CANCER IN HUMANS
## Cancer Statistics in USA – Est. 2016* and 2017**

<table>
<thead>
<tr>
<th></th>
<th>All sites</th>
<th>Lung</th>
<th>Breast (W)</th>
<th>Prostate</th>
<th>Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New cases</strong></td>
<td>1,685,000</td>
<td>224,000</td>
<td>249,000</td>
<td>181,000</td>
<td>95,000</td>
</tr>
<tr>
<td></td>
<td>1,689,000</td>
<td>222,000</td>
<td>255,000</td>
<td>161,000</td>
<td>96,000</td>
</tr>
<tr>
<td><strong>Deaths</strong></td>
<td>596,000</td>
<td>158,000</td>
<td>41,000</td>
<td>26,000</td>
<td>49,000</td>
</tr>
<tr>
<td></td>
<td>601,000</td>
<td>156,000</td>
<td>41,000</td>
<td>27,000</td>
<td>50,000</td>
</tr>
</tbody>
</table>

* Published 2016

** Published 2017
SEVEN WARNING SIGNS OF CANCER

- Change in bowel or bladder habits
- 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
Constitutional Symptoms and Survival

Hodgkin's Disease: Effect of Constitutional Symptoms (B) on Prognosis

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**

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1.</td>
<td>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</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about <strong>more than 50% of waking hours</strong></td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care, confined to bed or chair <strong>more than 50% of waking hours</strong></td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair</td>
</tr>
</tbody>
</table>
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

Patient’s tissue sample or blood sample

Pathology

Proteomic profile

Genomic profile
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
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

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

- Stage I: 100%
- Stage II: 50%
- Stage III: Lower than 50%
1. Substances (mostly proteins) found in blood, urine, tissue, or body fluids.

2. Gene expression or DNA changes found in tumor tissue.

They may:

• 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 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=0.07)
• **Protective effect of non-citrus fruits**
  (RR=0.6)
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

<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)*
Normal Chest X-ray
Chest CT Scan Showing Metastases
PET/CT scan
Positron Emission Tomography/Computer Tomography
PLEURA
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 $\Rightarrow$ 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 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
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
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

- 1% of patients are between 12-29 years old.
- 5% of patients are between 30-39 years old.
- 14% of patients are between 40-49 years old.
- 28% of patients are between 50-59 years old.
- 31% of patients are between 60-69 years old.
- 18% of patients are between 70-79 years old.
- 3% of patients are between 80-89 years old.
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


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

- Stage 0
- Stage I
- Stage II
- Stage III
- Stage IV
# Prognostic Indicators in Colorectal Cancer

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

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) → Heat + Reducing Acid or Intestinal Conversion → PORPHYRIN (Fluorescent) + Fe

CG: 113697-1
FIBERSCOPE
Familial Adenomatous Polyposis
Fibroscopic and Microscopic Views of a Colon Polyp
Colonoscopy – Colon Polyps

- Multiple pedunculated polyps
- Sessile polyp (may be multiheaded)
- Polyp with area of malignant transformation

Carcinoma in situ
Invasive carcinoma
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%

E. MORAN - 2018
MALE GENITAL APPARATUS

- Ureter (from kidney)
- Rectum
- Seminal vesicle
- Prostate gland
- Urinary bladder
- Erectile tissue
- Urethra
- Glans penis
- Epididymis
- Scrotum
- Testis
- Vas deferens
<table>
<thead>
<tr>
<th>PSA Value</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\leq 4.0$ (&quot;Normal&quot;)</td>
<td>High probability of localized disease</td>
</tr>
<tr>
<td>4-1 - 10.0</td>
<td>Very low risk of metastases (limited radiographic staging needed)</td>
</tr>
<tr>
<td>$&gt; 10.0 - 20.0$</td>
<td>Low risk of metastases</td>
</tr>
<tr>
<td>$&gt; 20.0$</td>
<td>Risk of metastases</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Grade</th>
<th>Well differentiated</th>
<th>Moderately differentiated</th>
<th>Moderately-poorly differentiated</th>
<th>Poorly differentiated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1+1=2</td>
<td>3+2=5</td>
<td>3+4=7</td>
<td>4+4=8</td>
</tr>
<tr>
<td>2</td>
<td>2+1=3</td>
<td>3+3=6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2+2=4</td>
<td>3+4=7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>4+3=7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td>5+5=10</td>
</tr>
</tbody>
</table>

Primary & secondary pattern summed for Gleason score sum:

- 2: "Good"
- 4: "Intermediate"
- 7: "Intermediate"/"Bad"
- 8: "Bad"
# PROSTATE CANCER

Occult Lymphnode Metastases vs. Tumor Stage and Grade

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>Tumor Grade (Gleason)</th>
<th>%</th>
<th>%</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Localized Dis.)</td>
<td>(Localized Dis.)</td>
<td>Well</td>
<td>Intermediate</td>
<td>Poor</td>
</tr>
<tr>
<td>T1, N0, M0</td>
<td>(2-4)</td>
<td>5</td>
<td>23</td>
<td>50</td>
</tr>
<tr>
<td>T2, N0, M0</td>
<td>(5-7)</td>
<td>5-28</td>
<td>20-27</td>
<td>27-38</td>
</tr>
<tr>
<td>T3, N0, M0</td>
<td>(8-10)</td>
<td>18</td>
<td>42</td>
<td>68</td>
</tr>
</tbody>
</table>
DIAGNOSIS of TESTICULAR CANCER
Ultrasound of the Scrotum: Right Testicle Cancer

Normal left testicle

Seminoma in right testicle (RT)
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