Principles of Cancer Treatment

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Objectives

• Describe the principles of cancer treatment
  – Surgery
  – Chemotherapy
  – Biotherapy and Targeted Therapy
  – Complementary and Alternative Medicine

• Additional treatment modalities:
  – Radiation therapy
  – Hematopoietic Stem Cell Transplant

SURGERY
Surgery

- Is the oldest form of cancer treatment!
- Used for several reasons:
  - Preventative
  - Curative treatment
  - Palliate symptoms
  - Obtain tissue/tumor samples
  - Diagnose and stage cancer

- May remove part or all of a tumor
- Can be before or after other modalities (chemotherapy, radiation)


Staging and Diagnosis

- Adequate tissue samples are essential for proper diagnosis and staging!
  - Used for genetic testing
  - Determine extent of disease

- Variety of biopsy methods available

- Treatment is often based on biopsy results and tissue analysis


Role of Cancer Surgery

- Preventative/Prophylactic
  - To prevent or reduce risk of cancer in high-risk patients
    - Esophageal resection with Barrett’s esophagus
    - Mastectomy with BRCA mutations
    - Thyroidectomy with suspicious/symptomatic nodules

Role of Cancer Surgery

- **Curative**
  - To remove entire tumor; must have well-defined margins (encapsulated)
    - Colon resection
    - Lobectomy
- **Palliative**
  - Used when cancer is not curable
    - Stent placement, etc
    - Reduce tumor burden (debulking)

Surgery Types

- **“Traditional”**
  - ‘going under the knife’
- **Minimally invasive**
  - Laparoscopic
  - Cryoablation
  - Thermal ablation
- **Stereotactic**
  - Cyberknife (uses radiation)

Nursing Role

- **Post-operative care**
  - Pain management
  - Prevention of SE associated with surgery and cancer
    - Pneumonia/atelectasis
    - Impaired wound healing
    - Bleeding/coagulopathies
    - Thrombosis
    - Infection
- **Psychosocial support is key!**
CHEMOTHERAPY

Chemotherapy

• Systemic therapy using a chemical substance
  – Frequently given in combination with other chemotherapy or non-chemotherapy drugs
  – Are toxic to both normal and cancerous tissues
    • Can be a limiting factor in dosage/use
  – Many routes of administration available
  – Often given in specific sequences (cycles) to maximize response and minimize side effects

Chemotherapy Classification

• Cell Cycle Specific
  – Antimetabolites
  – Plant alkaloids
    • Camptothecins
    • Epipodophyllotoxins
    • Taxanes
    • Vinca alkaloids
    – Miscellaneous

• Cell Cycle Non-Specific
  – Alkylating agents
  – Antitumor antibiotics
  – Nitrosureas

Cell Cycle

- G0—Resting/dormant phase
- G1—Synthesis of proteins and RNA; growth
- S—DNA is replicated
- G2—Preparation for mitotic spindle formation; growth
- M—Cell division occurs

Mechanism of Action

**Cell Cycle Specific**
- Exert an effect at a specific part of the cell cycle
- Work best when given in cycles or divided doses
- Most effective when patient kept on regular treatment schedule

**Cell Cycle Non-Specific**
- Exert effects in all phases of cell cycle, including G0
- Cell kill is directly proportional to the amount of drug administered.
- Dose dependent—easier to delay treatment so that higher dose can be given


Alkylating Agents

- Interfere with DNA replication by breaking DNA helix strand
- Examples:
  - Carboplatin/Cisplatin
  - Cyclophosphamide
  - Oxaliplatin
  - Ifosfamide
  - Dacarbazine

Side Effects

- Myelosuppression is main dose-limiting toxicity
- Many agents are irritants/vesicants
- Secondary malignancies are possible with some agents

Additional:
- Hemorrhagic cystitis
  - ifosfamide
  - cyclophosphamide
- Nephrotoxicity
  - cisplatin
- Anaphylactic Reactions
  - oxaliplatin, thiotepa, carboplatin

Common:
- Nausea/vomiting/diarrhea, decreased fertility, skin irritation, mucositis, alopecia, fatigue, neuropathy

Antitumor Antibiotics

- Cell cycle non-specific
- Bind with DNA; inhibits DNA/RNA synthesis
- Examples:
  - Bleomycin
  - Mitomycin
  - Mitoxantrone
  - Anthracyclines
    - Doxorubicin
    - Epirubicin
    - Idarubicin
    - Daunorubicin

Side Effects

- Myelosuppression is the most common dose limiting toxicity
- Many agents are vesicants
- Drugs are colored (not clear)
  - Teach patient that urine/sclera might be discolored after administration

Additional:
- Cardiotoxicity
  - Anthracyclines
    - Lifetime cumulative-dose limits
- Pulmonary toxicity
  - Bleomycin
    - Test dose often used
- Radiation Recall
- Photosensitivity
- Nephro/hepatotoxicity

Common:
- Nausea/vomiting, alopecia, electrolyte imbalance, decreased fertility, PPE (hand-foot syndrome), mucositis
Nitrosoureas

- Cell cycle non-specific
- Interfere with DNA replication by breaking DNA helix
- Cross blood-brain barrier
- Examples:
  - Carmustine
  - Lomustine
  - Streptozocin

Side Effects

- Additional:
  - Nephrotoxicity
  - Hepatotoxicity
  - Pulmonary fibrosis
    - Lomustine
  - Altered glucose metabolism
    - Streptozocin

- Common:
  - Nausea/vomiting, anorexia, impaired fertility

Antimetabolites

- Cell cycle specific
- Act in S phase; inhibit DNA synthesis and/or repair.
- Given via many different routes
- Examples:
  - Capecitabine
  - Cytarabine
  - Fluorouracil
  - Gemcitabine
  - Methotrexate
  - Pemetrexed
### Side Effects

**Additional:**
- Many agents are folic acid agonists or antagonists
  - Folic acid is either supplemented OR avoided!
- Patients with hematologic disease may require hydration/allopurinol to prevent TLS

**Common:**
- Nausea/vomiting, alopecia, photosensitivity, constipation, fatigue, peripheral edema

**Additional:**
- Myelosuppression
- Interstitial lung disease
  - Topotecan

**Common:**
- Nausea, vomiting, alopecia, anorexia, fatigue, mucositis

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### Camptothecins

- Plant alkaloid
- Cell cycle specific
- Act in S phase; inhibits topoisomerase I, causing double-strand DNA changes

**Examples:**
- Irinotecan
- Topotecan

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### Side Effects

**Additional:**
- Myelosuppression
- Interstitial lung disease
  - Topotecan

**Common:**
- Nausea, vomiting, alopecia, anorexia, fatigue, mucositis

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Epipodophyllotoxins

• Plant alkaloid
• Cell cycle specific
• Act in G2 and S phase; interfere with topoisomerase II
• Examples
  — Etoposide
  — teniposide

Side Effects

• Myelosuppression is major dose-limiting toxicity
• Can cause hypotension if administered rapidly
• Consider dose reduction in patients with renal/hepatic impairment

• Additional:
  — Hypersensitivity reactions

• Common:
  — Nausea, vomiting, alopecia, anorexia

Taxanes

• Plant alkaloid
• Cell cycle specific
• Act in G2 and M phases; inhibit cell division by stabilizing microtubules
• Examples:
  — Cabazitaxel
  — Docetaxel
  — Paclitaxel
**Side Effects**

- **Additional:**
  - Use of in-line filter is required in some agents
  - Paclitaxel
  - Consider dose adjustment or alternative agent in hepatic or renal dysfunction

- **Common:**
  - Hypersensitivity reactions
  - Premedicate with H2 antagonist, antihistamine, corticosteroid
  - Alopecia, facial flushing, fatigue, nausea, vomiting, myelosuppression, fluid retention

- Peripheral neuropathy is major dose-limiting toxicity
- Agents are irritants/vesicants
- Do not use PVC bag/tubing to administer

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**Vinca Alkaloids**

- Plant alkaloid
- Cell cycle specific
- Act in G2 phase to block DNA production, and M phase to prevent cell division
- Examples:
  - Vinblastine
  - Vincristine
  - Vinorelbine

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**Side Effects**

- Myelosuppression and neurotoxicity are major dose-limiting toxicities
- Agents are vesicants

- **Additional:**
  - FATAL IF GIVEN INTRATHECALLY!
  - Nephrotoxicity
  - Hepatotoxicity

- **Common:**
  - Constipation, alopecia, nausea, vomiting

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Miscellaneous Agents

- Cell cycle specific
- Has varied mechanisms of action
- Examples:
  - Arsenic trioxide
  - Hydroxyurea
  - Vorinostat
  - Asparaginase
  - Procarbazine
  - Ixabepilone


Side Effects

- Additional:
  - Alcohol should be avoided with procarbazine use
  - Antabuse-like reactions
  - Regular monitoring of labs and ECG needed with several agents
  - Asparaginase carries risk of anaphylactic reactions
- Common:
  - Nausea, vomiting, mucositis, hepatotoxicity, nephrotoxicity, fatigue, diarrhea


Routes of Administration

- Oral
- Intramuscular
- Subcutaneous
- Intravenous
- Intraperitoneal
- Intra-arterial
- Intrathecal
- Intrapleural
- Intravesicular

- Advantages and disadvantages for each route
- Additional care areas may administer by specialized route
  - Interventional radiology
  - Operating suite

Combination Chemo

• Many agents given in combination of two or more
• Different mechanisms of action maximizes cell kill
• Some agents have synergistic effects when utilized together
• Possible delayed drug resistance

Goals of Chemotherapy

• Adjuvant — used after primary treatment.
  • chemo after surgery or radiation
• Neoadjuvant — used before primary treatment.
  • Chemo used to shrink a tumor before surgery
• Palliative — used to control symptoms and improve quality of life
• Curative — intended to cure disease
• Myeloablative — Obliterates bone marrow
  • Used before BMT

Complications of Chemotherapy

• Hypersensitivity reaction — Often prevented by premedications
• Extravasation — Irritants — Vesicants
• Anaphylaxis — True allergic response
  • Can be a Code situation!
• Know your institutional policies!!
Hazardous Drugs

- Must meet one or more of these criteria:
  - Genotoxicity – causes DNA damage
  - Carcinogenicity – causes cancer development
  - Teratogenicity/developmental toxicity – fetal damage, loss
  - Reproductive toxicity – sterility, infertility
  - Organ toxicity – at low doses

Safe Handling Guidelines

- National Institute for Occupational Safety and Health (NIOSH) [www.niosh.com](http://www.niosh.com)
- Occupational Safety & Health Administration (OSHA) [www.osha.gov](http://www.osha.gov)
- Oncology Nursing Society (ONS) [www.ons.org](http://www.ons.org)
- American Society of Health-system Pharmacists (ASHP) [www.ashp.org](http://www.ashp.org)
- Washington State Hazardous Drug Law (ESB 5994) [http://www.lni.wa.gov/Safety/Topics/AtoZ/HazardousDrugs/](http://www.lni.wa.gov/Safety/Topics/AtoZ/HazardousDrugs/)
- Your own institutional policies and procedures

Principles of Safe Handling

- Preparation in biologic safety cabinet (BSC) under laminar flow hood
- Safe handling techniques during storage, mixing, and transport
- Processes in place for labeling, administration, and disposal
- Personal Protective Equipment
Potential Exposure Routes

- **Inhalation**
  - wear mask if risk of aerosolization.

- **Skin absorption**
  - wear chemotherapy-tested gloves
  - Double-gloving is best practice

- **Ingestion**
  - do not eat in areas where chemotherapy is prepared, stored or administered.

- **Eyes**
  - wear eye protection if there is any risk of splashing or aerosolization.

Washington State Law

- Passed in 2012 by state legislature
  - Requires all facilities that handle hazardous drugs to comply with NIOSH recommendations
  - List of hazardous drugs defined by NIOSH and formulary
  - Implemented in three stages:
    - January 1st, 2015 – written hazardous drug control program implemented
    - July 1st 2015 – provided employee training
    - January 1st, 2016 – installed appropriate ventilated BSC

- Through Department of Labor & Industries

Summary

- Chemotherapy can be classified according to effect on cell cycle and pharmacologic class
- Each class has different mechanisms of action and side effect profiles
- Special precautions must be taken when handling chemotherapy agents
- Many agencies regulate safe handling of hazardous drugs, including new state law

BIOTHERAPY AND TARGETED THERAPY

Biotherapy

• Harnesses the body’s immune system to fight cancer and other diseases
• Enhances immune response
• Prevents metastasis of cancer cells
• Helps normal cells repair following treatment
• Used as both cancer treatment and supportive care
• Includes:
  – vaccines
  – interleukins
  – interferons,
  – colony stimulating factors

Vaccines

• Two FDA approved for cancer prevention:
  – Hepatitis B
    • Can lead to hepatocellular carcinoma
  – Human Papillomavirus (HPV)
    • Gardasil protects against HPV types 6, 11, 16, 18
    • Cervarix protects against HPV types 16 and 18
• Vaccines for cancer treatment
  – Experimental
  – Results mixed

**Interferons**

- Immunomodulator
- Used in treatment of hematologic diseases, chronic hepatitis B and C, severe malignant osteoporosis
- Side effects include flu-like symptoms, hypersensitivity reactions, hepatotoxicity, depression/suicidal ideation, renal insufficiency


**Interleukins**

- Stimulates different immune cells to enhance tumor-fighting capabilities and immune response
- Used to treat renal cell carcinoma and metastatic melanoma
- Side effects include anaphylaxis, infusion reactions, flu-like symptoms, rash, edema, hepatic/renal/cardiac insufficiency


**Targeted Therapy**

- Tyrosine Kinase Inhibitors
- Cytotoxic Therapies

Targeted Therapy

- Substantial growth in field in last 10 years
  - The first three:
    - Rituximab approved 1997
    - Trastuzumab approved 1998
    - Bevacizumab approved 2004
  - Within the last three years, 36 new oncology drugs received FDA approval
    - Most were targeted therapies
- Monoclonal antibodies (mAbs) and Small Molecule Inhibitors


Mechanism of Action

- Signal transduction:
  - Generated inside or outside of the cell
  - Triggers a signaling cascade that directs the cell to do a specific activity
- Cell signaling directs cellular growth, function, and death
  - Done by biochemical or molecular messengers
    - Cytokines, enzymes, etc


Classifications

Monoclonal Antibodies

- Type of therapy derived from human and mouse antibodies.
- Target specific tumor markers on the outside of cells.
  - Key in lock
- Usually given IV
- Some incorporate radionuclides
- Often end in –mab

Small Molecule Inhibitors

- Consist of very small molecules
- Target intracellular pathways
  - Alarm code
- Requires long-term pathway inhibition; treatments are usually oral
- Often, but not always, end in –nib
  - One exception: temsirolimus

Examples of mAbs

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target</th>
<th>Source</th>
<th>Indication</th>
<th>Year Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>rituximab</td>
<td>CD20</td>
<td>Chimeric</td>
<td>Non-Hodgkins Lymphoma</td>
<td>1994</td>
</tr>
<tr>
<td>trastuzumab</td>
<td>HER-2</td>
<td>Humanized</td>
<td>Breast, gastric cancer</td>
<td>1998</td>
</tr>
<tr>
<td>cetuximab</td>
<td>EGFR</td>
<td>Chimeric</td>
<td>HN, colorectal cancer</td>
<td>2004</td>
</tr>
<tr>
<td>bevacizumab</td>
<td>VEGF</td>
<td>Humanized</td>
<td>Colorectal, GBM, NSCLC</td>
<td>2004</td>
</tr>
<tr>
<td>panitumumab</td>
<td>EGFR</td>
<td>Human</td>
<td>Colorectal cancer</td>
<td>2006</td>
</tr>
<tr>
<td>ofatumumab</td>
<td>CD20</td>
<td>Human</td>
<td>CLL</td>
<td>2009</td>
</tr>
<tr>
<td>Brentuximab vedotin</td>
<td>CD30</td>
<td>Chimeric</td>
<td>HD, anaplastic lymphoma</td>
<td>2011</td>
</tr>
</tbody>
</table>

Adapted from http://www.actip.org/pages/library/Table_Monoclonal_Antibodies.pdf

Side Effects

- Highly dependent on the cellular pathway being disrupted and agent administered
  - Hypersensitivity reactions are possible
    - Some agents require premedication
  - Dermatologic toxicities can be severe (acneform rash, PPE, dry/cracked skin, fissuring)
    - May require advanced supportive care; can be dose-limiting
  - Also cardiac dysfunction, hepatotoxicity, nausea, vomiting, hypertension, fatigue

### Small Molecule Inhibitors

![Diagram of Small Molecule Inhibitors]

### Examples

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target</th>
<th>Indication</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib (Velcade)</td>
<td>26S proteasome</td>
<td>Multiple myeloma, mantle cell lymphoma</td>
<td>IV, SC</td>
</tr>
<tr>
<td>Erlotinib (Tarceva)</td>
<td>EGFR</td>
<td>NSCLC, pancreatic cancer</td>
<td>PO</td>
</tr>
<tr>
<td>Everolimus (Afinitor)</td>
<td>mTOR</td>
<td>Breast, renal cell</td>
<td>PO</td>
</tr>
<tr>
<td>Imatinib mesylate (Gleevec)</td>
<td>MCR-ABL</td>
<td>Ph+ CML</td>
<td>PO</td>
</tr>
<tr>
<td>Sorafenib (Nexavar)</td>
<td>Multi-kinase</td>
<td>Hepatocellular, renal cell carcinoma</td>
<td>PO</td>
</tr>
<tr>
<td>Temsirolimus (Torisel)</td>
<td>mTOR</td>
<td>Renal cell carcinoma</td>
<td>IV</td>
</tr>
</tbody>
</table>


### Side Effects

- Very drug specific!
  - Dermatologic toxicities
    - Rash, acne, PPE, oral ulceration
  - Cardiac dysfunction
    - Edema, fluid retention, cardiomyopathy, decreased LVEF, QT prolongation, hypertension
  - Miscellaneous
    - Electrolyte imbalances, hair color changes, hepatotoxicity, skin discoloration,
Summary

- Effect specific cellular markers/signals on both healthy and cancerous cells
  - Cancerous cells overexpress tumor markers
- Infusion reactions are not uncommon in mAbs
- Many agents are PO
  - Patient education is important
  - Some agents cannot be crushed; know whether or not they can be taken with food
- Side effects are highly drug specific


COMPLEMENTARY AND ALTERNATIVE (CAM) THERAPIES

CAM Therapies

- Any medical system, practice, or product that is not thought of as standard care
  - Complementary Medicine
    - A CAM therapy used along with standard medicine
  - Alternative Medicine
    - A CAM therapy used in place of standard treatments
  - Integrative Medicine
    - Combines treatments from conventional medicine and CAM for which there is some high-quality evidence of safety and effectiveness

Prevalence in the US

- Approximately 38% of adults and 12% of children use CAM
  - Most use is underreported
  - Use has risen significantly in recent years
  - Spans all cultural/ethnic backgrounds
- $33.9 BILLION spent in 2007 alone
  - Out-of-pocket visits, supplies, materials
- Some CAM practices are more regulated than others
  - Supplements/herbals are NOT FDA regulated

Types of CAM

- Alternative Medical Systems
  - Acupuncture, TCM, naturopathy
- Energy Therapies
  - Reiki, Qi Gong
- Exercise Therapies
  - Tai Chi, Yoga
- Manipulative and Body-based Methods
  - Chiropractic, therapeutic massage, osteopathy
- Mind-body Interventions
  - Aromatherapy, support groups, meditation
- Nutritional Therapeutics
  - Macrobiotic diet, vitamins
- Pharmacological and Biologic Treatments
  - Herbals, hormones,
- Spiritual Therapies
  - Intercessory prayer, spiritual healing

Nursing Considerations

- Be aware of own attitudes, perceptions regarding CAM treatment
- Assess for CAM use with each patient
- Assist with finding evidence-based sources of information
  - ONS PEP
  - Natural Standard
- Support/empower patient choices
# Resources for Patients

- American Cancer Society Complementary and Alternative Medicine  

- National Center for Complementary and Alternative Medicine (NCCAM)  

- American Holistic Medical Association  
  - [http://www.holisticmedicine.org/index.asp](http://www.holisticmedicine.org/index.asp)  
  - Searchable provider database

- Society for Integrative Oncology  
  - [http://www.integrativeonc.org/index.php/patients](http://www.integrativeonc.org/index.php/patients)

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# Questions?

- Thank you!!