CANCER
Causes, Prevention, Screening, Early Diagnosis, and Treatment”

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Why this new course?

- Educated people should know the true facts
- To understand the known causes of cancer
- To be able to prevent the disease
- To understand the diagnosis and treatment
- To empower ourselves through knowledge
WHY DID I GET INVOLVED WITH THIS COURSE?

• I like teaching
• I am committed to helping people understand their health problems
• I believe that it is the duty of physicians to help people know the facts and avoid false advertisement
DISCLAIMER AND CREDITS

Disclaimer: Nothing to declare

Credits:

1. Personal teaching and clinical files
2. Multiple Internet programs
3. Books and journals
PLAN OF COURSE

1. **Basic Biology and Organism Functions:**
   a. Cell and tissues
   b. What is cancer and its causes

2. **Cancer Prevention and Cancer Screening**

3. **Early Diagnosis**

4. **Cancer Treatment**
LECTURE #1
Characteristics of life are traits that all living organisms share.

There are 11 characteristics of life that humans share with other organisms:

1. **Movement** – Self-initiated change in position, motion of the internal organs
2. **Responsiveness** - Ability to sense changes within or around the organism and react to them
3. **Growth** - Increase in body size
4. **Reproduction** - Produce offspring \( \Rightarrow \) producing new individuals
5. **Respiration** - Obtaining oxygen and releasing CO$_2$

6. **Digestion** - Chemically changing food substances, and getting rid of wastes

7. **Absorption** - Passage of digested products through membranes and into body fluids

8. **Assimilation** - Changing absorbed substances into chemically different substances

9. **Circulation** - Movement of nutrients throughout the body
CHARACTERISTICS OF LIFE (III)

10. Excretion - Removal of wastes

11. Metabolism –
  • A. The acquisition of food
  • B. Utilization of its energy
  • C. Waste excretion

How are the characteristics of life dependent on metabolism?
  • We need food and energy to be able to do all of the characteristics of life
MAINTENANCE OF LIFE: Requirements of Organisms (1)

- Life requires certain environmental factors:

1. **Water** - Most abundant compound in body, required for metabolic processes, transport of substances, and regulation of temperature

2. **Foods** - Provide chemicals and water, used for energy, making new living matter, or regulating chemical reactions

3. **Oxygen** - Used to release energy from food substances which drives metabolic processes

4. **Heat** - Form of energy, product of metabolic reactions
5. **Pressure** - Application of force to something helps humans breathe, also used inside body to push blood through blood vessels

6. **Digestion** - Chemically changing food substances, and getting rid of wastes

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HOMEOSTASIS

- Maintains an internal **stable environment** (water, nutrients, oxygen, and heat)
- The body does this with **homeostatic mechanisms** which are self-regulation control systems that have 3 components:

1. **Receptor** - provides info. about specific conditions (stimuli) in the internal environment
2. **Set point** - tells what a particular value should be (temperature of body 98.6°F)
3. **Effectors** - causes responses that alters condition in the internal environment
HOMEOPTASIS
FEEDBACK MECHANISMS

Phases

• Sensor mechanism senses disruption in homeostasis
• Control center
• Effector mechanism to restore homeostasis

Example

• High blood sugar
• Brain center
• Insulin ➤ Normal blood sugar
THE CELL
The Cell
THE CELL

**Nucleus**: Contains the DNA (genetic material)

**Cytoplasm**: Cell mass with organ-specific functions

**Organelles: Mitochondria** – cell energy (ATP)

- **Ribosomes** – protein synthesis and fat metabolism
- **Golgi apparatus** – processes proteins
- **Endoplasmic reticulum** – transports proteins and lipids
- **Lysosomes** – digestive enzymes

**Cell membrane** - Various constituents, biochemical and immunologic receptors
Fig. 3. Events in the cell cycle.
The Cell Cycle

- G2
  - Cell Growth
  - Duplication of Organelles
  - Prep Cell Division

- M
  - Mitosis
  - Cell Division

- G1
  - Cell Growth
  - Duplication of Organelles
  - Prep for DNA replication

- S
  - DNA Replication

18 – 24 hours
Cell Division (Mitosis)
**CELL DIVISION (MITOSIS)**

**Prophase:** Nuclear membrane dissolves
   Nuclear DNA ➢ Chromosomes. Each has a pair of chromosomes connected to a centromere by a spindle of fibers

**Metaphase:** Centromeres divide pulling the chromosomes apart

**Anaphase:** Centromeres separate and chromosomes are pulled toward opposite sides of the cell ➢ 46 chromosomes on each side of the cell

**Telophase:** New membrane around each set of 46 chromosomes., Spindle fibers disappear, cytoplasm divides. Two daughter cells
Tissues

Four types of tissue

Connective tissue

Epithelial tissue

Muscle tissue

Nervous tissue
From an Atom to a Man
ORGANIZATION OF THE HUMAN BODY

• Human organism is a complex structure composed of many parts

• It has several body cavities lined by membranes

• A variety of organ systems
Dorsal Cavity

Lateral view
ORGAN SYSTEMS (1)

• Body Covering:
  • **Integumentary system**

• Support and Movement:
  • **Skeletal system; Joints and Muscular system**

• Integration and Coordination:
  • **Nervous system; endocrine system** (hormones -secreting glands)

• Transport:
  • **Cardiovascular system; Lymphatic system**
• Absorption and Excretion:
  • Digestive system; respiratory system; urinary system

• Reproduction:
  • Reproductive system
Some Terms Used In These Lectures

Mitosis = Cell (nucleus) divides. Four phases.

Metabolism = Life-long biochemical processes

Atrophy = Cells shrink (skin, brain)

Hypertrophy = Cells increase its size (uterus in pregnancy)

Hyperplasia = Cells multiply (trained muscle)

Dysplasia = Changes due to chronic irritation (skin, bladder)

Degeneration = Changes in cytoplasmic components (water, fats, pigment, calcium)

Necrosis = Cell death
CELL INJURY
TYPES OF CELL INJURY

Cell aging – natural event

Toxic - endotoxic: diabetes, gout
- exotoxic: Alcohol, CO, lead, medications

Infections - viral, bacterial, protozoan, fungal

Physical - wounds, thermal (U/V, radiation, electrical)

Deficit: \( \text{H}_2\text{O}, \text{O}_2 \), nutrients, vitamins

Vascular - Lack of blood supply
CELL AGING

A normal biological process, with individual variances in absence of pathologic events

Skin and its glands and elastic tissue atrophy ➢ dry skin and wrinkles

Muscles atrophy, reduced muscle mass ✔️ strength

Arteries lose their elastic tissue ➢ hardening of their wall ➢ high blood pressure and decreased blood supply

Digestive glands atrophy ➢ ✔️ secretions ➢ impaired digestion and motility ➢ constipation

Nerve cells atrophy and death ➢ mental dysfunctions
PROTECTIVE MECHANISMS

Natural:

• **Skin and mucous membranes** integrity
• **Lysozymes**
• **Cilia** (hair-like threads) in the nose and pulmonary airways
• **Blood** white blood cells (granulocytes and lymphocytes)
• **Humoral:** Antibodies

**Acquired:** Vaccinations
CELL INJURY - REACTION

- Exposure to injury
- Cell may adapt its structure and function
- Homeostasis is disturbed
- Cell degeneration
- Cell death
- Disease (occult) → Illness (signs & symptoms)
CAUSES OF DISEASES

**Intrinsic:** Age, gender, heredity, habits, lifestyle

Diseases: Atherosclerosis, Diabetes mellitus, Cancer

**Extrinsic:** Infections, accidents

Environment

Stress
DISEASE EVOLUTION

1. Exposure to injury
2. Incubation
3. Prodromal signs
4. Acute phase of signs and symptoms
5. Recovery
6. Convalescence
7. Healing (?)
ONSET, COURSE, AND RECOVERY

Acute disease – End point is healing

Chronic disease – No healing, Exacerbations
STRESS AND DISEASE

**Stress:** Physiologic or psychologic ➢ Alarm reaction – “flight-or-fight” ➢ Central nervous system and hormones activity ➢ End of Stress, homeostasis restored

If stress continues:

Coping mechanisms activated ➢ Recovery

If no recovery:

Exhaustion of homeostasis ➢ Onset of disease
Standing Tube of Whole Blood

--- Plasma

--- White Blood Cells & Platelets

--- Red Blood Cells
BLOOD COMPONENTS

- **Plasma**
- **Cells:**
  - Red blood cells (RBC or erythrocytes)
  - White blood cells (WBC):
    - *Granulocytes: neutrophils, eosinophils, basophils*
    - *Lymphocytes*
    - *Monocytes*
  - Platelets
CELLULAR BLOOD COMPONENTS

RBC - Carry Oxygen and CO$_2$

WBC - Various functions

Neutrophils - Fight infections

Lymphocytes - Active in immune responses

Monocytes - Promote neutrophils

Eosinophils - Active in allergy

Platelets - Essential in initiating blood clotting
Blood film (smear) to show:
Red blood cells, white blood cells (neutrophils), and a platelet
Stem Cell and Blood Cells

Multipotent hematopoietic stem cell (Hemocytoblast)

- Common myeloid progenitor
  - Erythrocyte
  - Mast cell
  - Myeloblast
  - Megakaryocyte
  - Thrombocytes

- Natural killer cell (Large granular lymphocyte)
  - Monocyte
  - Macrophage

- Common lymphoid progenitor
  - Small lymphocyte
    - T lymphocyte
    - B lymphocyte
  - Plasma cell
White Blood Cells

- Monocyte
- Eosinophil
- Basophil
- Lymphocytes
- Neutrophil

White Blood Cells
LYMPHATIC SYSTEM

Lymph Capillaries in the Tissue Spaces

- Lymph capillary
- Arteriole
- Tissue fluid
- Tissue cells
- Tissue spaces
- Venule
- Lymphatic vessel
THE LYMPHATIC SYSTEM

- Intercellular space
- Lymphatic capillaries
- Lymphatic vessels (afferent and efferent)
- Lymph nodes, spleen (see the Immune System)
- Thoracic duct
- Blood
- Thymus
- Spleen
The Female Breast
The Spleen
The Host Defences

**Physical barriers**: Integrity of skin and mucous membranes (lining of the GI and GU system), conjunctiva, nasal membranes

**Chemical barriers**: Lysozymes (antibacterial substances) in tears, in the secretions of stomach, prostate, and vagina

The inflammatory response

The immune response
THE INFLAMMATORY RESPONSE

Vascular and cellular changes in presence of a change in homeostasis (physical or chemical injuries, infections, foreign bodies)

1. Vasodilation ➢ redness, local warmth
2. WBC infiltration
3. Swelling ➢ nerve irritation ➢
4. Pain
WOUND HEALING

A surgical cut is sutured:

1. Small amount of blood escapes from the blood vessels
2. Platelets from the blood arrest the bleeding
3. Blood clots on site
4. White blood cells and macrophages (scavenger cells) move to the site
5. Bacteria and any foreign matter are removed by these cells
6. Collagen is laid into the wound
7. Healing ensues in 10-14 days
THE IMMUNE SYSTEM
CELLULAR COMPONENTS OF THE IMMUNE SYSTEM

- Lymph nodes
- Spleen
- Thymus
- Tonsils and lymphatic tissue in the pharynx
- Lymphatic tissue in the GI tract
CELL-MEDIATED IMMUNITY

**T-lymphocytes** (activated in the thymus) 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 (from the bone marrow) 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)
- IgD
DISEASES THAT COMPROMISE THE HOST DEFENCE MECHANISM

Hodgkin’s disease
Lymphomas
Leukemias
Multiple myeloma
Carcinomas and sarcomas
Inherited or acquired primary immunodeficiency disease
GENETICS – STUDY OF HEREDITY

• Human gametes: Ovum (ova) and Spermatozoa
• Genetic material: DNA
• Chromosomes: 46 chromosomes in all body cells
  • 23 chromosomes in ova and spermatozoa (meiosis)
  • 46 chromosomes in the fertilized egg
• Genes: Dominant genes and Recessive genes on sites of the chromosomes
GENES AND ALLELES

• Genes control the transmitted traits through the alleles
• Alleles are the variations of genes (eye color)

• Alleles may be **dominant** or **recessive**
• **Dominant** alleles transmit the heredity even if on **one parental chromosome** (heterozygous)
• **Recessive** alleles transmit only if homozygous (on **both parental chromosomes**)

23 pairs of chromosomes
21 are autosomes
2 are x-linked: **XX** = Female offspring
**XY** = Male offspring
MODES OF GENETIC INHERITANCE

GENE ABNORMALITIES

Autosomal dominant - Produce abnormal traits in offspring even if only one parent has the gene.

Autosomal recessive - Don’t produce abnormal traits unless both parents have the gene.

X-linked dominant

X-linked recessive
INTERMISSION
CANCER = Malignant Tumor = Malignant Neoplasm

A tissue growth:

• Not necessary for body’s development or repair
• Invading healthy tissues
• Spreading to other sites of the body (metastasizing)
• Lethal because of its invasion, metabolism, and complications
Tissues

Four types of tissue

Connective tissue

Epithelial tissue

Muscle tissue

Nervous tissue
## Cancer Terms to Know

<table>
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<tr>
<th>Origin</th>
<th>Name</th>
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<tr>
<td>Epithelium (lining tissue)</td>
<td>Carcinoma</td>
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<tr>
<td>Glands</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Connective tissue</td>
<td>Sarcoma</td>
</tr>
<tr>
<td>Bones</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td>Muscles</td>
<td>Rhabdomyosarcoma</td>
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<tr>
<td>Brain tissue (glial cells)</td>
<td>Glioma</td>
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<td>Lymphatic glands, spleen</td>
<td>Lymphoma</td>
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<td>Blood cells</td>
<td>Leukemia</td>
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BENIGN TUMORS

Benign tumors do not invade surrounding healthy tissues.

Benign tumors do not spread out.

Benign tumors may cause complications due to
obstruction of natural conduits [bronchi (airways), intestine].

Terms: Adenoma, lipoma.
Abnormal Karyotype of a Patient With Leukemia
A highly regulated and controlled cell death. It results in changes that include, cell shrinkage, nuclear breakage, chromatin and chromosominal breakage, and global messenger RNA decay.

Defective apoptotic processes have been implicated in a wide variety of diseases. An insufficient amount results in uncontrolled cell proliferation, such as cancer.

Between 50 and 70 billion cells die each day due to apoptosis in the average human adult.
Phases of Apoptosis

- Nucleus condensing (pyknosis)
- Cell shrinkage
- Nucleus fragmenting (karyorrhexis)
- Apoptotic body
- Phagocyte engulfs apoptotic bodies
What Causes Cancer?

- Some viruses or bacteria
- Some chemicals
- Radiation

Heredity
Diet
Hormones
Heredity and Cancer

All Breast Cancer Patients

- Inherited factor(s)
- Other factor(s)

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CANCER SUSCEPTIBILITY
INTERINDIVIDUAL DIFFERENCES

Aryl Hydrocarbon Hydroxylase Inducibility

Debrisoquine Metabolic Phenotype
SPONTANEOUS MUTATIONS

OXYDATIVE DNA DAMAGE
POLYMERASE INFIDELITY
CHROMOSOMAL REARRANGEMENT
RECOMBINASE INFIDELITY
Oncogenes

Normal cell

Cancer cell

Mutated/damaged oncogene

Normal genes regulate cell growth

Oncogenes accelerate cell growth and division
Tumor Suppressor Genes Act Like a Brake Pedal
p53 Tumor Suppressor Protein Triggers Cell Suicide

Normal cell → Excessive DNA damage → Cell suicide (Apoptosis)

p53 protein
Chances of Genomic Instability

Human Body Cells $\sim 10^{14}$

Lifetime Cell Divisions $\sim 10^{16}$

Chances of Mutation $\sim 10^{124}$
EVENTS IN CARCINOGENESIS

- METABOLIC ACTIVATION OF CARCINOGEN
  - Cytochrome P-450 enzymes
- PROTOONCOGENES ACTIVATION
  - Hepatocellular carcinoma c/w Aflatoxin B₁ exposure
- LOSS OF TUMOR SUPPRESSOR GENES
  - p53 on chromosome 17
- LOSS OF ANTIMITASTASIS GENES
Cancer Risk and Aging

Number of CANCER Cases (per 100,000 people)

Age of Person (in years)

Cancer Risk and AGING

Colon

Breast

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## Known Factors Associated with Cancer Development

<table>
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<tr>
<th>Factor</th>
<th>%</th>
<th>Factor</th>
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<td>Diet</td>
<td>30</td>
<td>Occupation</td>
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<tr>
<td>Smoking</td>
<td>30</td>
<td>Family History</td>
<td>2</td>
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<tr>
<td>Infection</td>
<td>10</td>
<td>Pollution</td>
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<td>Sunlight</td>
<td>8</td>
<td>Food Additives</td>
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<tr>
<td>Alcohol</td>
<td>5</td>
<td>Industrial Products</td>
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*Modified from Doll, R. et al, 1981*
Populations - Based Studies

Regions of Highest Incidence

U.K.: Lung cancer
CHINA: Liver cancer
AUSTRALIA: Skin cancer
JAPAN: Stomach cancer
U.S.: Colon cancer
BRAZIL: Cervical cancer
CANADA: Leukemia


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Heredity? Behavior? “Acculturation”? 

**Colon Cancer**
(Number of new cases per 100,000 people)

- Japan: 5
- Japanese families in U.S.: 50
- U.S.: 100

**Stomach Cancer**
(Number of new cases per 100,000 people)

- Japan: 7
- Japanese families in U.S.: 70
- U.S.: 100

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<th>S.F.-BORN</th>
<th>U.S. WHITES</th>
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<td>Stomach</td>
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<td>Nasopharynx</td>
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</tr>
<tr>
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<td>Prostate</td>
<td>Pancreas</td>
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THE DAWN OF MOLECULAR EPIDEMIOLOGY OF HUMAN CANCER

"NO ONE SUPPOSES THAT ALL THE INDIVIDUALS OF THE SAME SPECIES ARE CAST IN THE VERY SAME MOLD"

C. Darwin, 1859
Example of Normal Growth

- Dead cells shed from outer surface
- Epidermis
- Dividing cells in basal layer
- Cell migration
- Dermis

Artwork by Jeanne Kelly, © 2004

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Loss of Normal Growth Control

Normal cell division

Cell damage—no repair

Cell Suicide or Apoptosis

Cancer cell division

First mutation
Second mutation
Third mutation
Fourth or later mutation

Uncontrolled growth

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The Beginning of Cancerous Growth
Tumors (Neoplasms)
Invasion and Metastasis

1. Cancer cells invade surrounding tissues and blood vessels.
2. Cancer cells are transported by the circulatory system to distant sites.
3. Cancer cells reinvade and grow at new location.
Malignant versus Benign Tumors

Benign (not cancer) tumor cells grow only locally and cannot spread by invasion or metastasis.

Malignant (cancer) cells invade neighboring tissues, enter blood vessels, and metastasize to different sites.

Time
Maturation of Cancer Cells

Cancer may be formed by cells in various degrees of maturation ("differentiation"):

- **Undifferentiated** – One cannot identify the tissue origin
- **Moderately well differentiated** – Some features suggest a tissue origin
- **Well differentiated** – One can identify a tissue origin and specific function (mucus secreting, keratin formation)

The degrees of cell differentiation correlate with the
- **progression** (undifferentiated are progressing fast)
- **response to chemoradiation** (undifferentiated have a better response)
Figure 1. Development of a tumor.
END OF LECTURE #1