Biomedical Engineering for Global Health

Lecture Twelve

Four Questions

- What are the major health problems worldwide?
- Who pays to solve problems in health care?
- How can technology solve health care problems?
- How are health care technologies managed?

Three Case Studies

- Prevention of infectious disease
  - HIV/AIDS
- Early detection of cancer
  - Cervical Cancer
  - Ovarian Cancer
  - Prostate Cancer
- Treatment of heart disease
  - Atherosclerosis and heart attack
  - Heart failure

Outline

- The burden of cancer
- How does cancer develop?
- Why is early detection so important?
- Strategies for early detection
- Example cancers/technologies
  - Cervical cancer
  - Ovarian cancer
  - Prostate cancer

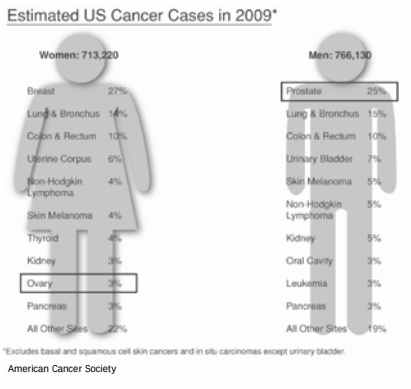
The Burden of Cancer: U.S.

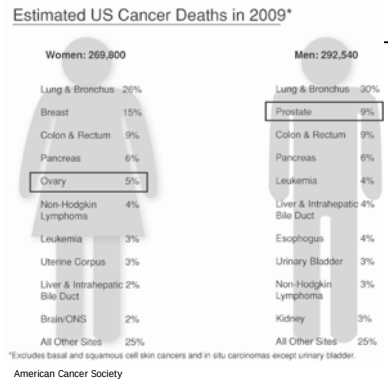
- Cancer:
  - 2nd leading cause of death in US
  - 1 of every 4 deaths is from cancer
- 5-year survival rate for all cancers:
  - 62%
- Annual costs for cancer:
  - $172 billion
    - $61 billion - direct medical costs
    - $16 billion - lost productivity to illness
    - $95 billion - lost productivity to premature death

U.S. Cancer Incidence & Mortality 2004

- New cases of cancer:
  - United States: 1,368,030
  - Texas: 84,530
- Deaths due to cancer:
  - United States: 563,700

www.cancer.org, Cancer Facts & Figures

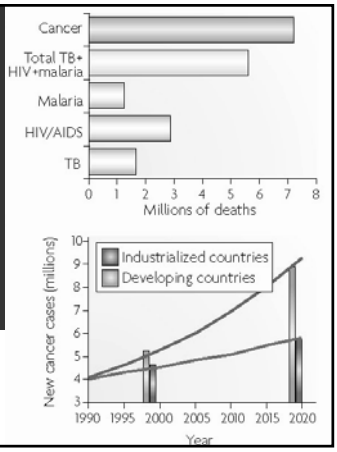




Worldwide Burden of Cancer

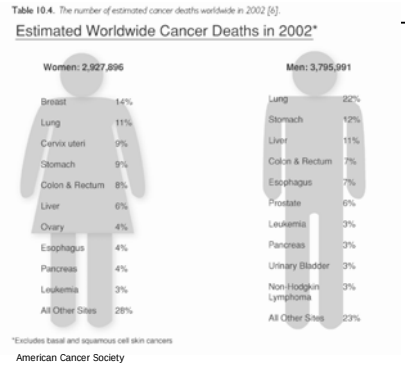
- Today:
  - 11 million new cases every year
  - 6.2 million deaths every year (12% of deaths)
- Can prevent 1/3 of these cases:
  - Reduce tobacco use
  - Implement existing screening techniques
  - Healthy lifestyle and diet
- In 2020:
  - 15 million new cases predicted in 2020
  - 10 million deaths predicted in 2020
  - Increase due to ageing population
  - Increase in smoking

Global Cancer Trends



Worldwide Burden of Cancer

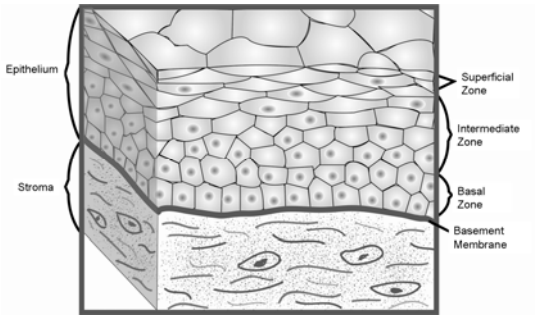
- 23% of cancers in developing countries caused by infectious agents
  - Hepatitis (liver)
  - HPV (cervix)
  - H. pylori (stomach)
- Vaccination could be key to preventing these cancers



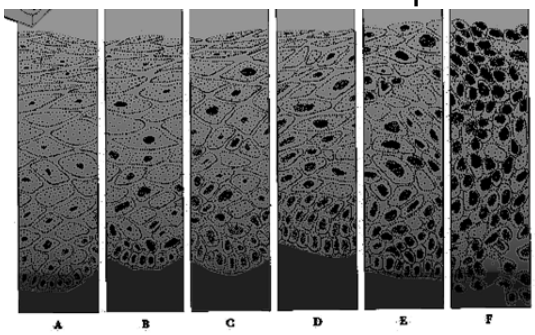
What is Cancer?

- Characterized by uncontrolled growth & spread of abnormal cells
- Can be caused by:
  - External factors:
    - Tobacco, chemicals, radiation, infectious organisms
  - Internal factors:
    - Mutations, hormones, immune conditions

Squamous Epithelial Tissue



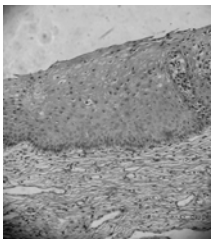
Precancer → Cancer Sequence



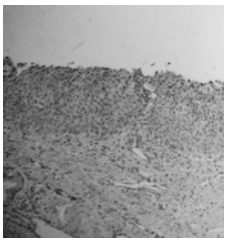
Journal of Nurse-Midwifery, **3b**(5), *McGraw R.K.,* Gynecology: A Clinical Atlas © *1991*

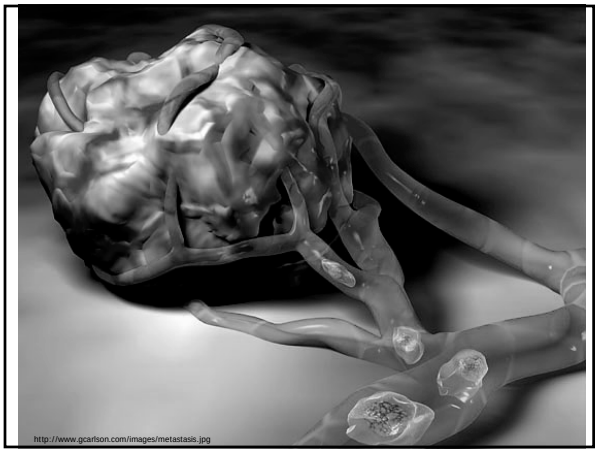
Histologic Images

Normal



Cervical Pre-Cancer





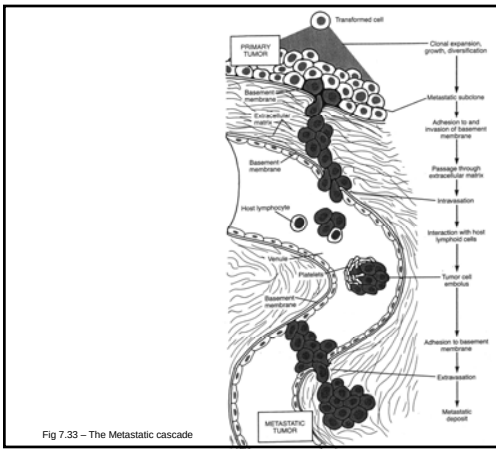
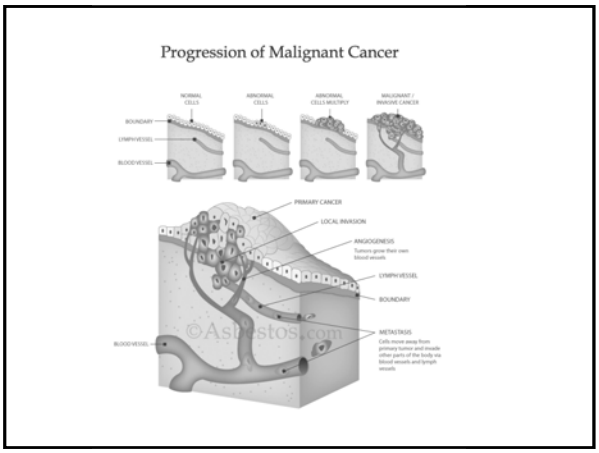


Fig 7.33 – The Metastatic cascade

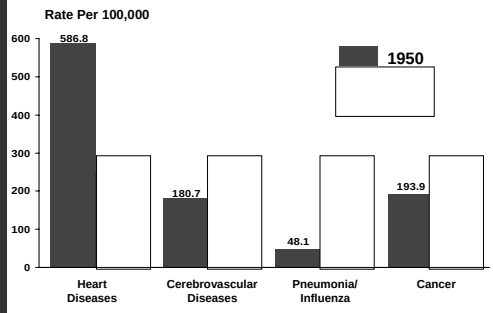
Neoplasia



The War on Cancer

- 1971 State of Union address:
  - President Nixon requested $100 million for cancer research
- December 23, 1971
  - Nixon signed National Cancer Act into law
  - "I hope in years ahead we will look back on this action today as the most significant action taken during my Administration."

Change in the US Death Rates* by Cause, 1950 & 2001



* Age-adjusted to 2000 US standard population.
Sources: 1950 Mortality Data - CDC/NCHS, NVSS, Mortality Revised.
2001 Mortality Data–NVSR-Death Final Data 2001–Volume 52, No. 3.
http://www.cdc.gov/nchs/data/nvsr/nvsr52/nvsr52_03.pdf

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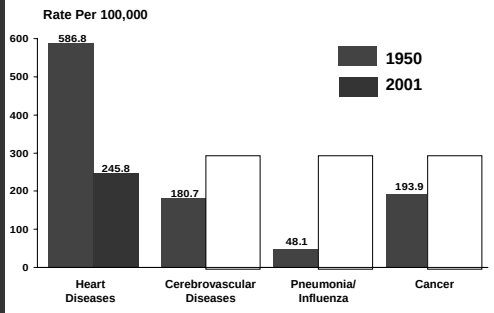

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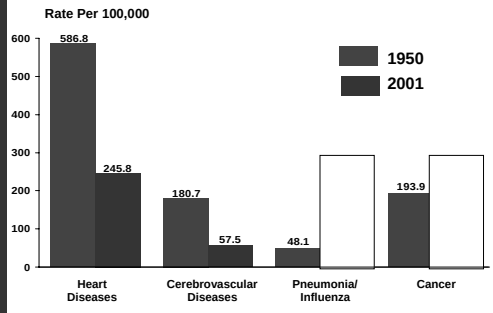

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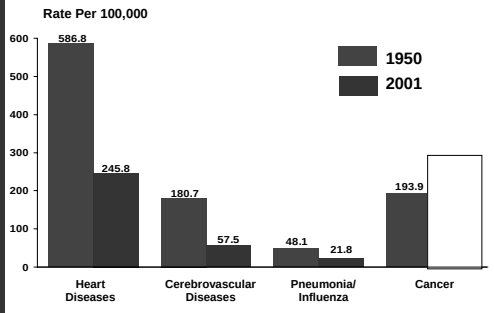

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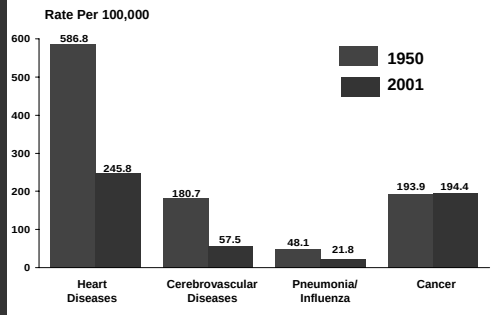

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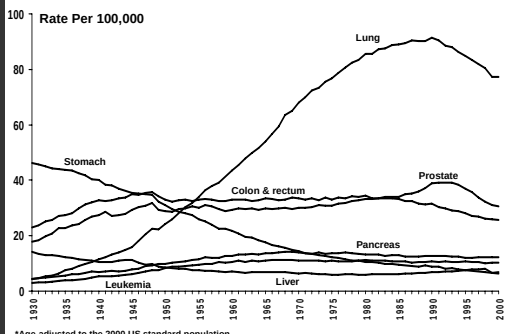
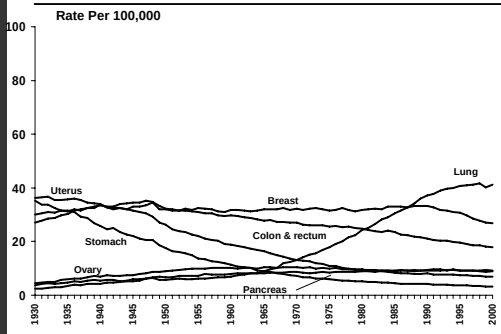
Cancer Death Rates*, for Men, US, 1930-2000



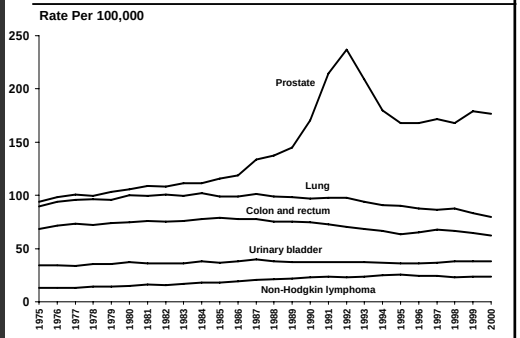
*Age-adjusted to the 2000 US standard population.
Source: US Mortality Public Use Data Tapes 1960-2000, US Mortality Volumes 1930-1959,
National Center for Health Statistics, Centers for Disease Control and Prevention, 2003.

Cancer Death Rates*, for Women, US, 1930-2000



*Age-adjusted to the 2000 US standard population.
Source: US Mortality Public Use Data Tapes 1960-2000, US Mortality Volumes 1930-1959,
National Center for Health Statistics, Centers for Disease Control and Prevention, 2003.

Cancer Incidence Rates* for Men, US, 1975-2000



*Age-adjusted to the 2000 US standard population.
Source: Surveillance, Epidemiology, and End Results Program, 1975-2000, Division of Cancer Control and
Population Sciences, National Cancer Institute, 2003.

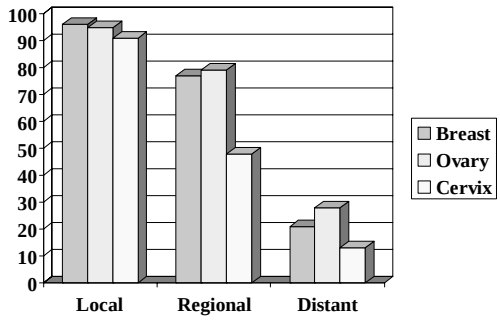
Relative Survival* (%) during Three Time Periods by Cancer Site

Site	1974-1976	1983-1985	1992-1999
All sites	50	52	63
Breast (female)	75	78	87
Colon & rectum	50	57	62
Leukemia	34	41	46
Lung & bronchus	12	14	15
Melanoma	80	85	90
Non-Hodgkin lymphoma	47	54	56
Ovary	37	41	53
Pancreas	3	3	4
Prostate	67	75	98
Urinary bladder	73	78	82

*5-year relative survival rates based on follow up of patients through 2000.
Source: Surveillance, Epidemiology, and End Results Program, 1975-2000, Division of Cancer Control and
Population Sciences, National Cancer Institute, 2003.

Importance of Early Detection

Five Year Relative Survival Rates



Screening

- Use of simple tests in a healthy population
- Goal:
  - Identify individuals who have disease, but do not yet have symptoms
- Should be undertaken only when:
  - Effectiveness has been demonstrated
  - Resources are sufficient to cover target group
  - Facilities exist for confirming diagnoses
  - Facilities exist for treatment and follow-up
  - When disease prevalence is high enough to justify effort and costs of screening

Cancer Screening

- We routinely screen for 4 cancers:
  - Female breast cancer
    - Mammography
  - Cervical cancer
    - Pap smear
  - Prostate cancer
    - Serum PSA
    - Digital rectal examination
  - Colon and rectal cancer
    - Fecal occult blood
    - Flexible sigmoidoscopy, Colonoscopy

Screening Guidelines for the Early Detection of Breast Cancer, American Cancer Society 2003

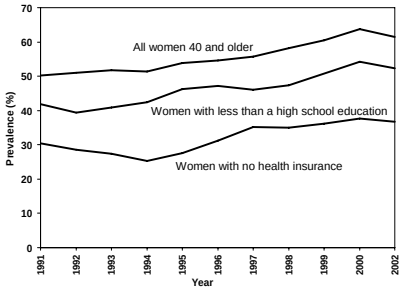
Yearly mammograms are recommended starting at age 40 and continuing for as long as a woman is in good health.

A clinical breast exam should be part of a periodic health exam, about every three years for women in their 20s and 30s, and every year for women 40 and older.

Women should know how their breast normally feel and report any breast changes promptly to their health care providers. Breast self-exam is an option for women starting in their 20s.

Women at increased risk (e.g., family history, genetic tendency, past breast cancer) should talk with their doctors about the benefits and limitations of starting mammography screening earlier, having additional tests (i.e., breast ultrasound and MRI), or having more frequent exams.

Mammogram Prevalence (%), by Educational Attainment and Health Insurance Status, Women 40 and Older, US, 1991-2002



*** A mammogram within the past year. Note: Data from participating states and the District of Columbia were aggregated to represent the United States.**
Source: Behavior Risk Factor Surveillance System CD-ROM (1984-1995, 1996-1997, 1998, 1999) and Public Use Data Tape (2000, 2002), National Centers for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention 1997, 1999, 2000, 2000, 2001,2003.

How do we judge efficacy of a screening test?

Sensitivity/Specificity

Positive/Negative Predictive Value

Sensitivity & Specificity

- Sensitivity
  - Probability that given DISEASE, patient tests POSITIVE
  - Ability to correctly detect disease
  - 100% - False Negative Rate
- Specificity
  - Probability that given NO DISEASE, patient tests NEGATIVE
  - Ability to avoid calling normal things disease
  - 100% - False Positive Rate

Possible Test Results

	Test Positive	Test Negative	
Disease Present	TP	FN	# with Disease = TP+FN
Disease Absent	FP	TN	#without Disease = FP+TN
	# Test Pos = TP+FP	# Test Neg = FN+TN	Total Tested = TP+FN+FP+TN

Se = TP/(# with disease) = TP/(TP+FN)

Sp = TN/(# without disease) = TN/(TN+FP)

Amniocentesis Example

- Amniocentesis:
  - Procedure to detect abnormal fetal chromosomes
- Efficacy:
  - 1,000 40-year-old women given the test
  - 28 children born with chromosomal abnormalities
  - 32 amniocentesis test were positive, and of those 25 were truly positive
- Calculate:
  - Sensitivity & Specificity

Possible Test Results

	Test Positive	Test Negative	
Disease Present	25	3	# with Disease = 28
Disease Absent	7	965	#without Disease = 972
	# Test Pos = 32	# Test Neg = 968	Total Tested = 1,000

Se = 25/28 = 89% Sp =965/972 = 99.3%

As a patient:

What Information Do You Want?

Predictive Value

- Positive Predictive Value
  - Probability that given a POSITIVE test result, you have DISEASE
  - Ranges from 0-100%
- Negative Predictive Value
  - Probability that given a NEGATIVE test result, you do NOT HAVE DISEASE
  - Ranges from 0-100%
- Depends on the prevalence of the disease

Possible Test Results

	Test Positive	Test Negative	
Disease Present	TP 25	FN 3	# with Disease = TP+FN = 28
Disease Absent	FP 7	TN 965	#without Disease = FP+TN = 972
	# Test Pos = TP+FP = 32	# Test Neg = FN+TN = 968	Total Tested = TP+FN+FP+TN = 25+3+7+965 = 1000

PPV = TP/(# Test Pos) = TP/(TP+FP) = 25/(25+7) = .781

NPV = TN/(# Test Neg) = TN/(FN+TN) = 965/(3+965) = .997

Amniocentesis Example

- Amniocentesis:
  - Procedure to detect abnormal fetal chromosomes
- Efficacy:
  - 1,000 40-year-old women given the test
  - 28 children born with chromosomal abnormalities
  - 32 amniocentesis test were positive, and of those 25 were truly positive
- Calculate:
  - Positive & Negative Predictive Value

Dependence on Prevalence

- Prevalence – is a disease common or rare?
  - p = (# with disease)/total #
  - p = (TP+FN)/(TP+FP+TN+FN) = (25+3)/(25+7+965+3) = 28/1000 = .028
- Does our test accuracy depend on p?
  - Se/Sp do not depend on prevalence
  - PPV/NPV are highly dependent on prevalence
- PPV = pSe/[pSe + (1-p)(1-Sp)] = .781
- NPV = (1-p)Sp/[(1-p)Sp + p(1-Se)] = .997

Is it Hard to Screen for Rare Disease?

- Amniocentesis:
  - Procedure to detect abnormal fetal chromosomes
- Efficacy:
  - 1,000 40-year-old women given the test
  - 28 children born with chromosomal abnormalities
  - 32 amniocentesis test were positive, and of those 25 were truly positive
- Calculate:
  - Prevalence of chromosomal abnormalities

Is it Hard to Screen for Rare Disease?

- Amniocentesis:
  - Usually offered to women > 35 yo
- Efficacy:
  - 1,000 20-year-old women given the test
  - Prevalence of chromosomal abnormalities is expected to be 2.8/1000
- Calculate:
  - Sensitivity & Specificity
  - Positive & Negative Predictive Value
  - Suppose a 20 yo woman has a positive test. What is the likelihood that the fetus has a chromosomal abnormality?

Summary of Lecture 12

- The burden of cancer
  - Contrasts between developed/developing world
- How does cancer develop?
  - Cell transformation → Angiogenesis → Motility → Microinvasion → Embolism → Extravasation
- Why is early detection so important?
  - Treat before cancer develops → Prevention
- Accuracy of screening/detection tests
  - Se, Sp, PPV, NPV