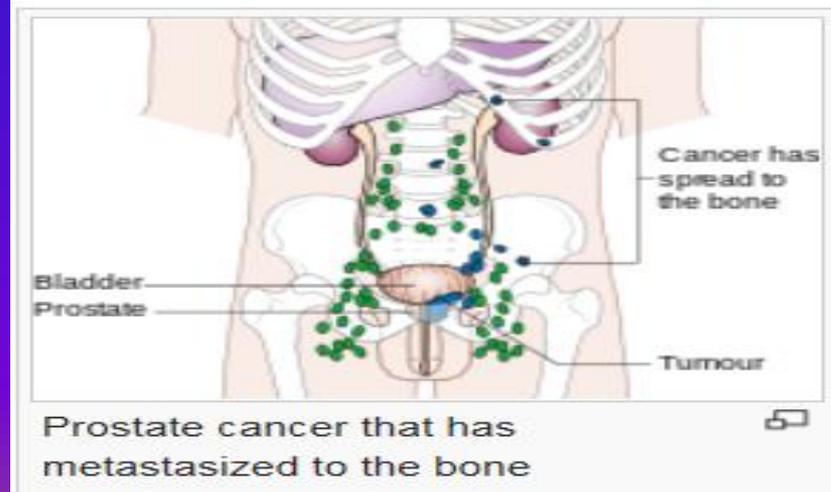
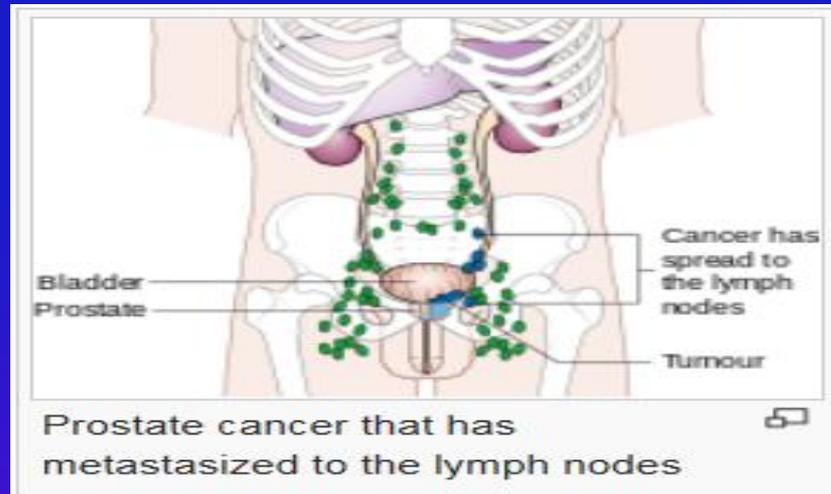
Prostate Needle Biopsy/ies



PROSTATE CANCER OCCULT LYMPHNODE METASTASES VS. TUMOR STAGE AND GRADE

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

Prostate Cancer Metastases



Metastatic Prostate Cancer to the Bones



PROSTATE CANCER

TREATMENT

Surgery

Radiation

Watchful Waiting

Hormone

Chemotherapy

SURGERY

What should we know?

- Disease control - rates?
- Side effects?
- Indicated for the particular patient?
- Quality of life?

Radical prostatectomy with removal of seminal vesicles

- Retropubic prostatectomy
- Perineal prostatectomy
- Laparoscopic/robotic prostatectomy

(Nerve-sparing technique and pelvic lymph node sampling are necessary)

Complications of Radical Prostatectomy

Estimated Overall Incidence

- Impotence 30–70%
- Bladder neck contracture 10–40%
- Incontinence 0–7%
- Mortality 0–3%

Smith, unpublished data

PROSTATE CANCER

RADIATION THERAPY

External beam ± hormones

3-D Conformal radiation therapy (3D – CRT)

Conformal proton beam radiation therapy

Intensity modulated radiation therapy (IMRT)

Interstitial (brachytherapy) – seeds or needles

Strontium-89 (Metastron®) for bone mets.

Clinically Localized Prostate Cancer

Prostate cancer Intervention Versus Observation Trial (PIVOT) Study

Prostatectomy vs. Observation

1994 – 2002 - 731 men, mean age 67 y.o.

Localized prostate cancer;

PSA median 7.8 ng/ml;

Any Gleason score;

Follow-up 8 yrs.

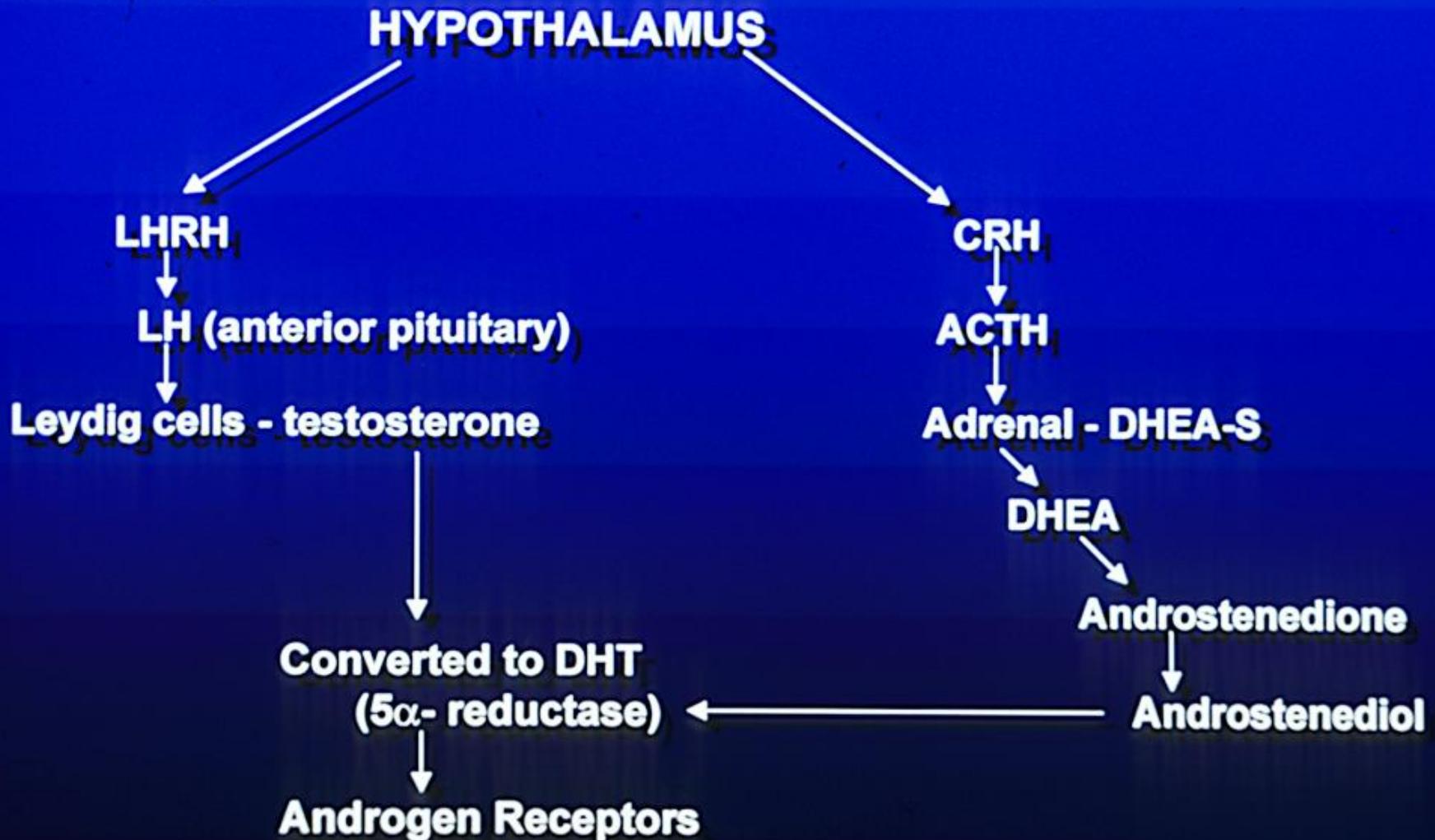
Conclusion: Prostatectomy did not reduce mortality rate

Prostate Cancer: Management of Advanced Disease

Androgen Deprivation

- **Standard treatment since the work of Huggins and Hodges (1941)**
- **Subjective response in 80% of patients**
- **Objective tumor regression measurable by bone scan, x-ray, and PSA**
- **Median duration of response: approximately 18 months**

HORMONAL CONTROL OF PROSTATE CANCER



Androgen Deprivation Therapy

LHRH agonists – Turn off the testicle production of male hormone. Shots given q. 3 – 12 months (Lupron™, Zoladex™)

Combined Androgen Blockade – LHRH agonist + antiandrogen (Flutamide™)

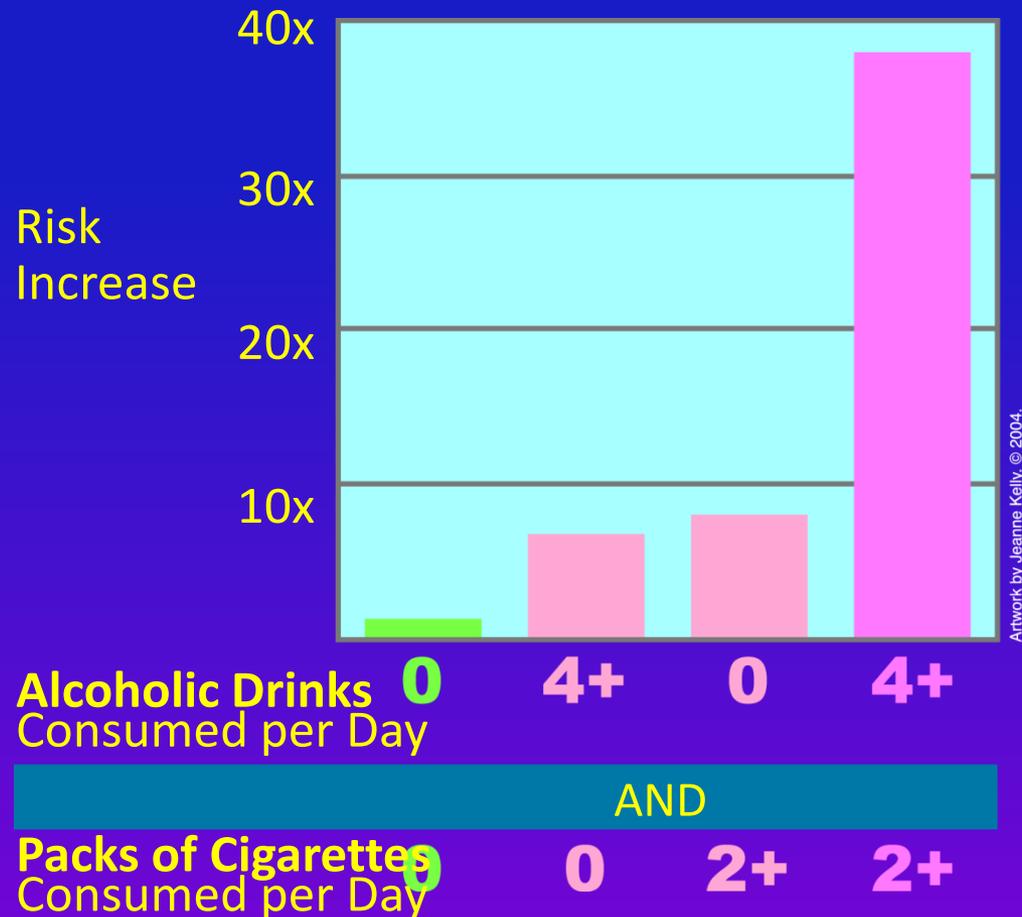
Side effects:

- Decreased libido
- Hot flashes
- Breasts enlargement
- Loss of muscle and increase in body fat
- Osteoporosis
- Risk of coronary heart disease and of Type 2 diabetes

UPPER GI CANCER

Limit Alcohol and Tobacco

Combination of Alcohol and Cigarettes
Increases Risk for **Cancer of the Esophagus**



CANCER of the ESOPHAGUS

Symptoms

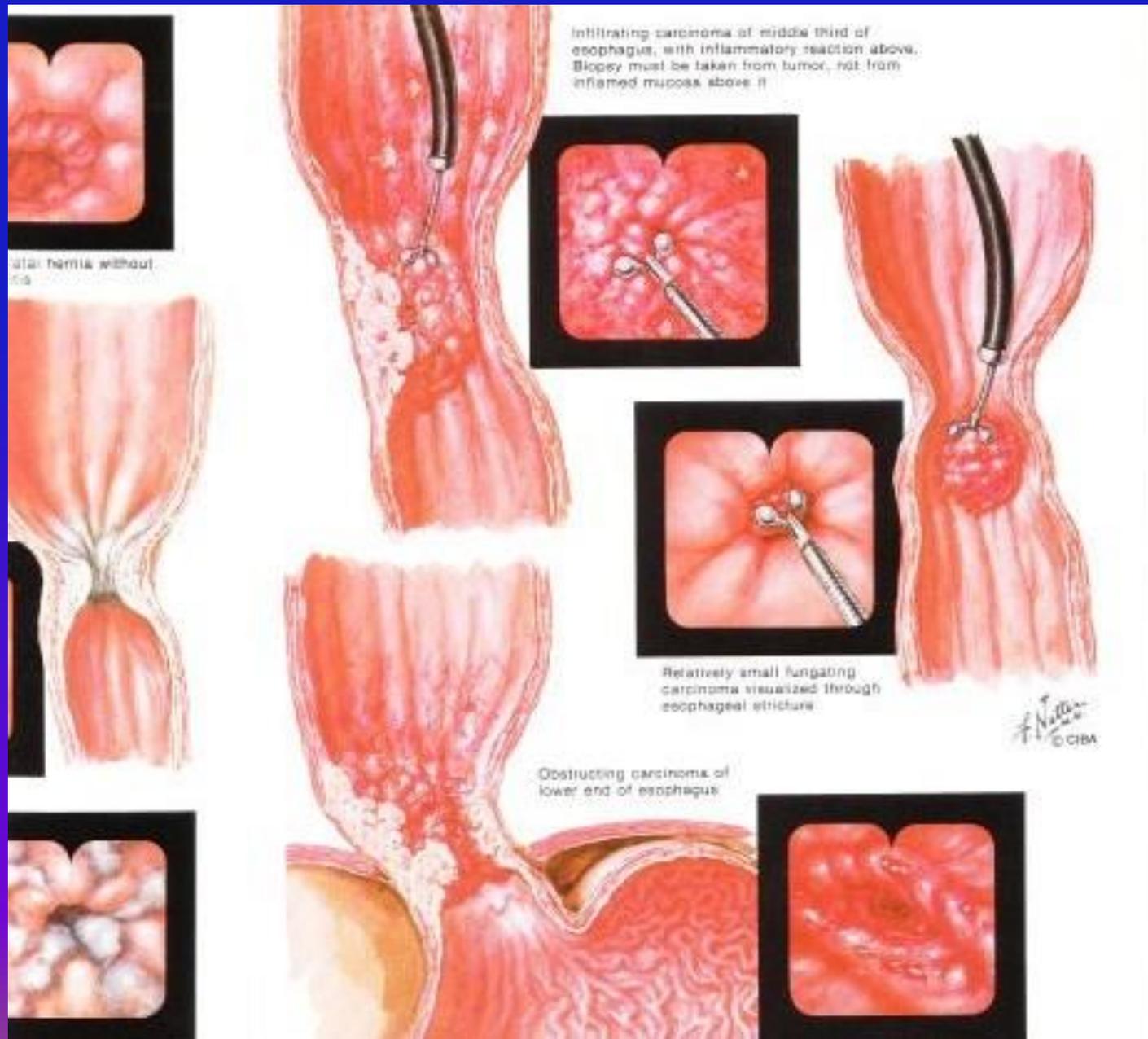
Difficulty swallowing solid foods

Later difficulty and pain swallowing fluids

Weight loss

Change in taste

Endoscopy – Esophageal cancer



STOMACH CANCER

Symptoms

Lack of appetite and Unexplained weight loss is a common sign of cancer.

Nausea & vomiting: Sometimes the vomit may have blood in it.

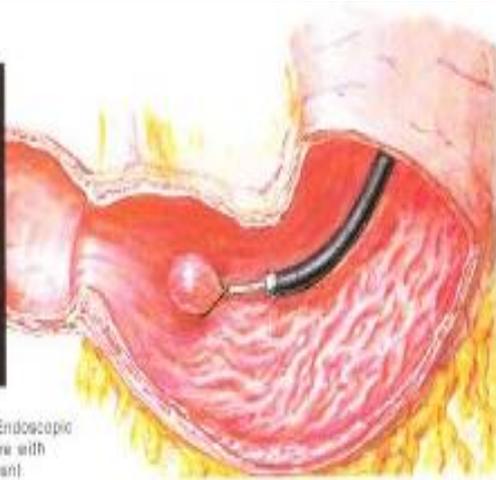
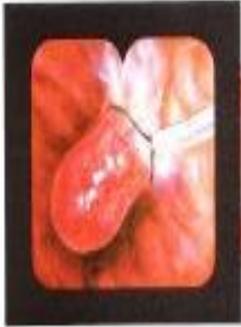
Stomach pain in the upper abdomen.

Early satiety (Feeling full after a small meal).

Heartburn.

In general, the symptoms occur when the cancer is advanced.

STOMACH



Gastric polyp. Endoscopic removal by snare with fulgurating current.



STOMACH CANCER

Treatment

Surgery with dissection and removal of the satellite lymph nodes.

Adjuvant chemotherapy.

5-year survival rates: 18% - 94%, depending on the stage

COLORECTAL CANCER

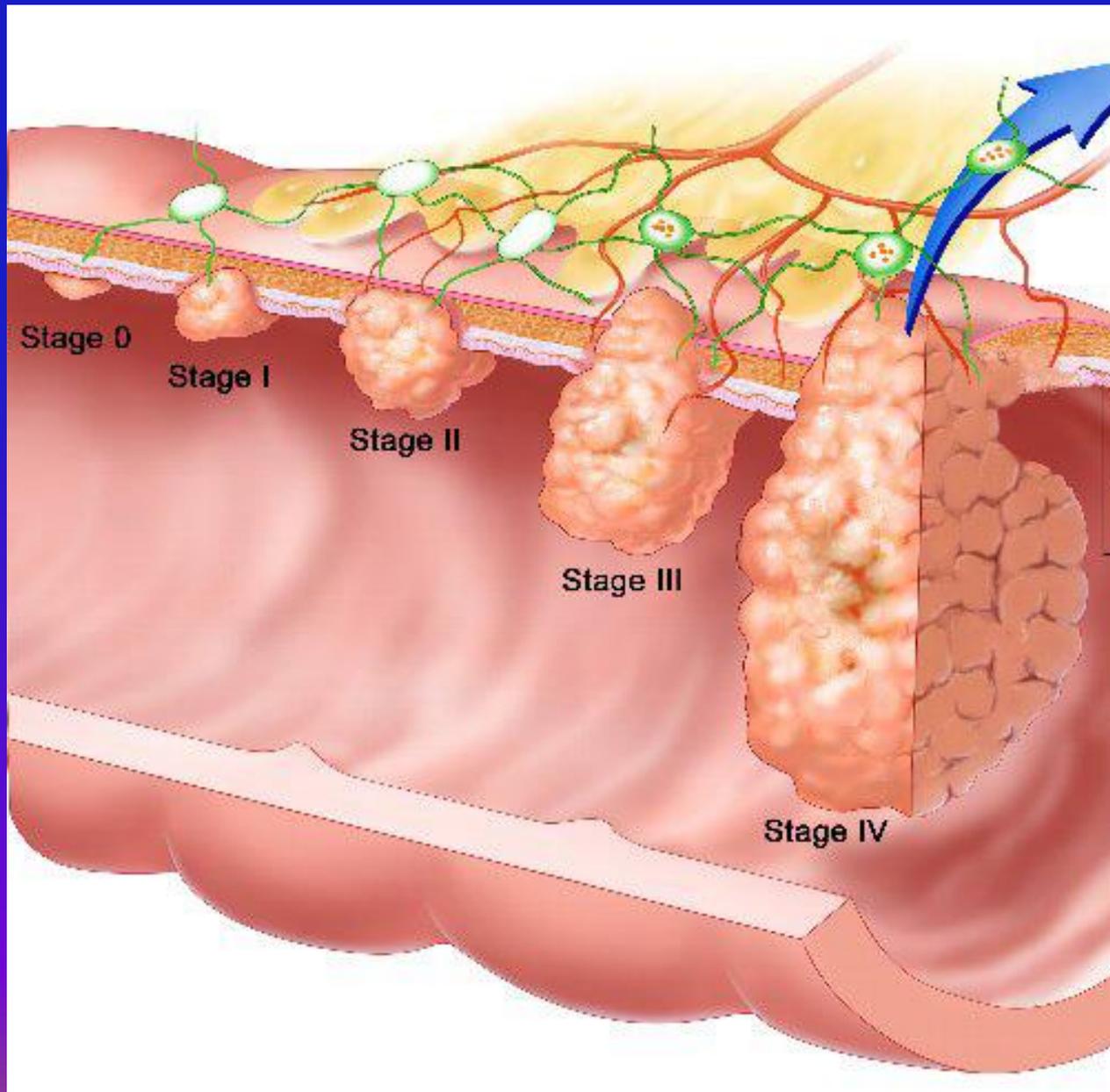
Risk Factors for Colorectal Cancer

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

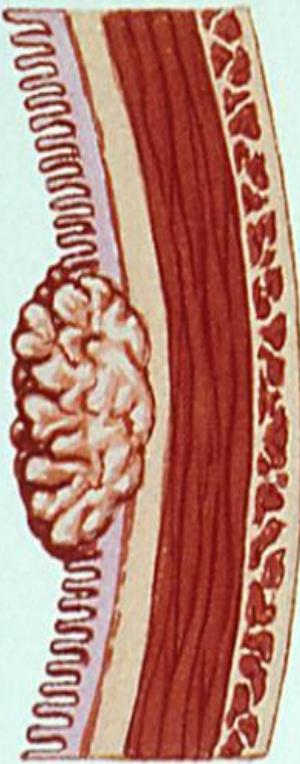
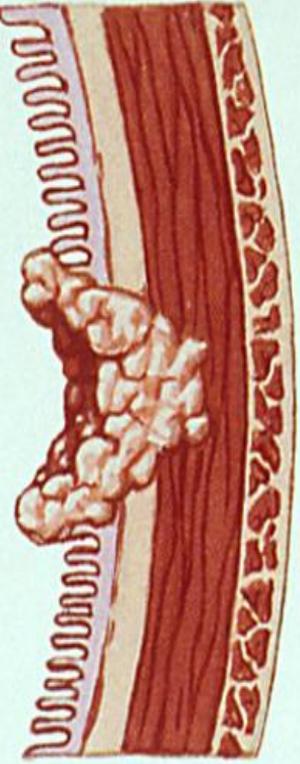
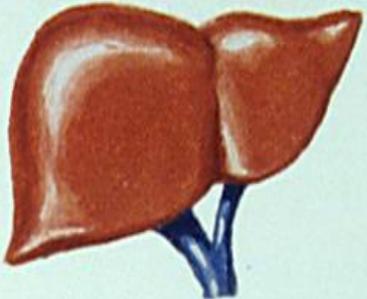
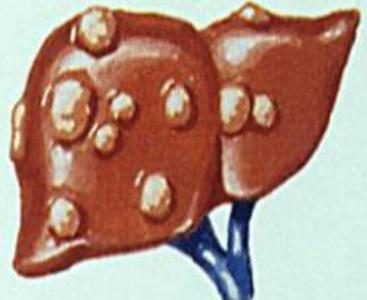
Colon Cancer

- 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

Stages in colon cancer development

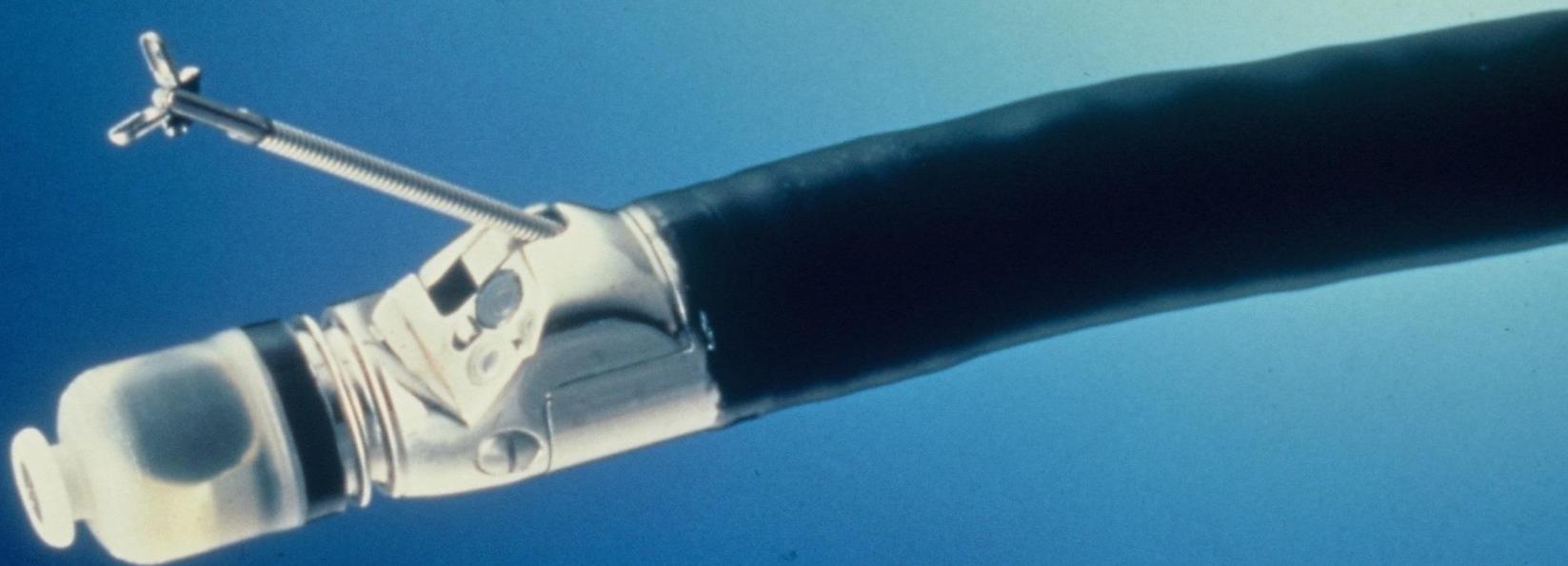


Prognostic Indicators in Colorectal Cancer

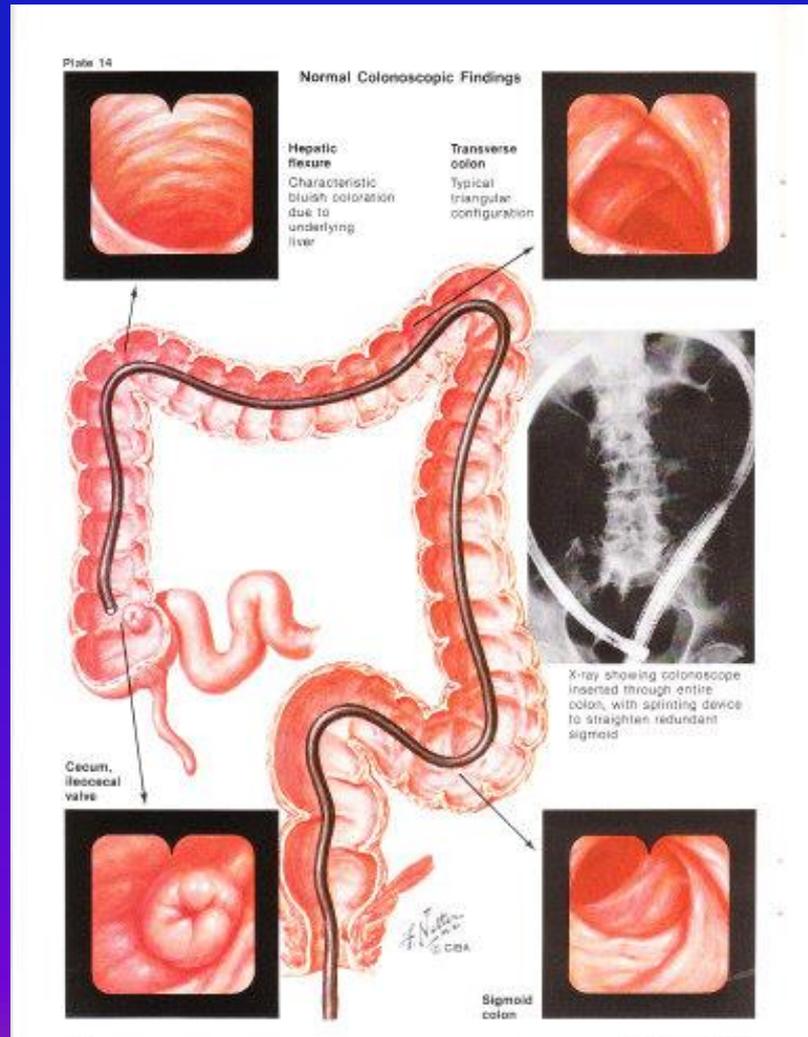
Tumor status			Node status	Systemic status
 <p>Limited to mucosa and submucosa (T₁)</p>	 <p>Invasion into, but not beyond, muscularis propria (T₂)</p>	 <p>Penetration of full thickness of bowel wall (T₃)</p>	 <p>Lymph nodes normal (N₀)</p>  <p>Lymph node metastasis (N₁)</p>	 <p>No distant metastasis (M₀)</p>  <p>Distant metastasis (M₁)</p>

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

FIBERSCOPE



COLONOSCOPY

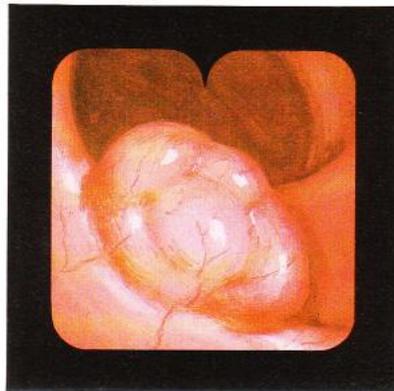


COLONOSCOPY – COLON POLYPS

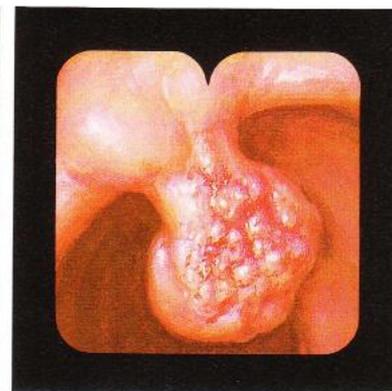
Polyps of Colon



Multiple pedunculated polyps

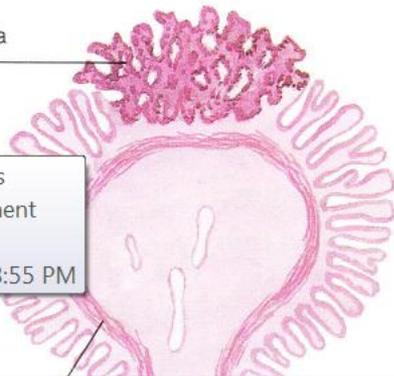


Sessile polyp
(may be multiheaded)

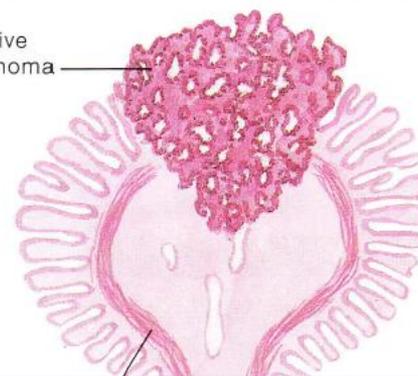


Polyp with area of
malignant transformation

Carcinoma
in situ



Invasive
carcinoma



Endo. esophagus
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Treatment of Colon Cancer

Surgery:

- Surgical removal of the area involved
- Careful dissection of satellite lymph nodes (N1-N3 sites)
- Examination of the liver

Chemotherapy

- If N+ (Stage 2) adjuvant
- If distant mets. (Stage 4)

RECTAL CARCINOMA RADIATION THERAPY

PREOPERATIVE

**REDUCES LOCAL RECURRENCE
IMPROVES RESECTABILITY RATE
REDUCES NODE METASTASES
IMPROVES SURVIVAL**

POSTOPERATIVE

EXCLUDES LOW RISK PATIENTS

PALLIATIVE

**RELIEVES: PAIN
TENESMUS
MUCOUS DISCHARGE**

TREATMENT of TESTICULAR CANCER

TESTICULAR CANCER

Presentation

- **Symptoms:**
 - Painless swelling in one testicle
 - Scrotal pain (rare)
 - Occasional: symptoms related to mets.
- **Signs:**
 - Firm testicular nodule or mass
 - Epididymis involvement
 - Hydrocele

TESTICULAR CANCER Management

Staging: Is the disease limited to the testicle?

Chest X-ray and abdominal CT scan

Biomarkers: Alpha-Fetoprotein (AFP)

β subunit of human chorionic gonadotropin

(beta-hCG)

Lactic dehydrogenase (LDH)

All biomarkers must become normal after orchiectomy

TESTICULAR CANCER

Tumor Markers

- After orchiectomy, **markers should become normal**
- Persistent elevation = residual disease
- Useful in dx. of relapse (clinical f/u)

TESTICULAR CANCER

Treatment

RADICAL ORCHIECTOMY (Removal of the testicle and of the spermatic cord = “the only acceptable diagnostic and therapeutic procedure”)

Retroperitoneal lymph node dissection

Radiation therapy for pure seminoma

Chemotherapy for extra-testicular disease

CANCER of the UTERUS

CANCER OF THE UTERUS

Risk Factors

- Menstruating at an early age.
- Starting menopause at a later age.
- Never giving birth.
- Taking estrogen only (HRT) after menopause.
- Taking tamoxifen to prevent or treat breast cancer.
- **Obesity** and **Metabolic syndrome**.
- Having **type 2 diabetes**.
- Having **polycystic ovarian syndrome**.
- Having a **family history** of endometrial cancer in a first-degree relative (mother, sister, or daughter).
- Having certain **genetic conditions**, such as Lynch syndrome.
- Having **endometrial hyperplasia**.

Cancer of the Uterus - Symptoms

Irregular periods

Menorrhagia

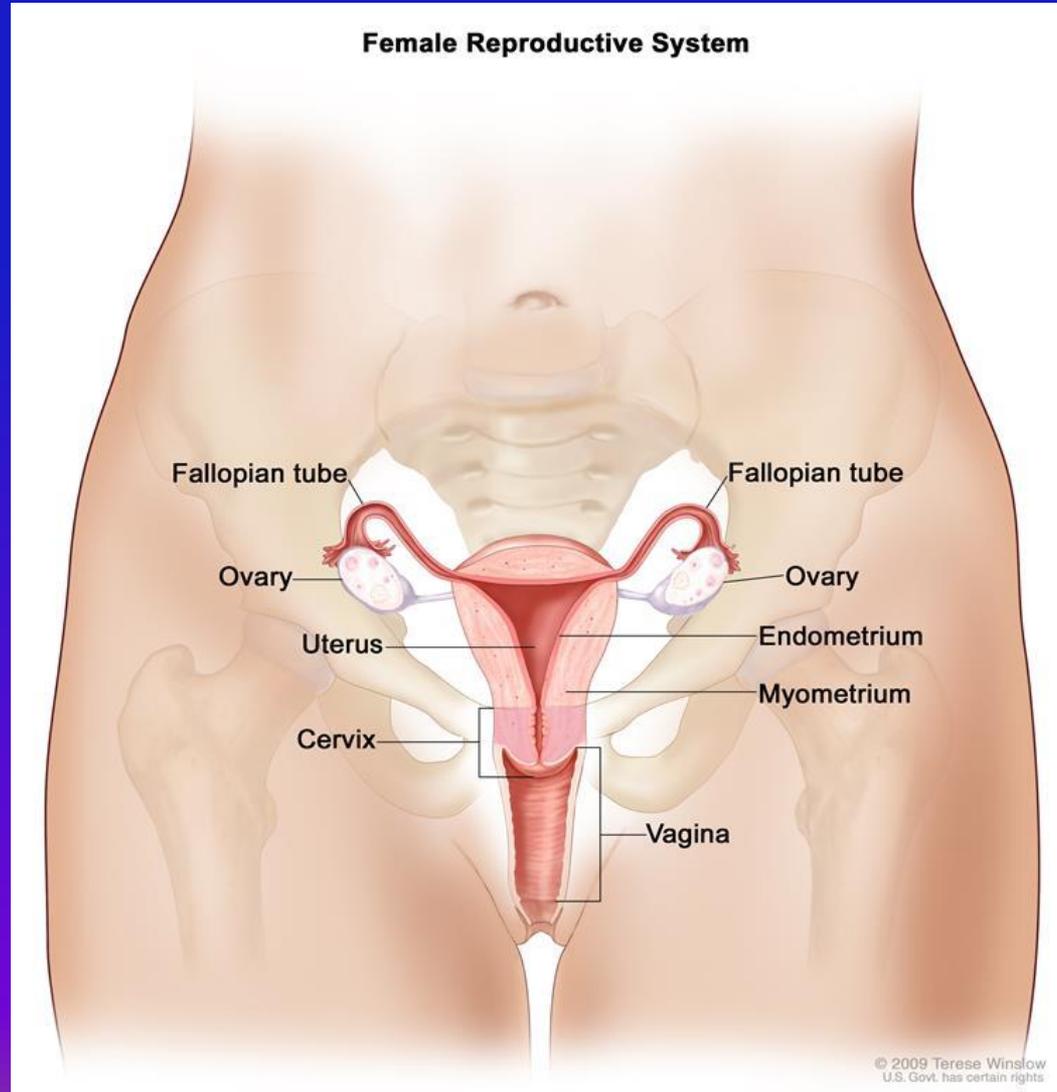
Abundant blood discharge – Metrorrhagia

Pelvic pain

Endometrial Cancer - Ultrasound



Cancer of the Uterus - Treatment

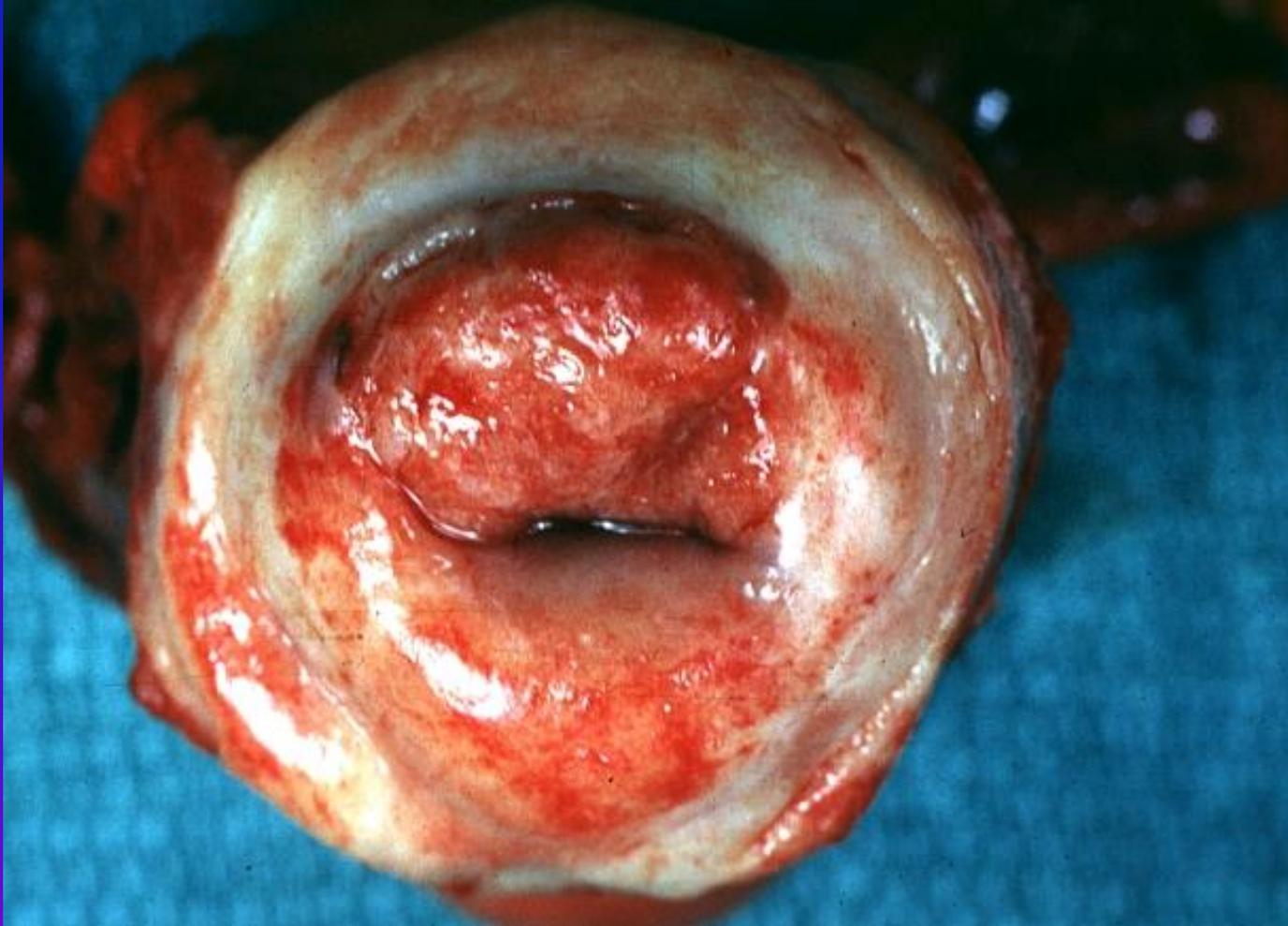


CANCER OF THE UTERINE CERVIX

Normal Uterine Cervix



Cervical Cancer (Invasive Carcinoma)



CERVICAL CANCER SCREENING

RECOMMENDATIONS

- All women who are or have been sexually active
- Papanicolaou (Pap.) test 3 yrs. after first vaginal intercourse and no later than 21 y.o.
- Pap. q. yr. in hi-risk cases
- After 30 y.o., if Pap. negative (x 3), screening with Pap. and HPV DNA testing q. 3 yrs.
- Pap. may be discontinued at 70 y.o. if previously normal

CANCER of the URINARY BLADDER

Cancer of the Urinary Bladder.

Symptoms are not specific

Blood in the urine

Having to urinate more often than usual

Pain or burning during urination

Urgency = feeling that one needs to go right away, although the bladder is not full

Having trouble urinating or having a weak urine stream

Late symptoms:

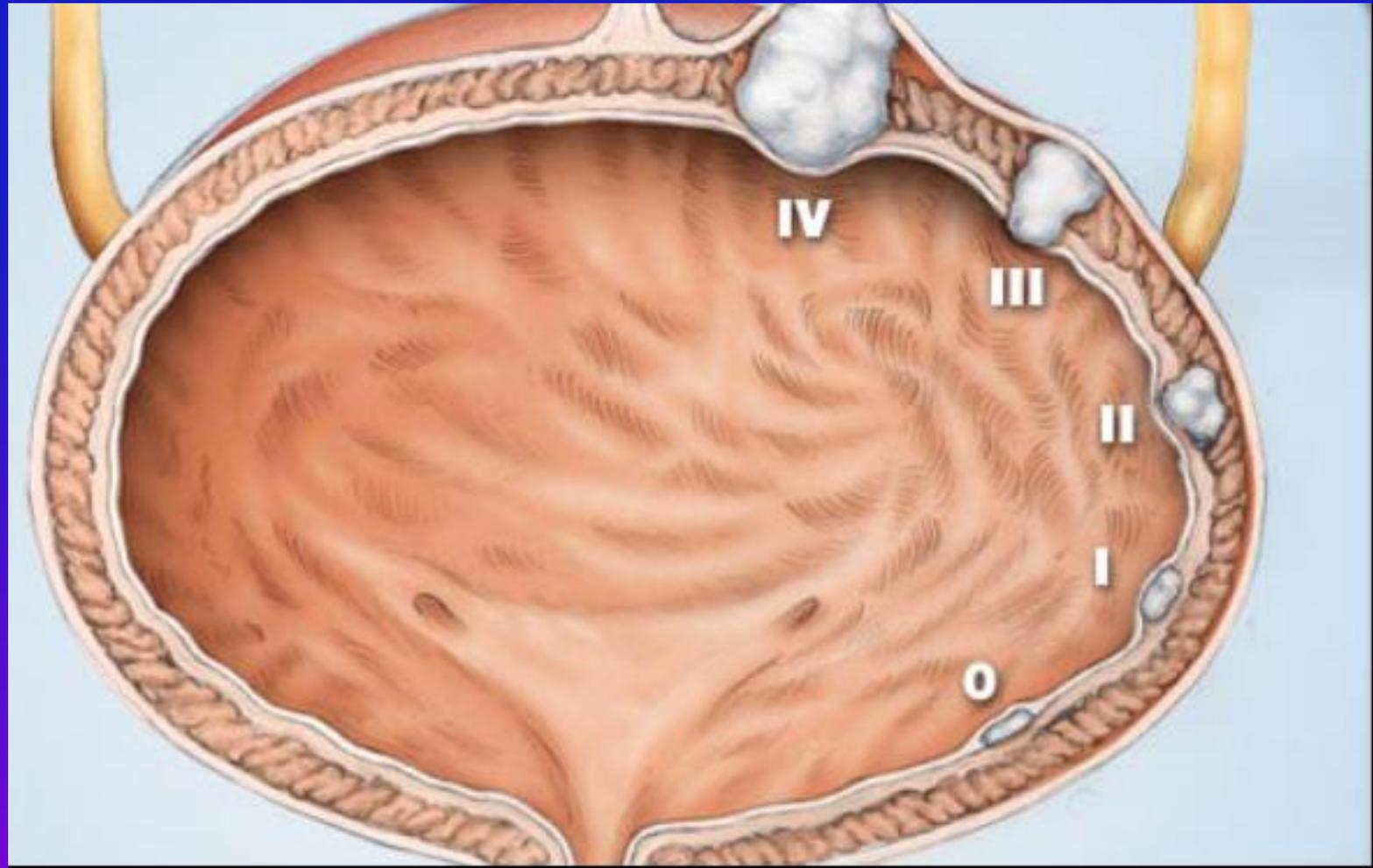
Being unable to urinate

Loss of appetite and weight loss

Feeling tired or weak

Bone pain

BLADDER CANCER STAGES



SKIN CANCER

SKIN CANCER SCREENING

Burden of Suffering

2017 - >5 million new cases in U.S.

>95% are basal cell or squamous cell carcinoma

Organ transplant patients x 100 times more likely

90% of non-melanoma are associated with exposure to
UV radiation

Actinic keratosis most common precancer

2017 – 87,000 malignant melanoma cases

2017 – 9,700 deaths

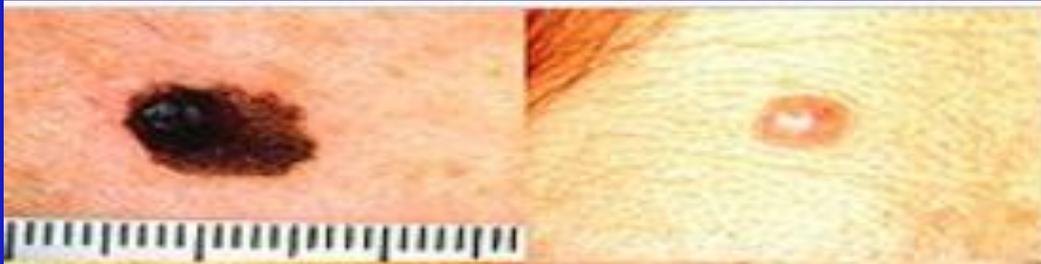
SKIN CANCER SCREENING

Risk Factors

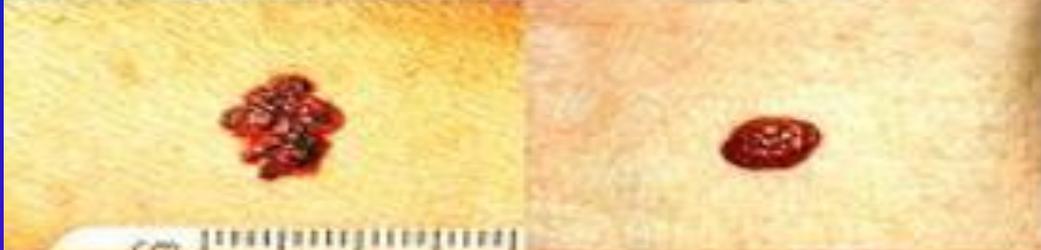
- Atypical moles (dysplastic nevi)
- Congenital moles
- Large number of common moles
- Immunosuppression
- Family/personal history of skin cancer
- Fair skin, poor tanning ability
- Intense sun exposure
- Severe sun burns in childhood

Malignant melanoma vs. Benign nevi (moles)

Asymmetry



Borders



Color



Diameter
changing

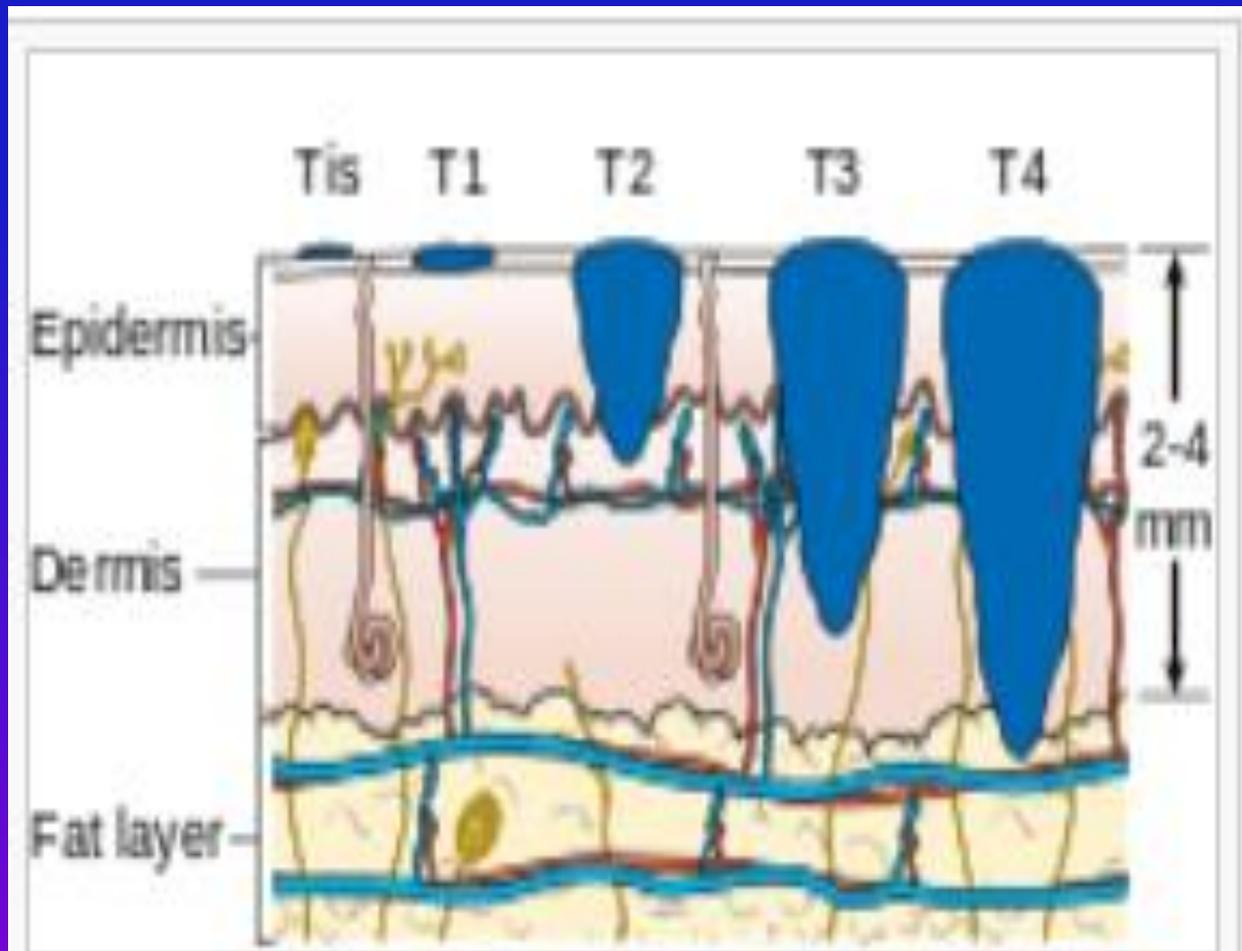


SKIN CANCER SCREENING

Recommendations

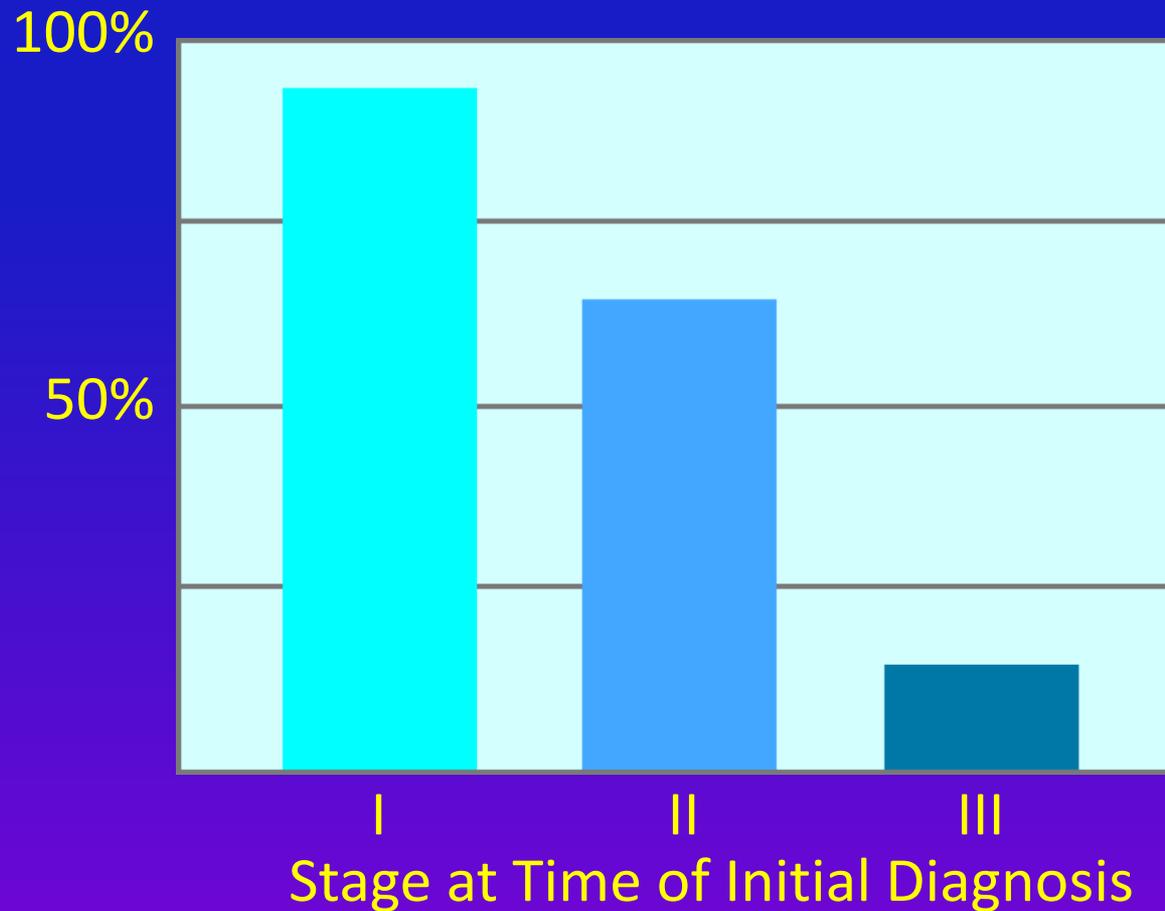
- Public education
- Avoidance of skin exposure
(protective clothing, sun screens)
- Biopsy of suspicious lesions

STAGES OF MELANOMA



Malignant melanoma – Stage and Survival

Five-Year Survival Rates for Patients with Melanoma (by stage)



Artwork by Jeanne Kelly. © 2004.

END OF LECTURE #5

END OF THIS CLASS

THANK YOU

