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Cancer refers to a group of more than 100 different diseases

characterized by abnormal and unregulated growth of cells

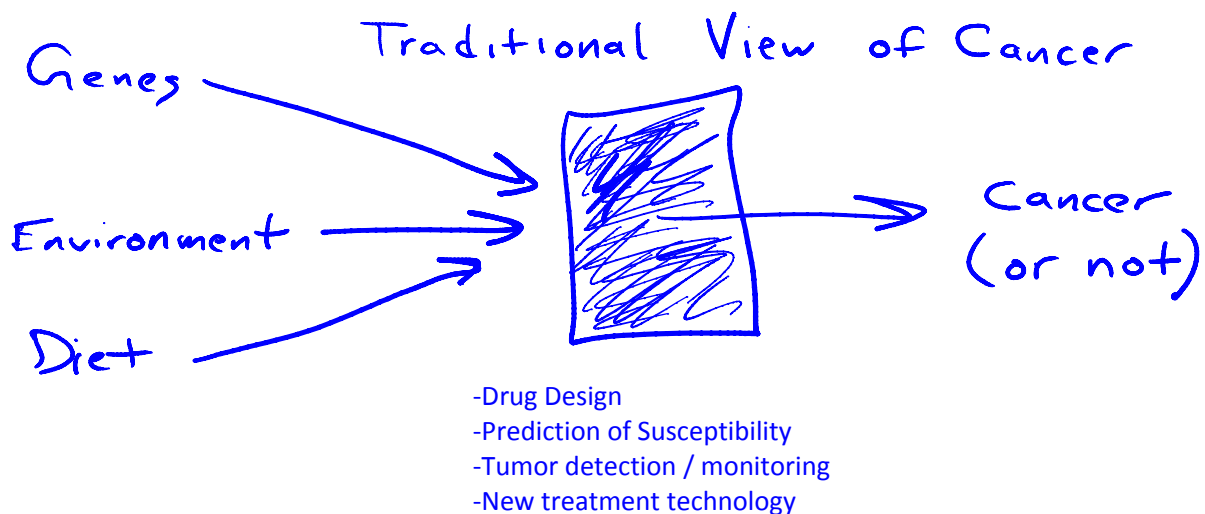
Destroys surrounding tissues Invades

May spread to other parts of the body

Origins

Greek Hippocrates (460-370)

Refers to non-ulcer forming and ulcer-forming growths



Between 50% _ 85% of women carrying the BRCA mutation will develop breast cancer by age 20

BRCA 1 is a gene that codes for a protein which repairs DNA during cellular division. When there is a larger degree of inbreeding, cancer rates can rise disproportionately high

1994 = BRCA gene was cloned.

Oncology: In biblical times the symbolic disease was leprosy. Later it was plague, then tuberculosis and syphilis. All of these diseases, long before the discovery of bacteria and protozoa, carried a faint taint, and aura of accursedness that required some holy intervention to cure. Meanwhile victims were shunned, segregated, often exiled. We may be somewhat more temperate today, but cancer is still thought of, by some, as a dirty, deadly disease, and its victims may be set apart.

11 different types of cancer = 80% of all cancers in the US

Carcinomas = cancer of tissue that makes up the lining of organs or within ducts within organs
Lung / Breast / Colon

Leukemias: spread in the body
Blood stream

Lymphomas: spread in the body via lymph nodes
Lymph Nodes

Sarcomas: cancer of mesodermally derived tissue
Fat, bone, muscle

Skin	600,000
Lung	
Colon	
Breast	
Prostate	

All cancers begin as genetic defects (inherited, acquired or both) that act on individual cells to change their structure and behavior

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- Examining the medical, genetic, and cellular basis of these diseases
- Relationship to normal control of cells and proliferation in multi-cellular organisms
- Media suggests that answers to cancer can be found in **population studies**, rather than true scientific experimentation by doctors. Leads to much more misinformation.

Skin Cancer:

Over a million people will be diagnosed with skin cancer.
The most common type of cancer
80,000 are diagnosed with melanomas (most aggressive)
1 in 71 people will get melanoma in lifetime

- An abnormal overgrowth (a tumor) of certain types of skin cells in the epidermis that began as normal skin structures
- A tumor can be either benign (generally localized and not life-threatening) or malignant (invasive or spreading, and may be deadly)
- Skin cancer is a malignant tumor able to invade surrounding tissues and metastasize (or spread) to other parts of the body but... is largely preventable (8000)
- Causes: solar / ultraviolet radiation is main cause. Artificially produced UV in tanning booths also. Predisposition (genetics), Chemicals like arsenic
- UVA / UVB rays cause sunburn (UVB more likely to cause sunburns) (UVA passes deeper into the skin)
- UVA can cause genetic mutations within the DNA beneath your skin
- Pre-cancerous
 - Actinic keratosis
- Cancerous = INFO AVAILABLE ON SECOND POWERPOINT
 - Basal cell carcinoma =
 - Squamous cell carcinoma =
 - Melanoma =
 - Others - of the specialized structures of the skin =
- Cancer exists as a continuum
- A cell that doesn't divide cannot ever become cancerous
- ABCD's of melanoma
 - A: Assymetry - sides do not match, not round nor square like benign ones.
 - B: Border - Irregular
 - C: Color - very uneven in color, some brown, black, etc.
 - D: Diameter - change in size, larger than a pencil eraser > larger = more dangerous

What is cancer biology?

Cell biology
Genetic
Molecular biology
Biochemistry
Developmental biology
Physiology
Histology
Anatomy
Pathology
Pharmacology
Epidemiology
Medicine - primary care oncology
Mental health- palliative care

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Pre-existing moles:

Early changes:

- New black area
- Scales
- Itching
- Texture changes
- Oozing, bleeding
- Usually do not cause pain

Secondary:

- Primary malignant neoplasm
- Vascularization
- Invasion
- Embolism
- Transport
- Arrest in organs
- Adherence
- Extravasation
- Establishment of microenvironment
- Tumor cell proliferation
- Metastases

Risk factors for skin cancer: light skin color, hair color, eye color, family history, personal history, certain types of moles, or larger numbers of them, freckles, which indicate sun sensitivity, chronic exposure to the sun, history of sun burns early in life.

Treatment: identify

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Prevalence indicates that there are people living with the disease

Death Rate / Mortality: number of people who die from a disease in a defined population in a given amount of time.

Cancer incidence, morbidity and mortality

1.1 million new cases per year in US.

12 million worldwider

.5 million deals per year in us

1,400 deaths per day in us.

6 million deaths worldwide

Cancer is a protracted degenerative, often dehumanizing disease

Hoped that study will be able to

- Improve management
- improve diagnosis
- Increase survival time
- Long term cures
- Prevention

1 in 3 americans will be diagnosed with cancer

1 in 4 deaths attributed to cancer

1 in 2 males get cancer

1 in 3 females get cancer

People over the age of 65 will have 50% of all cancers

30 years ago, 33% survived cancer, now over 50% do

30 years ago 5% of children survived leukemia, now over 70% do

30 years ago, 10% of testicular cancer survived, now 75% do

30 years ago, 50% of men with prostate cancer survived, now 90% survive

AIDS	Cancer
4 deaths per hour	1 death per minute
100 deaths per day	1400 deaths per day

1900's Pneumonia, influenza, tuberculosis, diarrhea, enteritis
1990's heart disease, cancer, stroke

Epidemiology: the study of the distribution and determinants of disease frequency in human populations

Cancer is not a random disease overall

Five main objectives

- To identify the cause of disease and its risk factors
- To determine the extent of disease found in the community
- To study the natural history and prognosis of disease
- To evaluate new preventative and therapeutic measures
- To provide a foundation for developing public policy

People who have no children are at greater risk than those who had children for breast cancer
1775 - Percival Pott - scrotal cancer higher in chimney sweeps

Incidence: a number of new cases in a specified population in a given amount of time

Prevalence: the number of existing cases of disease in a defined population in a given point in time

Primary Cancer: the first occurrence of cancer **Secondary Cancer:** Where it spreads to.

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- Since 1993, we are beginning to see a drop-off in the number of cancer deaths
- Socioeconomics may prevent people from getting testing results
- Graph of lung cancer deaths is very similar to graph of cigarette consumption
- Prostate cancer is probably found in a large majority of individuals
- Prostate cancer in older men is more slow growing
- Breast cancer in younger women is more aggressive than in older
- The age of the individual can affect how their cancer spreads.
- Pancreatic cancer is a perfect example of one with not enough education: there are no markers or anything that you can test to diagnose it.
- Testing with older cancer drugs was attempted as normal lab work. The problem was that people have multiple variable.
- Most cancer drugs work best in concert: "drug cocktails"
- Children are much more resistant and able to take higher dosages of drugs per pound of body weight.

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Etiological Risk Factors: Ones that can be eliminated

The older you get, the more likely you are to get cancer

This suggests something about the causes of cancer

Is not a single event... if it were, it would be just as likely to get it at a younger age as a later age.

Death from cancer is a result of the series of events which occur over time.

Cholera Deaths in London was the leading edge of cancer

Possible Risk factors for cancer:

Smoking, dietary factors, obesity, exercise, occupation, genetic susceptibility, infectious agents, reproductive factors, socioeconomic status, environmental pollution, UV light, radiation, prescription drugs, electromagnetic fields

Risk: an individual's risk for getting a disease

Relative Risk: your risk compared to others without (or with)

There is a time lag between the beginning of cancer and the starting of smoking

Epidemiology and Breast Cancer

Age at which a woman has first child is correlated with breast cancer

Person who has no children has an incidence equal to person whose first child is born when they are 35

Person whose first child is born when they are below 35 has less risk of breast cancer

Atypical Hyperplasia - first indication of irregularity (greater growth)

Mammogram -

Cervical Cancer:

PAP smears for women starting at 21, stopping by age 30 with 3 "normal" results

Colorectal Cancer:

Beginning at age 50 men and women should have one of the following exams

FOBT (fecal occult blood test) - once a year

FSIG (flexible sigmoidoscopy) - once every 5 years

Combination of the above two

Double-contrast barium enema - every 5 years

Colonoscopy - every 10 years

Looking for benign polyps - what do the cells look like on removal.

You want to catch cancer before it spreads

The prostate specific antigen (PSA) antigen test and the digital rectal examination should be offered annually, beginning at age 50 to men who have a life expectancy of at least 10 years

Men at high risk (african american males)

Japan has highest stomach cancer. Why?

Is it genes? Tremendous movement of people from Japan to USA?

Cancer: Definitions and Classifications

- Neoplasia = new growth
 - Abnormal mass of tissue with growth that exceeds and is uncoordinated with that of the surrounding normal tissues
 - Autonomous
- Tumor = synonymous with neoplasm
- Cancer = common term for malignant neoplasm
- Neoplasm have parenchyma and stroma
 - Parenchyma/ Stroma: the parenchyma of an organ consists of that tissue which conducts the specific function of the organ and which usually comprises the bulk of the organ. Stroma is everything else, connective tissue, blood vessels, nerves, ducts
 - The parenchyma / stroma distinction provides a convenient way to circumvent the listing of tissue types when discussing an organ.
- Benign and malignant tumors each have their own nomenclature.
- Neoplasia - definition:
 - A pathological process due to loss of normal genetic control of cellular proliferation differentiation and or cell death resulting in excessive and inappropriate growth of a cellular population which is genetically unstable, and which may progress through accumulation of further genetic alterations to become an invasive and metastatic tumor
- Benign/ Malignant Tumors
 - In the common use, the terms benign and malignant refer to the overall biological behavior of a tumor rather than to its morphological characteristics
 - In most circumstances, malignant tumors kill, whereas benign ones spare the host
 - However, so called benign tumors in critical locations can be deadly
 - The difference between their appearances is minimal compared to the behavior of the cells
 - Benign tumor may arise in any tissue, grow locally, and cause damage by local pressure and obstruction
 - The common feature is that they do not spread to distant sites (no metastasis)
- Benign vs. Malignant
 - Differentiation
 - Rate of Growth
 - Local Invasion
 - Metastasis

Types of cellular abnormalities which may lead to cancer.

Hyperplasia (non-neoplastic)

Abnormal increase in cell number without significant structural change (reversible)

Metaplasia (non-neoplastic)

Abnormal increase in cell where one type of cell substitutes for another (reversible)

Dysplasia (non-neoplastic or neoplastic)

Cell uniformity is lost and polymorphism exhibited. May be pre-cancerous (reversible)

Anaplasia (neoplastic)

De-differentiation of cells. Malignant (irreversible)

Non-neoplastic proliferation

Hyperplasia - an increase in the number of cells in a tissue or organ. Occurs only in cells capable of replication

Physiological: hyperplasia and hypertrophy of uterine smooth muscle erythropoiesis at high altitudes

Pathological: endometrial hyperplasia

Metaplasia - the replacement of one type of normal cell with another type of normal cell.

Reversible

Replacement of columnar epithelial cells with the more

Dysplasia

Denotes a loss of architectural organization and a loss of cell uniformity and epithelium
Pleomorphism and mitoses are more prominent than in the normal

Usually graded: mild, moderate, severe and carcinoma in situ

Mild to moderate dysplasia is potentially reversible

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- Dysplasia: denotes a loss of architectural organization and a loss of cell uniformity in epithelium
- Pleomorphism and mitoses are more prominent than in the normal
- Usually graded: mild, moderate, severe, and carcinoma-in-situ (is infact a cancer which has not yet spread)
- Mild to moderate dysplasia is potentially reversible

- Anaplasia: cells have really lost it:
- Irreversible loss of normal cell structure and function
- Positional anaplasia: size shape arrangement, and overall organization of cells in a tissue are altered
- Cytological anaplasia:

Differentiation and anaplasia

Differentiation = extent of which neoplastic cells resemble normal cells

Anaplasia = lack of differentiation

Cancer is not simply reverse differentiation

In general, benign tumors are well differentiated

Malignant tumors may be differentiated but most aggressive tend to appear undifferentiated

Characteristics of Anaplasia:

Severe Dysplasia - disordered growth

Pleomorphism

Abnormal cell positioning and size

Natural history of malignant neoplasm

- 1) Something happens to A SINGLE cell
- 2) Goes through some changes which are results of mutational changes
- 3) Undergoes a malignant transformation
- 4) Outgrows other cells and gets an advantage
- 5) Turns into a tumor as it gets bigger
- 6) Metastasis

Stages in human carcinogenesis

An initiated cell is one in which an environmental carcinogen has interacted with DNA to produce a mutation, often a single base alteration in the genome

Hyperplasia, look normal but continue dividing at a higher rate than normal

Clonal in appearance

An initiated cell is not a tumor cell because it has not yet acquired autonomy of growth

The DNA alteration may remain undetected throughout the life of the organism unless further events stimulate development of a tumor

Metabolism may activate or inactivate the chemical carcinogens

DNA repair: may either correct or introduce an altered base into the genome

Proliferation is necessary to permanently embed the change in the genome

Promotion: The clonal expansion of a changed cell which gives a mutation the selective advantage.

Conversion: clinically detectable - in situ, not doing anything bad yet, but ready to

Progression: anaplasia recognizable, cancer has spread with advantages

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Phenotypic changes (reflecting genotypic changes)

- Autocrine growth regulation
- Loss of responsiveness to environmental signals
- Altered immunological profile
- Accelerated growth
- Loss of growth controls
- Increased malignancy
- Increased invasiveness
- Changes in hormonal responsiveness
- Ability to metastasize
- Loss of susceptibility to antineoplastic drugs

From one transformed cell, to the smallest detectable mass takes 30 doublings (1 g)

To reach 1 kg needs only 10 more doublings

Cancer progression is a darwinian process: a cell is given an advantage

A tumor is not a single cell, though it does start as one. Over time it increases mutations and replications

Once you have the full tumor, it is made up of lots of different cells, not all will have the ability to metastasize, but a population does.

Final changes are the ability to invade and the ability to metastasize. Can infiltrate normal tissue and they have the ability to settle down in new areas of our bodies.

- Model for cancer growth
 - Initiation
 - Promotion
 - Progression
- Series of phenotypic changes in the cells
 - Loss of responsiveness to environmental signals
 - Altered immunological response
 - Accelerated growth (at least continuous)
 - Increased invasiveness
 - Changes in hormonal responsiveness
 - Ability to metastasize
 - Loss of susceptibility to antineoplastic drugs

Normal cells	Cancer Cells
Limited number of divisions 50+	Unlimited division
No telomerase synthesized	Cancer cells produce telomerase
• Need complex media (blood serum)	Grow in less complex media
Exhibit contact inhibition	No contact inhibition
Normal karyotype	Can cause cancer when injected into moice
	Polyploidy and or aneuploidy

- Angiogenesis: Blood systems; cancer tumors develop a blood system around themselves
- Lung Cancer a model for cancer:
 - The leading cause of death due to cancer in the US
 - There are two main types
 - Small cell (20%)
 - Non-Small Cell (80%)
 - Lung Cancer identification and staging
 - CT Scans, and observations during surgery
 - Determines type of treatment and prognosis
 - Lung cancers typically start in the spongy, pinkish gray walls of the bronchi
- Some cancers make proteins which can be easily detected because only they can make these
- Pockets of air in lung produce pockets on surface of lung
- Grayism mass of tissue starts to block air passages
 - Interferes with lung function
 - Lung tissue sick - not enough oxygen
 - Part of lung may collapse
- Basal cells taking over
- Hard masses keratin accumulate in tumor tissue
- Eventually, lung ceases to function
- Symptoms of lung cancer
 - Cough
 - Frequent attacks of pneumonia and bronchitis
 - Pain in chest
 - Coughing up blood
 - Weight loss
 - These symptoms are not specific to cancer, so they can be easily overlooked.

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- Chest x-ray with greater than 1 cm tumors
- Sputum test
 - Cells spit up with mucous from lung examined
- CAT scan
 - Uses x-rays aimed at different angles to make a 3D Image
- Fiberoptic bronchoscope
 - Tube with strands that transmit light... can do biopsy
- Surgery - looking at lung physically

- TUMOR CLASSIFICATION BY CELL TYPE: MALIGNANT AND BENIGN
 - Benign tumors:
 - Based on parenchymal component
 - Mesenchymal tumors add -oma to cell of origin
 - ◻ Fibroblasts - fibroma
 - ◻ Cartilage = condroma
 - ◻ Osteoblasts - osteoma
 - Epithelial tumors can be named for cell of origin, microscopic architecture, or macroscopic appearance
 - Adenoma - glandular appearance or from glandular tissue

- Egypt

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- ★ • Tumor Growth and Metastasis Depends on Angiogenesis
 - Invasion and Metastasis -
 - Attachment
 - Local breakdown
 - Locomotion
 - Secondary tumor (Metastasis)
 - What is Metastasis
 - The ability of cancer cells to penetrate into lymphatics and blood vessels
 - What is Angiogenesis
 - The development of a new network of blood systems into a tumor
 - One of the critical events required is the
 - Tumor angiogenesis is the proliferation of a network of blood vessels that penetrates into cancerous growths
 - Starts with cancerous tumor cells releasing molecules that send signals to surrounding normal host tissue.
 - The walls of blood vessel are formed by vascular endothelial cells.
 - These cells rarely divide
 - Angiogenesis can stimulate them to divide

VEGF = vascular endothelial growth factor

bFGF = basic fibroblast growth factor = most important

VEGF and bFGF are first synthesized inside tumor cells and then secreted into the surrounding tissue

Bind to receptors in the endothelial cells

This starts cascade of events turning on new genes to produce new endothelial cell growth

Clinical Trials

a research study
not random

Naming of
malignant tumors

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- Malignant Tumors usually called carcinomas
 - Squamous cell carcinoma - squamous pattern
 - Adenocarcinoma - glandular growth pattern
 - Can either be named for organ of origin or "poorly differentiated" or "undifferentiated"
- Mesenchymal tumors usually called sarcomas
 - Fibrosarcoma, liposarcoma, leiomyosarcoma, rhabdomyosarcoma, etc
- Many exceptions - some use common name
- More undifferentiated they are the more aggressive they are
- Malignant Tumors in epithelial cells
 - Well differentiated, moderately differentiated, poorly differentiated
 - Squamous carcinomas
 - Adeno-carcinomas
 - Alveolar
 - Papillary
 - Tubular, etc.
- Sarcoma
 - Malignant tumor arising from connective tissue of those structures derived from connective tissue, bone, muscle, subcutaneous tissue
 - Chondroma - cartilage
 - Osteosarcoma - bone
 - Angiosarcoma - blood vessel
 - Glioma - Brain (Glial Cells)
 - Rhabdomyosarcoma - muscle (striated)
- Tumor Identification
 - By organ of origin
 - Breast, prostate, lung, etc.
 - By Cell type
 - Benign
 - Often ends in
- **BRAIN TUMORS:**
 - An abnormal growth of tissue in the brain
 - More than 17,000 brain tumors are diagnosed in the US each year
 - There are two classifications of brain tumors
 - Considered benign if
 - Composed of non-cancerous cells
 - It has clearly defined borders
 - Does not spread beyond the part of the brain where it originates
 - It can usually be completely removed
 - It is unlikely to recur
 - They cause: severe pain, permanent brain damage, death... they can also become malignant
 - Considered Malignant if:
 - It's composed of cancer cells
 - Or it is composed of harmless cells located in an area where is suppressed one or more vital functions.
 - Do not have distinct borders
 - Tend to grow rapidly , increasing pressure in the brain

- Can spread in the brain and spinal cord past where they originated
 - Highly unusual for them to spread beyond the central nervous system
- Primary brain tumors: those that originate in the brain
 - Relatively rare type of cancer
 - Only 1% of all solid tissue cancers
- Secondary brain tumors: originate in other parts of body and travel to brain
- Low Grade brain tumor
 - Well defined borders
 - Some form in cysts
 - Grow slowly if at all
 - Spread throughout the brain
- Medium Grade to high grade tumors
 - Truly malignant
 - Grow much more rapidly
 - Infiltrate healthy tissue
 - Recur more often than low-grade tumors
 - The growth pattern makes it difficult to remove the entire tumor
- Hematological Malignancies
 - Clonal expansions of neoplastic cells derived from or resembling normal hematological cells
 - In general, leukemias and lymphomas are classified according to the stage of normal hematopoiesis at which their neoplastic cells appear to be locked.
 - Most hematological malignancies are either
 - Leukemias or lymphomas
 - Leukemia: malignant tumor of the blood forming tissues: chronic or acute
 - Lymphoma: malignant tumor of the lymphatic system (Hodgkins or non-Hodgkins)

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- Leukemia Classification and Incidence:
 - Acute and chronic leukemias are classified as lymphocytic or myelogenous according to the predominant cell type.
- **Acute Leukemia**
 - Progresses rapidly, characterised by ineffective immature cells in the bone marrow pushing out the normal cells
 - AML - acute myelogenous leukemia adults
 - ALL - acute lymphocytic leukemia
 - Symptoms: pallor, headache, fatigue, loss of appetite, enlarged spleen.
- Chronic Leukemia
 - Progresses slowly and rarely affects people under age 20
 - Chronic myelogenous leukemia CML strikes ages 40-50 more common in males
 - Chronic Lymphocytic leukemia (CLL) strikes after age 40 and is most common in older men
- Diagnosis of CML: Magic Bullet Treatment
 - Too many neutrophils and the Philadelphia chromosome
 - Chronic phase: follows an indolent course, mild symptoms, <10% blasts in marrow
 - Accelerated Phase: Characterized by spleen enlargement and progressive intermittent fevers, night sweats, and unexplained weight loss
 - Blast Phase: characterized by transformation to a very aggressive acute leukemia. Patients die in this phase.
- Lymphomas
 - Signs and symptoms
 - Enlarged lymph nodes are a hallmark of both types of lymphomas
 - Lymphomas are identified as type A (no symptoms) or type B symptoms including fatigue, fever, chills, night sweats
 - Diagnosis: biopsy of enlarged lymph nodes
- How far has cancer progressed?
 - Staging and Grading
 - Staging is based on clinical, radiological and surgical criteria such as tumor size, involvement of regional lymph nodes and presence of metastases.
 - Why?
 - Different behaviors, treatments and prognosis
 - Assists in finding etiology
 - Assists in evaluating various therapies
 - Grading: estimates aggressiveness based on anatomical cytological, differentiation and number of mitoses (degree of anaplasia)
 - Gross Form - enclosed vs. diffuse
 - Grades I, II, III, IV (most anaplastic)
 - TNM System:
 - T = tumor size and spread = grades 1 - 4
 - N = lymph node involvement, number, size, mobility
 - M = metastasis, number organs, impairment
 - Gives long term survival estimate
 - I: 70-80%
 - II: 45-55%
 - III: 15-25%
 - IV : Under 5%
- Metastasis:
 - Indicates Malignancy
 - A discontinuous spread of tumor

- Methods of metastasis include
 - Seeding of body cavities
 - Lymphatic spread
 - Hematogenous spread

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Breast	Axillary lymph nodes, opposite breast, lymphatics
Lung	Lymph nodes, liver, bone brain

- Cancer: cellular and molecular biology: cell cycle control
- Cancer is dysregulated or uncontrolled cell proliferation
- Cell proliferation is governed by the cell cycle
- To understand root causes and monitor the progression of cancer, one must examine the cell cycle
- G1 = first gap or growth phase during which the cell prepares for dna replication
- S = the time period during which dna synthesis occurs and a copy of the dna is created
- G2 = second gap or growth phase during which the cell prepares for mitosis or cell division
- Cyclins and cyclin dependent kinases
 - Two types of regulatory proteins are involved in cell control
 - Cyclins and cyclin dependent kinases (Cdk)
 - Kinases - take phosphate from ATP and add it to a protein or other substrate
 - CDKS - cyclin dependent kinases
- Cellular checkpoints are nothing more than chemical reactions which are made by DNA
- Mutations that alter gene control systems... (cancer is mutagenic)
- Cell cycle control at different levels
 - Extracellular signals
 - Receptors
 - Signal transducers
 - Transcription factors checkpoints and cell cycle regulators
 - Housekeeping genes

11 / 26 / 07 - 2nd Floor Kerr Hall (in study center)

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- Video was a story of one of the major cancer researchers and physicians
- Working on a different approach to cancer
 - Trying to get the immune system to recognize cancer cells
 - Some cancer cells make markers (gene products)
 - If you can get white blood cells to attack markers, you can attack cancer cells
- ★• Review sheet for final exam
- ★• Sample exam - to prepare for final (check for chapter reviews on website)
- Cancer is a genetic disease of somatic cells. Mechanisms that normally control proliferation and cell death are subverted
- Cell cycle is key to understanding cancer
- Each human cell contains approximately 25-35000 genes
- Some genes are responsible for control of cellular proliferation
- If these genes become mutated, cell proliferation becomes abnormal
- Abnormal cell proliferation is a hallmark of cancer
- Progression through the cell cycle and ultimately cell division is controlled by the regulated expression of genes
- Involves equilibrium between expression of genes responsible for positive regulation of cell proliferation and expression of genes responsible for negative regulation of cell proliferation
- G1/S: monitors cell size and for DNA damage
- G2 /M: replication complete, DNA Damage
- M: spindle fibers connected etc
- G0: does body require more of my type of cell
- Alterations in three types of genes cause cancer
 - Oncogenes: related to cells moving forward in cell cycle
 - Tumor suppressor: make proteins which stop cells from dividing when they should stop
 - Stability genes: move cells through the dying cycle
- Proto-Oncogenes
 - These are normal genes present in every cell that act to promote cell division
 - Proto-oncogenes are tightly controlled and only act when conditions are appropriate for cell division
 - When mutation increases the activity of proto-oncogenes or remove their normal controls, the proto-oncogenes become an oncogene - a step toward CA
 - Proto-oncogenes promote cell growth and require the alteration of only one allele to create out of control cellular growth
 - Dominant genes
 - Mutated in ways that cause genes to be constitutively active or active under conditions when wild type gene is not
 - Can result from chromosomal translocation, intragenic mutation and gene amplifications
 - The normal counterpart of oncogenes are called proto-oncogenes (wild type allele)
- Normal cells growing in culture need growth factors present in the medium to divide
 - PDGF: (platelet derived growth factor) is encoded by the oncogene SIS
- Signals for normal mitosis and oncogenes
 - Binding of growth factor to its receptor triggers a cascade of signaling events within the cytosol. Many of these involve protein kinases

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- Oncogenes
 - Characteristics of oncogenes
 - Usually exhibit a dominant phenotype at cellular level
 - Only one copy needed to give effect
 - Usually requires that more than single mutation in this cell class to turn into neoplasia
 - May be transmitted from generation to generation when mutation occurs in germ lines
 - Rarely occurs (in the gametes) screws up replication from the beginning

Gene	Function	Familial Disorders	Sporadic
DCC	Cell surface interactions	Unknown	Colorectal cancer
WT1	Transcription	Wilm's tumor	Lung cancer
Rb1	Transcription	Retinoblastoma	Small-lung carcinoma
P53	Transcription	Li-fraumeni syndrome	Breast, colon, and lung cancer

- Retinoblastoma 1 Gene
- Involved in breast, bone, lung, bladder, and retinal cancers (among others)
- Inheriting one mutated (inactivated) copy of gene

- Oncogenes and tumor suppressor genes drive the neoplastic process by increasing the cell number through the stimulation of cell death
- Housekeeper genes
 - Third class of genes called stability genes or caretakers
 - This class includes the mismatch repair nucleotide excision repair and base excision repair genes responsible for repairing subtle mistakes made by DNA replication or by exposure to mutagens
 - If a mutation occurs in somatic cells then this would potentially cause a sporadic case of cancer
 - If only a single mutation was necessary to cause cancer, you would always be likely to get cancer... since it takes time for mutations to occur, it is a strong suggestion that it takes multiple genes making it a disease of the elderly

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★ THE ENDS OF CHROMOSOMES ARE CALLED??????
Possibly two points on the final exam

Telomeres are

Repetitive DNA sequences at the ends of all human chromosomes
They contain thousands of repeats of the six nucleotide sequences
Cancer cells have a lot of telomerase