COLON CANCER
### CANCER STATISTICS IN USA – 2015*

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*Published 2/15
COLORECTAL CANCER
BURDEN OF SUFFERING

- Lifetime risk in U.S. = 2.6%
- Average life loss = 13 yrs.
- 60% of cases are advanced at time of diagnosis
- 5-yr. survival
  - localized = 91%
  - regional = 60%
  - distant = 6%
HEMOQUANT TEST

HEMEL (Non-Fluorescent) → Heat + Reducing Acid or Intestinal Conversion → PORPHYRIN (Fluorescent) + Fe
COLONSCOPY
PREVALENCE OF PROXIMAL VS. DISTAL COLON CANCER BY AGE GROUP

Mantel-Haenszel Chi-Square Test
p = 0.0481
Stages in colon cancer development
# Prognostic Indicators in Colorectal Cancer

<table>
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<tr>
<th>Tumor status</th>
<th>Node status</th>
<th>Systemic status</th>
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<tr>
<td>Limited to mucosa and submucosa ($T_1$)</td>
<td>Lymph nodes normal ($N_0$)</td>
<td>No distant metastasis ($M_0$)</td>
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<tr>
<td>Invasion into, but not beyond, muscularis propria ($T_2$)</td>
<td>Lymph node metastasis ($N_1$)</td>
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<tr>
<td>Penetration of full thickness of bowel wall ($T_3$)</td>
<td></td>
<td>Distant metastasis ($M_1$)</td>
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Tumor staging assesses depth of invasion (T) into or through bowel wall, presence or absence of lymph node (N) and distant organ metastasis (M).
COLON POLYPS MUST BE REMOVED. THEY ARE PRECURSORS OF CANCER
COLONOSCOPY – COLON CANCER
COLON CANCER - TREATMENT

Surgery
Chemotherapy + Surgery
Chemotherapy
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
HUMAN ANATOMY AND PHYSIOLOGY

• The Nervous System
• The Endocrine Glands
• The Hemopoietic System
• The Circulatory System
• The Respiratory Tract
• The Digestive Tract
• The Urinary Tract
• The Reproductive System
• The Locomotor System
• The Skin
THE URINARY TRACT

1. Kidneys
2. Ureters
3. Bladder
4. Urethra
POSITION OF KIDNEYS
KIDNEY FUNCTION
SEMIPERMEABLE MEMBRANE
GLOMERULAR FILTRATION

1. Filtration
2. Reabsorption
3. Secretion
4. Excretion

Excretion = Filtration – Reabsorption + Secretion
KIDNEY GLOMERULUS
Microscopic hematuria

Gross hematuria (red urine)

**Causes:** Urinary tract infections (UTI)

- Kidney or bladder stones
- Disorders of the clotting system (Medications: Aspirin, warfarin, clopidogrel)
- Prostate enlargement (BPH)
- Cancer of kidney, bladder, prostate
KIDNEY (RENAL) FUNCTIONS

Excretion of wastes:
- Urea from protein catabolism
- Uric acid from nucleic acid metabolism

Reabsorption of vital nutrients: Glucose

Acid-base homeostasis

Regulation of osmolality: ADH ➤ water reabsorption

Regulation of blood pressure: Plasma Na conc. ➤
- renin ➤ angiotensin

Hormone secretion: Erythropoietin ➤ production of RBC’s in the bone marrow
DISEASES OF THE URINARY TRACT

**Kidneys:** Infections: Pyelonephritis, Glomerulonephritis

- Stones
- Cancer
- Infarct

**Ureters:** Stones

**Bladder:** Infections

- Stones
- Cancer

**Prostate:** Enlargement (Benign Prostatic Hypertrophy = BPH)
URINARY TRACT INFECTIONS

**Pyelonephritis:** Infection of the kidneys from lower part of the tract or from blood

**Symptoms:** Fever, shaking chills, painful urination, back pain, abdominal pain, nausea

**Diagnosis:** Urine culture, kidney ultrasound

**Treatment:** Antibiotics

**Glomerulonephritis:** Several acute or chronic diseases affecting the glomeruli or the small vessels in the kidneys. Frequently after a strep throat infection.

**Diagnosis:** Edema, hematuria, proteinuria
KIDNEY STONES (CALCULI)

Are formed from minerals in the urine.

**Symptoms:** Excruciating pain = renal colic. Comes in waves lasting 20 to 60 minutes. Associated symptoms include: N+V, blood in the urine, painful urination.

Stones ≤ 3mm may pass spontaneously.

**Causes:** Genetics, overweight, not drinking enough fluids.

Calcium oxalate (urine acidic), calcium phosphate (urine alkaline), uric acid (urine acidic), struvite (infections)

**Diagnosis:** CT scan

**Treatment:** Extracorporeal shockwave lithotripsy, Uteroscopy laser lithotripsy

Avoid colas (phosphoric acid)
Kidney stone  8mm
Renal Colic
RENAL FAILURE

**Acute:** Infarct, Glomerulonephritis, Shock

**Chronic:** End stage of glomerulonephritis
            Chronic pyelonephritis
            Nephrosclerosis
            Nephrotic syndrome
            Uremia
CANCER OF THE KIDNEY (RENAL CELL CARCINOMA (RCC) or HYPERNENPHROMA

**Burden of suffering:** US 2015 Est. 61,560 new cases

**Risk factors:** smoking, obesity, and high blood pressure have been estimated to account for up to 50% of cases

**Symptoms:**
- Hematuria (40%)
- Flank pain (40%)
- Weight loss (33%)
- Fever (30%)
- High blood pressure (20%)
**KIDNEY CANCER**

**Diagnosis:** Blood: aspartate aminotransferase and alanine aminotransferase are high

**X-ray:** IVP, Ultrasound, CT scanning, MRI, renal angiography

**Treatment:**
- Radical nephrectomy
- Nephron-sparing nephrectomy (T < 4 cm)
- Laparoscopic nephrectomy
- Surgical removal of metastases
URINARY BLADDER
CANCER OF THE URINARY BLADDER

Burden of suffering: US 2015 Est. 74,000
(M = 56,320; F = 17,680)

Risk factors: 50% of cases related to smoking
30% related to occupational exposure to dyes

Symptoms: Hematuria (blood in the urine) = not specific
Tenesmus and pain = not specific

Diagnosis: Cystoscopy – biopsy – pathologic examination

Treatment: If superficial – TURBT, BCG
If infiltrating the muscle – Intravesical chemotherapy
BLADDER CANCER STAGES
THE GENITAL AND REPRODUCTIVE SYSTEMS
THE FEMALE GENITAL SYSTEM
FEMALE GENITAL APPARATUS - SCHEMA

- Ovary
- Fimbria
- Uterine cavity
- Fallopian tube
- Internal os
- Cervix
- External os
- Ectocervix
- Endocervix
- Endocervical canal
- Uterus
- Vagina
FEMALE GENITAL APPARATUS
CANCER OF THE OVARY

Burden of suffering: US 2015 Est. 21,290 new cases

Risk factors: Nulliparous, menarche at a young age, late menopause, hormones after menopause, fertility meds, inherited genetic risk (\(BRCA1\) and \(BRCA2\) – 50% risk), obesity. Use of talc powder?

Decreased risk: Pregnancies, hormonal birth control (\(\checkmark\) 50%), breast feeding, diet.

Symptoms: Bloating, abdominal discomfort, distension
CANCER OF THE UTERUS
(ENDOMETRIAL CANCER)

Burden of suffering – US 2015 Est. 54,870 newly diagnosed

Risk factors:
- Obesity (40%),
- Excessive estrogen exposure - Estrogen exposure   risk
- Estrogen + Progesterone (most birth control pills)   risk
- HTN, diabetes,
- Endometrial hyperplasia, uterine polyps

Symptoms: Vaginal bleeding (metrorrhagia), pelvic pain

Diagnosis: Endometrial biopsy, D&C

Treatment: Hysterectomy + salpingo-oophorectomy - 5-yr. survival 80%
ENDOMETRIAL CANCER - ULTRASOUND
CERVICAL CANCER
CERVICAL CANCER
BURDEN OF SUFFERING

- Increased incidence last 40 yrs.

- Lifetime risk in U.S. = 0.3%

- 5-yr. survival - localized = 90%
  - advanced = <14%
1. Early onset of sexual intercourse
2. History of multiple sex partners
3. Low socioeconomic status
4. HIV and HPV infection
5. Immunosuppression
6. *In utero* exposure to DES
Normal Uterine Cervix
Cervical Cancer (Invasive Carcinoma)
RISK FACTORS FOR CERVICAL CANCER

- Chronic HPV infection
- Previous CIN2, CIN3, carcinoma (continue annual screening x 20 years)
- History of multiple sexual partners
- HIV (OR 4-6)
- Early age of first intercourse (under 17)
- Exposure to an STI (OR 2.1)
- Mother/sister with cervical cancer (OR 2.6)
HUMAN PAPILLOMAVIRUS (HPV)

- 6.2 million new infections per year in US (20.6 cases per 100,000 population)
- Thought to be responsible for 5% of all types of cancers worldwide
  - 100% of cervical cancers
  - 90% of anal cancers
  - 40% of penile, vaginal, and vulvar cancers
  - 25% of oral cavity cancers
  - 35% of oropharyngeal cancers

E. MORAN - 2016
HUMAN PAPILLOMA VIRUS

- 20 million Americans currently infected
- 1/3 of US women infected by age 24
- 75% of sexually active women will be infected at some point during lifetime
- 75-90% of HPV infections will clear in 1 year; host may remain immune to that subtype for up to 3 years
- New infection less likely with older age
CERVICAL CANCER SCREENING
RECOMMENDATIONS

• 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
THE BREAST
BREAST CANCER
## CANCER STATISTICS IN USA – 2015*

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BREAST CANCER

BURDEN OF SUFFERING

- Incidence = 110/100,000 women/yr.
  \(\uparrow 55\%\) between 1950-1991

- Mortality = 22/100,000 women/yr.
BREAST CANCER RISK FACTORS

**Major:**
- Age
- Family history
- History of breast cancer

**Minor:**
- Early menarche
- Late menopause
- First child at >30 y.o.
- Obesity
- Radiation
FEMALE BREAST CANCER RISK FACTORS

U.S. Woman’s average risk of breast cancer = 12% during her lifetime

**Personal history:** Breast cancer in one breast ➤ 1% - 2% chance/year of developing a second breast cancer

**Family history:** First-degree relative of maternal or paternal site ➤ x 5 times the average risk
BREAST CANCER
RISK FACTORS

- Older age at pregnancy, nulliparity
- High socioeconomic status (diet? lifestyle?)
- Hx. of high-dose radiation exposure
- Oral contraceptives, long-term estrogen Rx.
- Obesity, high-fat diet
BREAST CANCER SCREENING
MAMMOGRAPHIC SIGNS OF CANCER

Irregular Mass

Microcalcifications
BREAST CANCER SCREENING
RECOMMENDATIONS

- Age 20-39: Clinical Breast Exam q. 3 yrs.
- Age >40, as long as candidate for treatment:
  - Clinical Breast Examination - q. yr. and
  - Mammography (low-dose) q. 1-2 yrs.

Note: Insufficient evidence in favor of:
  - Mammography in women >70 y.o.
  - Breast self examination
BREAST CANCER

EARLY DETECTION

- 2-view mammography ± CBE →
  Mortality ↓ 20-30% in 50-69 y.o.
The Female Breast
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 – 3

EXAMINE AXILLAE

PALPATE BREASTS
PATIENT SUPINE
Breast cancer – T4
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

ESTROGEN RECEPTOR

AFFECTS DNA SYNTHESIS

NUCLEUS

CYTOPLASM

BREAST CELL
<table>
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<th>Progesterone Receptor +</th>
<th>Responsive to Endocrine Therapy</th>
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<tr>
<td>ER−</td>
<td>0%</td>
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<tr>
<td>ER+</td>
<td>54%</td>
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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) ➤ ⚠ CHF
- As single drug ➤ ⚠ (NYHA III-IV 5%)
- Combined with AC ➤ ⚠ 28% (NYHA III-IV 19%)
PROGNOSIS
BREAST CANCER PROGNOSIS

- Presence of metastases
- Size of tumor
- Location of tumor within the breast
- Supraclavicular or internal mammary nodes
- Axillary nodes
- Vascular invasion
- Cytological pattern
- Histological grade
- ER, PR, Her2 receptors
- Molecular biology characteristics
TREATMENT OF FEMALE BREAST CANCER
TREATMENT OF BREAST CANCER

Surgery

Radiation therapy

Hormonal therapy (anti-estrogens):
   Tamoxifen
   Aromatase inhibitors

Biologicals:
   Monoclonal antibodies
   Tyrosine kinase inhibitors

Chemotherapy
State after Left Total Mastectomy
LYMPHEDEMA OF THE ARM AFTER BREAST CANCER SURGERY
LOCAL RECURRENCE AFTER RADICAL MASTECTOMY
BREAST CANCER
REGIONAL SPREAD

LYMPHATIC
AXILLARY
SUPRACLAVICULAR
INTERNAL MAMMARY
SKIN
SUBCUTANEOUS TISSUES
NIPPLE
CHEST WALL
LYMPHATIC SPREAD OF BREAST CANCER
Frequency of internal mammary metastases in the different zones of the breast in 900 patients:

- Upper Inner: 217 cases
- Lower Inner: 55 cases
- Central: 195 cases
- Upper Outer: 351 cases
- Lower Outer: 82 cases
NEW APPROACHES

- Stereotactic Breast Biopsy
- Scintimammography
- Sentinel Node Biopsy
- Neoadjuvant Therapy
SENTINEL LYMPH NODE BIOPSY
TREATMENT OF BREAST CANCER
MODIFIED RADICAL MASTECTOMY
LIMITED SURGERY WITH RADIATION THERAPY VS. RADICAL MASTECTOMY

Actuarial Disease-Free Survival

PROBABILITY

YEARS

HALSTED

QUADRANCTECTOMY

E. MORAN - 2015
Tamoxifen Citrate
Nolvadex®
INDICATIONS

Oral palliative treatment of advanced breast cancer in postmenopausal women

Patients who have had a recent negative estrogen receptor assay are unlikely to respond
ANTIESTROGEN
NOLVADEX® (tamoxifen citrate)

ESTROGEN ANTAGONIST

\[
\begin{align*}
&\text{O} \quad \text{(CH}_2\text{)}_2\text{N(CH}_3\text{)}_2 \\
&\text{C}_6\text{H}_8\text{O}_7 \\
&\text{C}_2\text{H}_5
\end{align*}
\]

(NON-STERoidal)

INHIBITS

- Estrogen binding in estrogen receptor positive breast cancer cells
- Further estrogen receptor protein formation
- Cell division
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
END OF LECTURE #7