Scientific Basis for Practice

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2017 OCN Test Blueprint Content Areas

<table>
<thead>
<tr>
<th>Content Area</th>
<th>Percentage of 2017 Test</th>
<th># of Scored Questions*</th>
</tr>
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<tbody>
<tr>
<td>Health Promotion, Screening &amp; Early Detection</td>
<td>6%</td>
<td>9</td>
</tr>
<tr>
<td>Scientific Basis for Practice</td>
<td>9%</td>
<td>13</td>
</tr>
<tr>
<td>Treatment Modalities</td>
<td>16%</td>
<td>23</td>
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<tr>
<td>Symptom Management</td>
<td>22%</td>
<td>32</td>
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<tr>
<td>Psychosocial Dimensions of Care</td>
<td>8%</td>
<td>12</td>
</tr>
<tr>
<td>Oncologic Emergencies</td>
<td>12%</td>
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<tr>
<td>Survivorship</td>
<td>8%</td>
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<tr>
<td>Palliative &amp; End of Life Care</td>
<td>11%</td>
<td>16</td>
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<tr>
<td>Professional Performance</td>
<td>8%</td>
<td>12</td>
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</table>

*To determine the number of scored items from each subject area, multiple the percentage by 145.


Scientific Basis for Practice

Questions on this section tend to be knowledge-based.

A. Carcinogenesis
B. Immunology
C. Genetic risk factors
D. Research protocols
E. Clinical trials
F. Regarding specific cancer types:
   1. pathophysiology
   2. common metastatic sites
   3. diagnostic measures
   4. prognosis
   5. classification
   6. staging
   7. histologic grading

Study Resources

  - Chapter 1: Biology of Cancer
  - Chapter 2: Staging & Performance Status
  - Chapter 4: Genetic Risk for Developing Cancer

  - Part 2: Scientific Basis for Practice

http://www.oncc.org/TakeTest/Certifications/media/0ncc/docs/certification/ocn_blueprint.pdf
Questions in this section tend to be knowledge based!

Objectives

- Discuss the biology of cancer and carcinogenesis.
- Identify how malignant tumors are classified according to naming (nomenclature), staging, and grading.
- List types and features of hereditary cancer syndromes.
- Identify the purpose and nursing implications of each phase of cancer clinical trials.

Carcinogenesis

Becoming Cancer

Along time ago in a body far, far away...

- A normally functioning cell joined the dark side
Definitions

• Cancer
  • A neoplasm characterized by the uncontrolled growth of anaplastic cells that tend to invade surrounding tissue and metastasize to distant body sites
• Cancer development
  1. Multiple mutations in a cell’s genes
  2. Genomic instability
  3. Inflammation

What are mutations in DNA?

• Mutations in DNA are the result of mistakes during the copying of DNA (remember the copying that takes place going from one DNA molecule to two)
• These mutations are thought to be the root cause of cancer, and it takes more than one mutation to lead to cancer
• Mutations can be:
  • Germline: Inherited; you get the mistake(s) from your parent(s)
  • Somatic: Spontaneous; occur during your life time
    Rare: 1 mutation per 1 million cell divisions

Mutations in Cell Regulators

• The Good News: DNA repair genes
  • Able to correct mistakes caused by carcinogens during replication
  • Called “Caretaker Genes”

• The Bad News: In some, genes are non-functioning and allow mutations to result in cancer
  • BRCA1 and BRCA2 in an inherited mutation (breast, ovarian, and prostate)

Mutations in Cell Regulators

• Proto-oncogenes → Oncogenes
  • DNA coders for controlled cell growth
  • When mutated: enable cancer cell to grow without governance: Foot stuck to the gas pedal
  • Ras mutations are an example proto-oncogene turned oncogene by point mutation (pancreatic & colon)

http://cisncancer.org/research/what_we_know/advances/oncogenes.html
Mutations in Cells Regulators

• Tumor suppressor genes
  • Control proliferation by preventing uncontrolled growth
  • Brake pedal that doesn’t work
  • RB gene mutation is an example of tumor suppressor gene (retinoblastoma, lung, breast, bone)

http://coniarcancer.org/research/what_we_know/advances/oncogenes.html

p53 Tumor Suppressor Gene

• Protein that checks DNA for errors
• If p53 gene damaged:
  • DNA does not get checked
  • Mistakes passed on to daughter cells
• p53 mutations occur in approximately 50% of human cancers
  • Melanoma, colorectal, lung, breast, testes, bladder, & prostate


Mutations in Cell Regulation

• Epigenetic Changes
  • Addition of subtraction of methyl groups to DNA (doesn’t change DNA, but changes expression)
• Chromosome translocation
  • Burkitt lymphoma MYC normally on chromosome 8 but relocated to chromosome 14
  • Philadelphia chromosome in CML (9 moves to 22)

Genomic Instability

• Cancer cells have defective replication/regulation
• Genetic materials are more fragile
• Leads to clonal evolution (changes in tumor over time)
  • Hereditary nonpolyposis colon cancer (HNPCC)
    • Characterized by microsatellite instability (genetic markers on cells)
Inflammation

- Inflammation may activate bioactive molecules that enhance carcinogenesis
- Tumor necrosis factor (TNF) is an inflammatory cytokine that plays a role in cancer creation (though has a large impact on immune surveillance and prevention)

Inflammatory Cause and Effect

- Chronic inflammatory conditions associated with tumor formation
  - Long-term indwelling urinary catheter-associated cystitis
  - Chronic Pancreatitis (pancreatic cancer)
  - Chronic Bronchitis (lung cancer)
  - Sunburn (SCC, Basal Cell, Melanoma)
  - Lichen sclerosis (vulvar cancer)
  - Sjogren syndrome, Hashimoto thyroiditis (lymphomas)

The Cancer 3-Step (Carcinogenesis)

1. Initiation
   1. Lightening strike
2. Promotion
   1. Micro-environment recruitment
3. Progression
   1. Growth and invasion

Application

- Environmental DNA Damage (Radiation, Chemicals, Viruses)
- Normal Cell
- DNA Damage
- Failed DNA Repair
- Mutations in cell genome
- Inactivation of tumor suppressor genes
- Activation of growth-promoting oncogenes
- Alteration of apoptosis genes
- Inherited Mutations

Successful DNA Repair
Carcinogens

• Physical
  • Radiation
    • Mostly from RADON
    • Thyroid cancer and AML are most closely tied to radiation exposure
  • Young children are more susceptible
• UV
  • Sun, tanning beds → skin cancers
  • UVB spectrum is the strongest offender

Question!

• Cancer can arise because of the combination of which three pathophysiologic factors? (Select all that apply.)
  1. Inflammation
  2. Apoptosis
  3. Contact Inhibition
  4. Genomic Instability
  5. Multiple Mutations in Regulatory Cells

Question!

• Ras is an example of a
  1. Mutated tumor suppressor gene
  2. Mutated proto-oncogene
  3. Mutated DNA repair gene
  4. Chromosome translocation

Carcinogens

• Chemical
  • First observations made in professions with an increased CA incidence
  • Normal cell function can fix chemical-related changes
  • Mutations create the problems
    • Smoking, asbestos, smoked/salted/pickled foods, antineoplastic agents, chromium VI, arsenic, coal tar, mustard gas, soot, nickel
Carcinogens

- Viral
  - RNA and DNA viruses are linked to human cancer
  - Viruses hijack cell machinery to create more virus
  - Cellular mutations are triggered
    - Hepatitis A/B/C virus (hepatocellular carcinoma)
    - Herpes viruses EBV (lymphoma), KSHV (Kaposi sarcoma-associated)
    - HPV 16, 18, 33, 39 (anogenital cancers & upper airway)
    - BK virus, JC virus

Cell Changes

- Structural changes
  - Shape, size, nuclear characteristics
  - Chromosomal variability (translocations, deletions, amplification)
- Cell membrane changes
  - Allow invasion and metastasis
  - Loss of “self” labeling antigens and production of “new self” antigens
    - Her-2/neu, CEA, Alpha-fetoprotein, PSA
- Abnormal glycolysis
  - Anaerobic glycolysis makes cell less dependent on oxygen
    (deregulated cellular energetics)

Hallmarks of a Cancer Cell

- Biologic capabilities that a cell acquires in a progressive, multistep process that transforms normal into abnormal into malignant

Metastasis

- “Highly inefficient process in that less than 0.01% of circulating tumor cells eventually succeeds in forming secondary tumor growths”
- Locomotion moves the cancer cell from extracellular matrix through basement membrane
Dissemination

• Direct organ to organ invasion
• Dissemination through lymphatic system
  • Primary node entrapment (sentinel node)
  • Skip metastasis (bypass sentinel and hit further downstream)
• Seeding throughout body cavities
• Blood vessel - arterial or venous

Implications of Metastasis

• Mets contribute to pain and suffering
• Is the major cause of death from cancer
• Understanding process of metastasis helps lead to therapies targeting molecular changes associated disease

Common Sites

• Most common, all cancers
  • Bones, lungs, liver, and CNS
• Breast
  • Bone, lung, brain, liver
• Colon
  • Liver, potentially lungs
• Colorectal
  • Liver, lung, and brain
• Lung Cancer
  • Adrenal gland, liver, bone, and brain

QUESTION!

• What is the process of initiation and promoting cancer through the action of biological, chemical, and physical agents?
  1. Mutagenesis
  2. Teratogenesis
  3. Carcinogenesis
  4. Immune Surveillance
QUESTION!

- Carcinogenesis is a multi-step process. The first stage is:
  A. Promotion
  B. Initiation
  C. Alteration
  D. Progression

Classification of Cancer

Classification of Cancer

- Classification systems provide a standardized way to:
  - Communicate with health care team
  - Prepare and evaluate treatment plan
  - Determine prognosis
  - Compare groups statistically

Classification of Cancer

Tumors Classified by:

- Histology
  - Grade
- Extent of disease
  - TNM Classification (solid tumors)
  - Staging

Tumor Grading & Staging

- **Grading** (done by Pathologist)
- **Staging** (done by Oncologist)

Tumor Grading
(Done by Pathologist)

- Method of classification based on microscopic characteristics of tumor
- Determines degree of malignancy of tumor cells
- Compares degree of “differentiation” & “mitotic activity” with normal cells

American Joint Committee on Cancer Classification

- Gx: Grade can not be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated
- G4: Undifferentiated

Tumor Grade

- A well-differentiated tumor is composed of cells that closely resemble the cell of origin
- Poorly differentiated tumors have cells that are difficult to recognize as to their cell of origin
  - Associated with poor outcome
- Grading used to predict outcome by assessing tumor characteristics that predict aggressiveness
Grading Classifications

- Low numeric grades
  - Also called “low-grade” tumors or “well-differentiated” tumors
  - Deviate least from normal
- High numeric grades
  - Also called “high-grade” or “poorly-differentiated” tumors
  - Most deviant (anaplastic) from normal

Staging (Done by the Oncologist)

- Evaluation of the extent of the tumor
- Not necessarily related to grade
- Purpose: quantify anatomic extent of disease
- Considerations
  - Size of cancer
  - Invasion of adjacent structures
  - Regional lymph node involvement
  - Distant metastasis

Tumor Staging

- Reasons for staging
  - Treatment planning
  - Prognostic information
  - Evaluate results of treatment
  - Facilitate exchange of information between treatment centers
  - Contribute to research

TNM Staging System

- T = Primary tumor size
- N = Absence or presence of regional lymph node metastasis
- M = Absence or presence of distant metastasis
Table 3-8. Basic Characters Used in the Tumor-Nodule-Metastasis Staging System

<table>
<thead>
<tr>
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<th>Description</th>
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<tbody>
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<td>Cancer in situ</td>
</tr>
<tr>
<td>1</td>
<td>Tumor limited to tissue of origin; localized tumor growth</td>
</tr>
<tr>
<td>2</td>
<td>Limited local spread</td>
</tr>
<tr>
<td>3</td>
<td>Extensive local and regional spread, extends beyond organ capsule</td>
</tr>
<tr>
<td>4</td>
<td>Metastasis</td>
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**Performance Scales**

**Karnofsky**
- 100% - normal, no signs of disease
- 90% - capable of normal activity, few symptoms
- 80% - normal activity with some difficulty
- 70% - can perform self, not capable of normal activity on work
- 60% - requires some help, takes care of most needs
- 50% - requires help often, requires frequent medical care
- 40% - disabled, requires special care and help
- 30% - severely disabled, hospital admission indicated
- 20% - very ill, requires admission, requires supportive measures or treatment
- 10% - bedbound, rapid progression of disease processes
- 0% - death

**ECOG**
- 0 - Asymptomatic (Fully active)
- 1 - Symptomatic but completely ambulatory
- 2 - Symptomatic, <50% in bed during the day
- 3 - Symptomatic, >50% in bed, but not bedbound
- 4 - Bedbound (Completely disabled)
- 5 - Death

**Classification of Cancer**

Clinical staging classifications

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**Question!**

A patient newly diagnosed with cancer tells the nurse, "The doctor ordered all of these tests for clinical staging. What does that mean?" The nurse’s best response is based on the knowledge that staging:

A. Predicts response to treatment
B. Compares treatment results across populations
C. Assesses the usual patterns of spread of specific cancers
D. Evaluates the extent of local and potential metastatic disease
Questions!

Tumor grading refers to the:

A. Expression of tumor-associated antigens
B. Degree of differentiation of malignant cells
C. Extent of chromosomal aberrations
D. Likelihood of metastatic spread

Questions!

According to the TMN staging system, which of the following is indicative of highly advanced disease?

A. T1 N1 M0
B. T3 N0 M0
C. T3 N3 M1
D. T2 N1 M1

Question!

Which of the following represents a high-grade, poorly differentiated cancer?

a. Grade I
b. Grade II
c. Grade III
d. Grade IV

Question!

A patient has just been diagnosed with stage III breast cancer, grade II. She asks the nurse what that means. The nurse explains to her that the primary tumor has

1. Spread to her lymph nodes and is moderately differentiated (an intermediate-grade tumor), meaning that the tumor cells somewhat resemble normal cells
2. Spread to her lungs and liver and is poorly differentiated (high grade), meaning that the tumor cells have some normal cell characteristics
3. Not spread to her lymph nodes and is well differentiated (low grade), meaning the tumor cells have some normal characteristics
4. Spread to her lymph nodes and lungs and is undifferentiated (a high-grade tumor), meaning that the tumor cell doesn’t resemble normal cells
Tumor Nomenclature

- Tumors usually named according to tissues of origin (numerous exceptions exist)
- Benign tumors
- Malignant tumors

Benign Tumors

- Labeled by adding the suffix "oma" to the tissue of origin
- Examples:
  - Lipoma — benign tumor composed of lipid tissue
  - Adenoma — benign tumor composed of glandular tissue

Malignant Tumors

- Carcinomas
  - Arise from epithelial tissue
- Sarcomas
  - Arise from connective tissue

Carcinomas

- Originate from epithelial tissue
- Prefixes describe specific type of epithelial tissue
  - Adeno
    - Tumors arising from glandular epithelium
    - Origin of organ also included
    - Example: “pancreatic adenocarcinomas” — malignant epithelial tumors arising from pancreas
  - Squamous
    - Tumors arising from squamous epithelium
    - Origin of organ included
    - Example: “squamous cell carcinoma of skin”
Sarcomas

- Originate from connective tissue
- Prefixes for specific connective tissue included:
  - Osteo – arising from bone
  - Chondro – arising from cartilage
  - Lipo – arising from fat
  - Rhabdo – arising from skeletal muscle
  - Leiomyo – arising from smooth muscle

Hematologic Malignancies

- Leukemias
  - Arise from hematopoietic cells
  - Classified according to cell type & maturity (Acute & Chronic)
  - Lympho – leukemia of lymphoid origin
  - Myelo – leukemia of myeloid origin
  - Chronic/Acute

- Lymphomas
  - Malignancies of lymphocytes
  - Sub classified as: Hodgkin’s disease (HD)
    Non-Hodgkin’s Lymphoma (NHL)

- Multiple myelomas
  - Arise from plasma cell (B lymphocyte line)

Immunology

Self v. Non-Self

Definitions

- Immunology
  - Study of recognition of cellular and tissue changes, as well as invasion of microbes

- Immunosurveillance
  - Immune recognition and control of tumor cells

- Immune Escape
  - Loss of recognition by immune cells, leading to escape and proliferation of tumor cells
Hematopoiesis

Lymphoid Organs
- Primary (maturation and growth of lymphocytes)
  - Bone
  - Thymus
- Secondary (sites where foreign antigens encounter lymphocyte immune response)
  - Mucosa-associated lymphoid tissue
  - Spleen
  - Bone

Cells
- B Cells
  - Mature in the _____________
  - B Cells multiply on recognition of specific antigen and further differentiation into plasma cells
    - Plasma cells produce five different immunoglobulins
- T Cells
  - Mature in the _____________
  - Role in immune surveillance
  - T helper cells (CD4) type 1: secrete cytokines and recruit monocytes
  - T helper cells (CD4) type 2: interact with B Cells
  - T cytotoxic cells (CD8) destroy host cells

Phagocytes
- Polymorphonuclear granulocytes
  - Migrate to tissues → inflammatory response
- Neutrophils (polys/segs & bands)
  - Make-up 60-70% of WBC differential
  - Short lived, migrate into tissues
  - Initiate inflammatory response
  - Engulf & destroy material
- Eosinophils
  - Attracted to parasites
- Basophils
  - Move to tissues where antigens are present
    - Hypersensitivity reaction

http://www.niaid.nih.gov/topics/immuneSystem/Pages/structureImages.aspx
Phagocytes

- **Mononuclear**
  - Fixed & mobile phagocytic cells
  - (monocytes/macrophages)
  - Start out as monocytes, when move into tissue become macrophages
  - “macro-” = big, “big eaters”
  - Slower to respond than granulocytes, but live longer
  - Alert the rest of the immune system of the invader

Cells

- **Dendritic Cells**
  - Starfish that **present antigens** to T cells and B cells
  - Effective at stimulation of antitumor immune response

- **Null Cells**
  - NK
  - Secret perforin to punch holes in cell walls
  - ID tumor and virus-containing cells
  - Activity is increased in presence of IL2, interferon

- **Mast Cells**
  - Contain multiple immune mediators

Cytokines

- Enhance communication and induce growth and differentiation of lymphocytes
- INF: limit spread of viral infections
- IIs: made mostly by T cells; communication, maturation, differentiation
- Hematopoietic growth factor: differentiation of bone marrow stem cells
- Tumor Necrosis Factor: mediate inflammation and cytotoxic reactions
- Chemokines: drive leukocyte movement

Major Histocompatibility Complex (MHC)

- Genetic region responsible for “self-recognition”
- MHC genes
  - Coded on chromosome 6 in humans
  - Expressed on surface of human cells
  - Also known as human leukocyte antigens (HLA)
Immune Response:
  Innate Immunity
  • Does not rely on memory
  • Natural Barriers
    • Physical
      • Epithelial cells of intact skin
      • Mucus membranes
    • Mechanical
      • Sneezing, coughing, vomiting, urination
    • Biochemical
      • Mucus, sweat, saliva, tears, GI flora, earwax

Immune Response:
  Inflammatory Response
  • Rapid activation of several plasma proteins, mast cell
degranulation, vascular changes, and influx of
  lymphocytes

Tumor Immunology
  • Tumor-associated antigens: induce protective
    immunity
  • Tumor associated antigens: may appear on the
    surface of a cell that has transitioned from normal
to cancer
  • HYPOTHESIS: immune system can protect host from
cancer
    • Examples- PSA, CEA

Why do tumor cells evade
  immune surveillance?
  • T-cell immunodeficiencies (Epstein-Barr Virus, HIV)
    • T cells play critical role in immune surveillance
  • MHC expression “deregulated” by tumor cell
    • Not targeted by T cells
  • Tumor cells created from host cells
    • May too closely resemble/function similar to normal cells
  • Tumor cells fail to recruit T cells
    • Too closely resemble self
  • Cell turnover & rapid growth rates in malignant
tumors may overpower immune system
QUESTION!

• Which of the following are natural barriers to prevent damage by environmental substances and thwart infections by pathogens?
  1. Histochemical
  2. Physical
  3. Mechanical
  4. Skeletal
  5. Biochemical

QUESTION!

• Which of the following result in the rapid activation of several plasma protein symptoms, mast cells degranulation, and influx of leucocytes?
  1. Human stress response
  2. Krebs citric acid cycle
  3. Hepatoenticular degeneration
  4. Inflammatory response

QUESTION!

• Which of the following describes an organ of the immune system rather than a barrier to bacterial invasion?
  1. Mucous membranes
  2. Lymphoid tissue
  3. Saliva
  4. Gastric secretions

Question!

• A 77 year-old patient was diagnosed with prostate cancer 14 years ago. He had a partial suprapubic prostatectomy and did not require chemotherapy or radiation. Her has taken two separate hormonal therapies since that time. Her recently had a change in urinary and bowel habits with increased urinary frequency and smaller caliber stools, to soft diarrhea stools, and he has noticed some intermittent blood in his urine. A colonoscopy did not show any abnormalities. An advance in his prostate cancer is suspected because of the presence of
  1. Tumor protective agents
  2. Mononuclear phagocytes
  3. Tumor-associated antigens
  4. Immature dendritic cells
Genetic Risk Factors

Genetic Structure

- Chromosomes are thread-like structures containing genetic information
- 46 chromosomes
- 23 pairs
- 22 autosomes
  - P or “petite” arms and q legs
- #23 associated with gender
  - X/Y

DNA

- 4 base pairs
  - Purines
    - Adenine
    - Guanine
  - Pyrimidines
    - Thymine
    - Cytosine
  - Base pairs are complimentary C-T, A-G

Genetic Mechanism for Cancer

- Many things happen simultaneously to create a cancer
- Genetic mutations are the basis for cancer
- Most mutations are NOT inherited
- Acquired genetic mutations have both biologic (indigenous) and environment (exogenous) basis
### Autosomal Dominance

- 50% chance of having an affected child
- WITH EACH PREGNANCY

### Autosomal Recessive

- 25% chance of having an affected child
- WITH EACH PREGNANCY

### Features of Hereditary Cancer

- Family member with known germline deleterious mutations in cancer susceptibility gene
- Early age of onset
- Cancer of rare histology
- Cancer in two or more close biologically related relatives
- Bilateral cancer in paired organs
- Multiple primary cancers in one person
- Constellation of cancers in the family par of a know hereditary cancer syndrome

### Syndrome Table

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Clinical Manifestation</th>
<th>Gene</th>
<th>Mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Ovarian cancer syndromes</td>
<td>Breast, ovarian, fallopian tube, prostate, pancreas</td>
<td>BRCA 1</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td></td>
<td>Breast, ovary, fallopian, prostate, pancreas, melanoma</td>
<td>BRCA 2</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Familial adenomatous polyposis</td>
<td>Colon polyposis, thyroid cancer, hepatoblastoma, desmoid tumors</td>
<td>APC</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Lynch Syndrome (Formerly HNPCC)</td>
<td>Cancers of the colon, rectum, stomach, small intestine, biliary tract, brain, endometrium, ovary, renal/urothelial</td>
<td>MSH1, MSH2, MSH6, MSH5, PMS1, 2</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Wilms Tumor</td>
<td>Wilms tumor and nephrogenic rests</td>
<td>WT1</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Fanconi Anemia</td>
<td>Leukemia, hepatocellular carcinomas, squamous cell carcinomas of head and neck</td>
<td>FANCA FANCB FANC</td>
<td>Autosomal recessive</td>
</tr>
</tbody>
</table>

*many of these are tumor-suppressor genes*
Indications for Cancer Predisposition Testing

• Confirmed family history consistent with hereditary cancer syndrome
• A test that can be interpreted once performed
• The test will be used to assist with medical decision making or will assist in diagnosis of a condition
• Informed consent
• Testing done in the context of pre and post genetic counseling
  • Genetic counseling defined as “the process of helping people understand and adapt to the medical, psychological, and familial implications of genetic contributions to disease”
  • Providers may be physicians, nurses, genetic counselors with specialized training in genetics

Outcomes for Predisposition Testing

• Predictive value of a negative result varies depending on whether a genetic mutation exists
• A negative result in the presence of a known genetic mutation indicates that the client is within the general population risk of cancer associated with that branch of the family
• Family history of OTHER parent also influences risk

Medical Management

• Surveillance: monitoring to detect cancer at earliest stages
• Risk-reducing surgery: removal of as much susceptible tissue to reduce risk
• Chemoprevention: take medicine, vitamin, other substance
• Risk avoidance: avoidance of exposures that could increase risk of certain cancers
• Healthy behaviors: diet and exercise

Ethical, Legal, Social Issues

• Psychologic consequences
  • Survivor’s guilt
  • Transmitter guilt
  • Heightened anxiety
  • Depression and anger
  • Personal identity issues
  • Regret for decisions made prior to results
  • Uncertainty
  • Intrafamilial issues
  • Stigmatization within family/social group
  • Incidental finding
Ethical, Legal, Social Issues

- Social Consequences
  - Financial issues
    - Tests are expensive, cost may not be covered by insurance
    - Surveillance may not be covered by insurance
  - Lack of QA test standard
  - Lack of qualified genetic counselors

- Legal
  - Discrimination against those harboring altered cancer genes as they have increased cost to insure or employ
    - Health insurance
    - Life insurance
    - Disability insurance
    - Long-term care insurance
    - Education
    - Employment

Protection

- HIPAA states that genetic information cannot be used as a preexisting condition or to determine insurance eligibility
- Does not protect from rate increases, insurers requesting genetic testing

GINA

- Genetic Information Nondiscrimination Act from 2008 applies to health insurance coverage and employment discrimination based on genetic information
- Employer may not request or access genomic information
Informed Consent

- Purpose of the test
- Motivation of test
- Risks of testing
- Benefits of testing
- Limitations of testing
- Inheritance patterns
- Risk of misidentified paternity
- Accuracy and sensitivity of testing
- Outcomes of testing
- Confidentiality
- Possibility of discrimination
- Alternatives to testing
- Impact on decision making
- Cost
- Right to refuse
- Testing in children
- Management of incidental findings

Nursing Implications

- Description of role of genetic material in cancer genetics and genetic testing
- Assessment of client beliefs and knowledge of cancer causes; correct misconceptions
- Discuss process and risks of genetic testing
- Rationale for tumor profiling

Nursing Implications

- Interventions to decrease perceived and actual barriers to cancer risk management
- Education on self-surveillance techniques
- Education on risk management
- Facilitating reimbursement for cancer risk management procedures
- Encourage communication

Nursing Implications

- Referral for client, family, or both to community support services
- Referral to professional counseling, when needed
- Encourage coping strategies
QUESTIONS!

• Nurses can advocate for individuals with known cancer risk mutations by
  1. Referring to the NCI Physician Data Query Summaries on Genetics
  2. Supporting HIPAA guidelines for the use of genetic information
  3. Discourage them from sharing their information
  4. Encourage to have testing repeated in 6 months

QUESTION!

• An individual who has known colon cancer susceptibility in his family has tested negative. His colon cancer risk
  1. Cannot be established
  2. Is at least equivalent to the general population
  3. Is nil
  4. Is still elevated

QUESTIONS!

• The son of a patient is happy to see the results of his genetic testing were negative. What is important for him to understand about his level of risk? (select all that apply)
  1. A negative result in the presence of a known genetic mutation means that the client is within the general population's risk of cancer associated with that branch of the family
  2. Because the results of the test are negative, his risk for cancer is minimal
  3. Without knowing the type of cancer his parent has, you cannot give accurate information about his risk level
  4. You do not know if his parent's cancer is the result of a genetic mutation. You need more information to help him determine his results and assess risk
  5. It is still important for him to have the surgery for removal of tissue at risk for cancer

QUESTION!

• Which of the following is a clinical feature of hereditary cancer?
  1. Older age of cancer onset
  2. Telomerase
  3. Multiple primary cancers in a single person
  4. Presence of metastases at time of diagnosis
QUESTIONS!

• Mutations in which gene have been correlated with both breast and ovarian cancer?
  1. p53
  2. PTEN
  3. BRCA1
  4. APC

QUESTIONS!

• Many of the gene mutations responsible for familial cancer syndromes are
  1. Proto-oncogenes
  2. Oncogenes
  3. Tumor suppressor genes
  4. Mismatch repair genes

QUESTIONS!

• If a parent has a hereditary cancer that is autosomal dominant inheritance. What is the percent chance of transmitting that gene mutation to a child?
  1. 75%
  2. 50%
  3. 25%
  4. 10%
What?

• Research Protocol: detailed, written plan of a clinical research study
• Clinical research study
  • Human subjects
  • Interventional
    • Prevention, screening, improving diagnostics, quality of life, and supportive care, treatment
  • Observational
    • Epidemiologic

Interventional Study

• Purpose
  • To assess safety, efficacy, and effectiveness of biomedical or behavioral interventions
• Interventions
  • New treatment, devices, behaviors
  • One or more, or none (control)
  • Assignment defined by protocol

Observational

• Purpose
  • Assess biomedical and health outcomes in groups of humans
  • May be sub-grouped by trait (men, over 50; women, under 40)
  • No intervention

Review and Approval

• All research regarding human subjects requires approval by institutional review board (IRB) or independent ethics committee (IEC)
• IRB purpose: protect and safeguard the rights and welfare of the human subjects in a clinical trial by providing independent review
  • Reviews protocol and consent
Criteria for IRB Approval

- Minimal risk to subjects
- Risk to benefit
- Unbiased selection of subjects
- Informed and voluntary consent
- Data monitoring to ensure the subjects’ safety
- Privacy and confidentiality of subject and data maintained
- Vulnerable subjects protected from coercion

Phase 0

- Exploratory study using small doses of investigational agent
  - Limited drug exposure for limited days (<7)
  - No therapeutic intent
  - Precedes Phase 1
- Goals
  - Provide human pharmacodynamic, pharmacokinetic data
  - Determine mechanism of action is observable
  - Enhance development
  - Around 10-12 subjects

Phase I

- Traditional first in-human dose finding study
  - Dose finding in use with concurrent therapies
- Goals
  - Evaluate safety and tolerability
  - Determine maximum tolerated dose
  - Determine dose-limiting toxicity
- Who?
  - 20-100, Healthy and patient volunteers, many cancer types, refractory to standard therapy, adequate organ function

Phase II

- Phase IIA: Proof of concept to provide information on activity of intervention to justify larger study
- Phase IIB: Optimal dosing
- Goals:
  - Proof of concept, intervention in the intended population
  - Evaluate safety
- Who?
  - 80-300, more homogenous population based on Phase I data, patients must of disease that can be measured and reproduced
Phase III
- Randomized controlled trial
- Goal
  - Compare intervention to a control group
  - Evaluate for safety
- Who?
  - Hundreds to thousands
  - Homogenous population

Phase IV
- Postmarketing study
- Goals
  - Continue to evaluate safety
  - May or may not be required by FDA
  - Compare another drug that is similar
  - Long-term monitoring
  - Food/drug interaction
- Who?
  - 100s to 1000s

Role of the Nurse in Any Phase
- Patient safety is the highest priority
- Protection of patients rights
- Promotes communication
- Promotes informed consent
- Assesses, monitors, and reports adverse events, and manages as necessary
- Documents in clinical record accurately
- Give voice to ethical considerations/concerns

QUESTIONS!
- A colleague indicates she would like to conduct a research study, but she does not want to do all of the work of an IRB application. What should the priority message for the nurses’ response?
  1. The research must involve no risk to the subjects, or it must be submitted for IRB review and approval
  2. The purpose of the IRB review is to protect and safeguard the rights and welfare of human subjects
  3. If it is not an interventional study, IRB is not required; it’s alright to begin data collection
  4. With electronic medical records, it’s very easy to just extract data on the clients the nurse is already seeing
QUESTIONS!

How would the nurse respond to a comment by family members that a phase IV clinical trial is really making a “guinea pig” out of their loved one?

1. Encourage them to talk with the study coordinator to address any concerns
2. Ask them about their experience with involvement in research studies in the past
3. Reassure them that research in cancer treatment over the past years has led to many advances
4. Explain that this trial involves agents that have been already tested and approved by the FDA for use in the clinical setting

QUESTIONS!

A Phase I treatment clinical trial is designed to evaluate:

A. Drug toxicities
B. What tumor will be responsive to a drug
C. New areas of use after FDA approval
D. Activity of a new combination in relation to the standard of treatment

Specific Cancer Pathophysiology

Bonus Round Questions!

Lung Cancer

- Lung Changes with Cancer
  - “Multihit” theory of carcinogen exposure, DNA damage, and mutation
  - Chromosome 15 alterations
- Presentation
  - Incidental finding or disease-related symptoms
- Common Metastatic Sites
  - Brain, liver, adrenals, bone
  - At risk for paraneoplastic syndromes (SIADH, hypercalcemia of malignancy, SVCS, SCC, etc.)
### Lung Cancer

- **Diagnostic Measures**
  - No known tumor marker
  - PFT to establish baseline respiratory status
  - CXR,
  - CT chest/abdomen
  - PET?
- **Overall Survival (OS) for all stages** is 16% at 5 years
  - 1 year survival rates have increased to 44%
  - NSCLC
  - SCLC

### Breast

- **Most common cancer in women worldwide**
- 100 times more common in women than men
- BRCA1 and BRCA2 associated gene mutations
- **Screening**
  - Self exam/Mamogram
  - Early detection increased OS
- Biopsy, grade, ER/PR & Her-2/neu testing
- Ductal carcinoma most prevalent
- Inflammatory breast cancer—extremely aggressive

### Breast

- **Staging**
  - Surgical, imaging
- **Metastases**
  - Regional lymph nodes, contralateral breast, bone, skin, lung, liver, eyes, bladder, brain, spinal cord

### Prostate

- **95% Adenocarcinomas**
- Tied to BRCA1 & BRCA2 and HPC1, as well a familial-non-mutation ties (increased x2-3 with first degree relatives)
- PSA, Digital rectal exam, transrectal ultrasound, biopsy (Gleason Scoring)
- MRI, bone scan
- Metastases
  - Bones, lymph nodes, lung, liver, and brain
Colorectal Cancer

- Risk
  - Smoking, age, alcohol, high fat diet, hereditary polyposis
- Adenocarcinoma accounts for 95% of cases
- Early presentation
  - Vague abdominal pain, changes in BM with or without bleeding
- Late presentation
  - Weight loss, distention, fatigue
- Metastases
  - Extension through bowel penetration
  - Liver and lung via hematologic spread

Pancreatic

- Smoking, obesity, dietary factors
- Adenocarcinoma accounts for 95% of cases
- Occasional neuroendocrine tumors
- Presentation
  - Weight loss, abdominal pain, indigestion or bloating, N/V
- Metastases
  - Liver and lung via hematologic spread
  - Will follow lymph chains

Question!

RM is a 77 year old woman who was diagnosed and treated for HER 2 positive breast cancer 2 years ago. She appears at her appointment complaining for feeling worn out, not able to do her usual light housework because her back hurts, and she appears short of breath while at rest. RM received trastuzumab within the past year but has not been seen in recent months because of the death of her spouse. Considering her symptoms, the nurse should be most concerned about the possibility of:

1. Axillary involvement, liver metastases, and lung metastases
2. Brain metastases, bone metastases, and lung metastases
3. Axillary and supraclavicular lymph node involvement, and colon metastases
4. Cardiac failure, lung metastases, and spinal cord involvement

Question!

Given the description of symptoms for RM above, the nurse would expect which of the following tests to be ordered to evaluate her present condition?

1. Electrocardiography, complete blood count, chest radiography, abdominal ultrasonography
2. Echocardiogram, complete metabolic panel, computed tomography (CT) of the chest, and bone scan
3. Computed tomography (CT) of the abdomen and pelvis, sentinel lymph node biopsy
4. Mamma print, magnetic resonance imaging, and pulmonary function tests
• A female patient has been diagnosed with stage IIIA breast cancer. Her tumor measures 45 mm, with one small axillary lymph node involved. Her anatomic stage of IIIA means she has
  1. T2, N2A, M0
  2. T1c, N2, M1
  3. T3, N1, M0
  4. T1a, N3, M1

• Work up for lung cancer would include
  1. Tumor markers, chest radiography, complete metabolic profile
  2. Chest and abdominal computed tomography and alpha-feta protein
  3. Chest CT, positron emission tomography (PET) scan, magnetic resonance imaging of the brain (MRI) of the brain
  4. Pulmonary function tests

• A common metastatic site for lung cancer patients is the brain. What type of radiation therapy would be most likely ordered to reduce risk?
  1. Stereotactic ablative radiation therapy (SRT)
  2. Radiofrequency ablation radiotherapy
  3. Prophylactic cranial irradiation
  4. Radioactive seed implant therapy (seed therapy)

• Which tumor marker is commonly used as an indicator of tumor burden and for monitoring of recurrence in colorectal cancer?
  1. CA 19-9
  2. CA 27-29
  3. Carcinoembryonic antigen (CEA)
  4. Alpha-feta protein (AFP)
Question!

Which of the following tumor markers are usually elevated in 80% of the patients with advanced epithelial ovarian cancer?

1. CA-125
2. CEA
3. CA 19-9
4. CA 27-29