Chemotherapy of Neoplasms

PHRM 203
Allison Beale
Overview

• Neoplasms
  – Introduction
  – Causes
  – Types
• Antineoplastic agents
  – Introduction
  – Examples

• Chemotherapy often associated with:
  – Secondary malignancies
  – Seizures (~13% of patients)
  – Nausea & vomiting
Neoplasms
Introduction

• 2nd leading cause of death in US after CV

• All cancers start with a cell or cells that is genetically different from the surrounding cells; all cell types can become cancerous

TERMS

– Anaplasia
  • Loss of cellular organization

– Autonomy
  • Ignore growth regulations

– Metastasis
  • Spread into other tissues

– Angiogenesis
  • Create their own blood supply
Neoplasms Causes

- Genetic predisposition
  - Li-Fraumeni Syndrome
  - Familial Adenomatous Polyposis
- Viral infection (e.g., herpes, HPV, EBV, HBV)
- Nematode infection (e.g., *Spirocerca lupi*)
- Constant irritation or inflammation
- Stress
- Chemicals (mutagens, carcinogens, e.g., Cisplatin)
- Radiation (uv, ionizing)
• Solid
  – Carcinomas
    • Tumors of epithelium
      – Adenomas versus adenocarcinomas
      – Melanoma versus malignant melanoma
        (melanocarcinoma)
  – Sarcomas
    • Tumors of mesenchymal origin
      – Fibroma versus fibrosarcoma
      – Lymphoma versus lymphosarcoma
      – Osteoma versus osteosarcoma
• Hematological malignancies
  – Leukemia (general term for cancer of white blood cells)
Carcinomas by WHO’s ICD-O* Code

* International Classification of Diseases for Oncology

- Epithelial NOS
- Squamous cell
- Basal cell (skin)
- Transitional cell
  - Papillomas
- Adenomas (glandular)
- Adnexal (uterine)
- Mucoepidermoid
- Specialized gonadal

- Cystic, mucinous or serous
- Ductal, lobular or medullary
- Acinar (pancreas, breast, salivary glands)
- Complex epithelial
- Paragangliomas or glomus
- Nevi or melanoma
Carcinomas—many possibilities in one organ

- **Lung carcinomas**
  - Adeno-
    - Glandular tissue origin, usually Goblet cells in the lung
    - Common, 30-40% of all lung carcinomas
  - Squamous cell
    - Usually hilar origin, 20-30%
  - Small cell
    - Smoking related, may secrete ADH (patient becomes hyponatremic)
      - Syndrome of inappropriate ADH secretion (SIADH)
  - Large cell undifferentiated
    - Aggressive, difficult to recognize, 10-15%
  - Sinonasal undifferentiated

*Lung cancer is notorious for paraneoplastic syndrome*

*Paraneoplastic syndromes: Effects caused by hormones (e.g., ADH, ACTH) secreted by tumors*

*Paraneoplastic syndromes may take endocrine (SIADH, Cushing’s), neurological, hematological or other forms*
Sarcomas

connective tissue tumors

• **Bone**
  – Chondro-
  – Osteo-
  – Parosteal osteo-
    • Metaphysal
  – Periosteal osteo-
    • Anywhere else on surface
  – Periosteal chondroma
    • Cartilagenous tumor
  – Small cell osteo-
  – Ewing’s

• **Soft tissue**
  – Muscle
    • Rhabdomyo-
    • Leiomyo-
  – Fat
    • Lipo-
  – Nerves
    • Malignant peripheral nerve sheath tumor
  – Blood vessels
    • Angio-
  – Fibrous tissue
    • Fibro-
    • Myxofibro-
Hematological

• Acute lymphoid leukemia (ALL)
  – Lymphocytes
• Acute myeloid leukemia (AML)
  – Granulocytes
  – Acute promyelocytic leukemia (APL)
• Chronic forms of above:
  – CLL
  – CML
  – CPL

• Meningeal leukemia
• Hodgkin’s lymphoma
  – Reed-Sternberg cells (altered B-cells)
• Non-Hodgkin’s
  – T-cell types
    • Mycosis fungoides (skin)
  – B-cell types
    • Burkitt’s lymphoma
      – EBV = cause
    • Diffuse large B-cell lymphoma

• Myelomas

All of these are diseases with too many of the affected cells
Antineoplastic drugs

Overview

• Mechanisms vary
  – Alter cell survival
  – Alter immune response

• Classes
  – Alkylating agents
  – Antimetabolites
  – Natural products
  – Hormones and hormone modulators
  – Miscellaneous agents

Focus on Tumor Lysis Syndrome

• Break-down products from dead cells
  – Hyperkalemia (cardiotoxic)
  – Hyperphosphatemia*
  – Hyperuricemia*
  – Hypocalcemia (tetany)
  – Acute renal failure (ARF)

• Allopurinol or Rasburicase ↓ hyperuricemia

* These conditions may cause ARF
Effectiveness of cancer chemotherapy by disease

1. Curative
   • ALL, Hodgkin’s, diffuse histiocytic lymphoma, Burkitt’s lymphoma, Testicular cancer, choriocarcinoma (placental)

2. Probably curative
   • AML, small cell, breast, osteogenic sarcoma

3. Major therapeutic benefit
   • Head & neck, cervical, metastatic breast, ovarian, soft tissue sarcomas, nodular lymphomas, chronic leukemias, insulinomas

4. Limited effectiveness
   • Lung, GI, prostate, melanoma
Mechanisms of Resistance

Adapted from pages 493-4, Brenner, Pharmacology 2nd ed.

• **Innate: ABC Transporters**
  - P-glycoprotein efflux pumps
    * Anthracyclines, taxanes and vinca alkaloids
  - Multidrug resistance protein pumps
    * Organic Anion Transporter (OAT) subfamily
    * Glutathione conjugated drugs are pumped out
    * Anthracyclines, methotrexate and vinca alkaloids

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Innate means the tumor has resistance BEFORE therapy
Mechanisms of Resistance

Adapted from pages 493-4, Brenner

• Acquired
  – Gene mutations
    • Topoisomerase
      – Etoposide
    • Dihydrofolate reductase
      – Methotrexate
    • Tubulin or microtubule proteins
      – Vinca alkaloids and taxanes
  – Altered gene expression
    • Dihydrofolate reductase over-expression
      – Methotrexate
    • Antiapoptotic protein induction

Acquired resistance are changes that are a RESULT of therapy
General Toxicity of Neoplastic Agents

Adapted from page 494, Brenner

- **Inhibition of cell replication**
  - Bone marrow, GI, Hair follicles
  - Worst
    - Nitrosoureas (carmustine)
  - Intermediate
    - Methotrexate, fluorouracil, cyclophosphamide
  - Least
    - Bleomycin, cisplatin, vincristine

- **Chemoreceptor trigger zone in medulla**
  - Nausea, vomiting
    - Worst: cisplatin and carmustine

Irritant antineoplastics trigger 5-HT release from enterochromaffin cells in the GIT leading to hypermotility of the GIT (vomiting, diarrhea, nausea)

Some 5-HT is absorbed into blood where platelets absorb it. Excess 5-HT triggers 5-HT3 receptors in CTZ.
Hematopoietic Agents

Colony stimulating factors

WBC growth factors

Hormones that trigger stem cell differentiation into WBCs in bone marrow. Important to replace neutrophils (granulocytes & Macrophages, too).

- Pegfilgrastim (Neulasta)
- Filgrastim (Neupogen)
- Sargramostim (Leukine)

RBC growth factors

Erythropoietin is a hormone produced by endothelial cells in the liver and kidney

- Epoetin alfa (Procrit) – rDNA erythropoietin
- Darbepoetin alfa (Aranesp)
  - Synthetic erythropoietin

SC, IV
### Antiemetic Therapy

Adapted from “Protocol for the use of antiemetics to prevent chemotherapy-induced nausea and vomiting” VHA Pharmacy Benefits Management Strategic Healthcare Group and Medical Advisory panel

<table>
<thead>
<tr>
<th>Antiemetic</th>
<th>Class</th>
<th>Receptor</th>
<th>Site of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aprepitant</td>
<td>Substance P antagonist</td>
<td>GI</td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>Phenothiazine</td>
<td>DA</td>
<td>GI &amp; CNS</td>
</tr>
<tr>
<td>Haloperidol, droperidol</td>
<td>Butyrophenone</td>
<td>DA</td>
<td>GI &amp; CNS</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Benzamide</td>
<td>DA, 5-HT</td>
<td>GI &amp; CNS</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Antihistamine</td>
<td>Histamine</td>
<td>CNS</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>Anticholinergic</td>
<td>ACh</td>
<td>CNS</td>
</tr>
<tr>
<td>Dronabinol C-III</td>
<td>Cannabinoid</td>
<td>CB₁, CB₂</td>
<td>CNS</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>Serotonin antagonist</td>
<td>5-HT</td>
<td>GI &amp; CNS</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Corticosteroid</td>
<td>UNK</td>
<td>GI</td>
</tr>
</tbody>
</table>
## Antineoplastic Drugs

### Alkylating Agents - nitrogen mustards

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorambucil (Leukeran)</td>
<td>Lymphomas and leukemias including Hodgkin’s disease; under consideration to treat rheumatoid arthritis; Off label - amyloidosis, polycythemia vera, autoimmune hemolytic anemia, etc.</td>
</tr>
<tr>
<td>Cyclophosphamide (Cytoxan)</td>
<td>In cocktails to treat lymphoma, myelomas, leukemias etc. (Also used to treat autoimmune conditions: MS, rheumatoid arthritis, Lupus…).</td>
</tr>
</tbody>
</table>

Table adapted from: *Focus on Nursing Pharmacology, 4th Ed.*, by AM Karch, Lippincott, Williams & Wilkins, 2008
# Nitrogen Mustard ADRs

<table>
<thead>
<tr>
<th>Drug</th>
<th>ADRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common to the class</td>
<td><strong>Seizures</strong>, nausea, vomiting, <strong>myelosuppression</strong>, liver failure, <strong>pulmonary fibrosis</strong>, Steven’s-Johnson, <strong>Secondary malignancies</strong> (carcinogens, mutagens &amp; teratogens)</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td><strong>Azoospermia</strong></td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td><strong>Cardiotoxicity</strong>, <strong>hemorrhagic cystitis</strong>, SIADH, alopecia, anaphylaxis</td>
</tr>
</tbody>
</table>
Antineoplastic drugs

Alkylating Agents - nitrosoureas

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
</table>

Carmustine ADRs include: Brain edema, kidney &/or liver failure, bone marrow suppression, pulmonary fibrosis, intense pain at injection site and secondary malignancies. It will stain skin BROWN.
Antineoplastic drugs
Alkylating Agents

• Mechanism of action of nitrogen mustards and nitrosoureas
  – Alkylate (cross-links) DNA (& RNA) which blocks the formation of the DNA-RNA complex in transcription
# Antineoplastic Drugs

## Alkylating Agents - Platinum

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisplatin</td>
<td>Combo therapy for metastatic testicular or ovarian tumors, advanced bladder cancers, small cell carcinoma of lung, etc.</td>
</tr>
</tbody>
</table>

- **Cisplatin (Platinol)**
  - IV infusion
  - Inadvertent overdose a problem

Cisplatin ADRs include: Seizures, **tinnitus**, **ototoxicity**, nausea/vomiting, kidney failure, myelosuppression, **anaphylaxis** and serious alterations in electrolytes.
Antineoplastic drugs

Alkylating Agents - Platinum

• Mechanism of action
  – They form platinum complexes in the nucleus that cross link DNA.
  – Cisplatin first discovered in 1845, but not known to be cytotoxic until 1965.
  • Enhances radiation therapy effects
Antineoplastic drugs

Alkylating Agents - Alkyl sulfonates

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Busulfan</td>
<td>Chronic myelogenous leukemia with the Philadelphia chromosome, bone marrow transplants</td>
</tr>
</tbody>
</table>

Mechanism of action

Cross links DNA-DNA as well as DNA-protein

Serious ADR: interstitial fibrosis

Table adapted from: Focus on Nursing Pharmacology, 4th Ed., by AM Karch, Lippincott, Williams & Wilkins, 2008
Antineoplastic drugs

Alkylating Agents - Others

• Hydrazines
  – Procarbazine

• Triazenes
  – Dacarbazine, temozolomide

• Aziridines
  – Carboquone, Triaziquone, Triethylenemelamine
Antimetabolites

- Folic acid analogs
  - Methotrexate, Pemetrexed
- Pyrimidine analogs
  - Fluorouracil, Cytarabine, Gemcitabine
- Purine & related analogs
  - Mercaptopurine, Pentostatin, Cladribine, Fludarabine

Methotrexate has many boxed warnings
### Antineoplastic drugs

#### Antimetabolites - Folic acid

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate (Trexall, Rheumatrex)</td>
<td>Leukemia, choriocarcinomas (germ cell cancers), breast &amp; lung carcinomas, osteosarcomas &amp; many other cancers, psoriasis, rheumatoid arthritis &amp; other autoimmune diseases</td>
</tr>
</tbody>
</table>

**Contraindications:** live vaccines, pregnancy, lactation

- PO
- Keep Cool
Antineoplastic drugs
Antimetabolites - Folic acid

• Mechanism
  – Analogs of folic acid
  – $\Theta$ dihydrofolate reductase
    • $\otimes$ activation of folate
      – $\Theta$ DNA, RNA and protein synthesis
  – Nutrients affecting/or affected by methotrexate
    • Folic acid
      – ↓ Methotrexate activity
    • Vitamin A
      – ↑ Methotrexate activity
    • Vitamin $B_{12}$
      – Levels of cobalamin are reduced by methotrexate
Methotrexate ADRs & ☐

- Severe bone marrow suppression (myeloablation)
- Sudden Death
- Lung disease
- Malignant lymphomas
- Fetal toxicity/death
- Fatal skin reactions including Steven’s-Johnson
- Kidney or liver failure
- Tumor Lysis Syndrome

- Bacterial infection
- GI problems (anorexia, hemorrhage, ulcers or perforations, vomiting, gingivostomatitis, diarrhea)
  - Photosensitivity
  - Seizures
  - Azotemia
  - ↑ risk of CVA
    - ↑ [homocysteine]
## Antineoplastic drugs
### Antimetabolites - Purines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cladribine</td>
<td>Active hairy cell leukemia</td>
</tr>
<tr>
<td>Clofarabine</td>
<td>Acute lymphocytic leukemia (ALL) after 2 relapses on another regimen</td>
</tr>
<tr>
<td>Fludarabine</td>
<td>Chronic lymphocytic leukemia (CLL); unresponsive B cell CLL</td>
</tr>
<tr>
<td>Pentostatin</td>
<td>Hairy cell leukemia in adults refractory to α interferon therapy</td>
</tr>
<tr>
<td>Thioguanine</td>
<td>Acute leukemia</td>
</tr>
</tbody>
</table>

Table adapted from: *Focus on Nursing Pharmacology, 4th Ed.*, by AM Karch, Lippincott, Williams & Wilkins, 2008
Antineoplastic drugs
Antimetabolites: purines

• Mechanism
  – purine analogs, so interfere with DNA activities
## Antineoplastic drugs

### Antimetabolites - Pyrimidines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorouracil (5-FU, Adrucil, Carac) ![icon]</td>
<td><em>Palliative</em> treatment of various GI cancers, advanced breast &amp; pancreatic carcinomas; Off label: topical basal cell carcinoma and actinic and solar keratoses; esophageal, cervical, urinary bladder, kidney, head &amp; neck cancers</td>
</tr>
</tbody>
</table>

*Discoloration doesn’t affect it, but if a precipitate forms, heat to 140 degrees Fahrenheit and shake vigorously.*

*IV*
Antineoplastic drugs
Antimetabolites - Pyrimidine

• Mechanism
  – Pyrimidine analog.
  – **Fluorouracil** developed in 1957 after observation that cancer cells used uracil more efficiently than normal cells.
    • Θ thymidylate synthetase and the normal production of thymidine
  – **5-FU ADRs** (*serious and/or life threatening only*)
    • Weakness, myocardial ischemia, GI ulcers and bleeding, nausea and vomiting, myelosuppression, alopecia, pain and dermatitis
Natural Products

- Enzymes
- Vinca alkaloids
- Taxanes
- Epipodophyllotoxins
- Camptothecins
- Antibiotics
- Anthracenedione
Antineoplastic drugs

Natural Products - Enzymes

- Asparaginase (Elspar) 🚫 ⚪ ✓
  - Indication: acute lymphoblastic leukemia (ALL)
  - Contraindications:
    - Allergy
    - Thrombosis prior to therapy
    - Pancreatitis ❌ ❌ ❌
    - Serious hemorrhage events ❌ ❌ ❌
  - Mechanism
    - ALL cells lack asparagine synthetase
    - Asparaginase converts asparagine to aspartic a. & then to ammonia, depriving the ALL cells of circulating asparagine

Discontinued, but other forms of asparaginase are still available.

Can cause hyperglycemia and permanent glucose intolerance

IV, IM, SC
Serious Asparaginase ADRs

- Vomiting/nausea/anorexia
- Hemorrhagic pancreatitis
- Azotemia (abnormally high levels of nitrogen-compounds, eg urea)
- Kidney failure
- Hemorrhage due to suppression of clotting factor synthesis
- Liver failure (hepatitis)
- Rash
- Glucose intolerance & hyperglycemia
## Antineoplastic drugs

### Natural Products: Mitotic inhibitors/spindle poisons

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Taxanes</strong></td>
<td></td>
</tr>
<tr>
<td>Docetaxel</td>
<td>Breast cancer and non-small cell lung cancer</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Ovarian cancer, breast cancer, non-small cell carcinoma, AIDS-related Karposi’s sarcoma “Taxol” from Western Yew Bark</td>
</tr>
<tr>
<td><strong>Vinca alkaloids - Madagascar periwinkle</strong></td>
<td></td>
</tr>
<tr>
<td>Vincristine (Oncovin)</td>
<td>Acute leukemia, lymphomas, various sarcomas (including neural) &amp; carcinomas</td>
</tr>
</tbody>
</table>

Table adapted from: *Focus on Nursing Pharmacology, 4th Ed.*, by AM Karch, Lippincott, Williams & Wilkins, 2008
Antineoplastic drugs

Natural Products: Mitotic inhibitors/spindle poisons

• **Vincristine** mechanism of action
  – Binds to tubulin dimers
  • Blocks the polymerization of the dimers into microtubules. Microtubules form the spindles necessary to separate the DNA during cell division, so mitosis is blocked. This affects all dividing cells, not just cancer cells.
  • Vinca alkaloids discovered & in use since 1959

• **Serious ADRs**
  – Alopecia, neurotoxicity (coma, seizures), paresthesias, **severe constipation**, ↓ deep tendon reflexes, myelosuppression, SIADH (urine retention), intestinal necrosis, bronchospasm
## Antineoplastic drugs

### Natural Products: Topoisomerase inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epipodophyllotoxins (Mandrake)</td>
<td>Testis, small cell and other lung cancers, breast cancer, Hodgkin’s and non-Hodgkin’s lymphomas, acute myelogenous leukemia, Kaposi’s sarcoma</td>
</tr>
<tr>
<td>Etoposide (Eposin)</td>
<td>PO, IV</td>
</tr>
<tr>
<td>Teniposide</td>
<td>Same as above, plus acute lymphoblastic leukemia in kids</td>
</tr>
<tr>
<td>Camptothecins</td>
<td></td>
</tr>
<tr>
<td>Topotecan</td>
<td>Ovarian cancer, small-cell lung cancer, colon and lung cancer.</td>
</tr>
<tr>
<td>Irinotecan</td>
<td>Same as above</td>
</tr>
</tbody>
</table>

Table adapted from: *Goodman & Gilman’s The Pharmacological Basis of therapeutics, 11th Ed, chp51 McGraw Hill, 2006*
## Antineoplastic drugs

### Natural Products: Antibiotics - anthracyclines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daunorubicin</td>
<td>Advanced HIV infection and associated Kaposi’s sarcoma</td>
</tr>
<tr>
<td>Doxorubicin (Adriamycin)</td>
<td>Leukemias, and many other cancers including Kaposi’s sarcoma (liposomal formulation)</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Adjunct after resection of primary breast tumor</td>
</tr>
<tr>
<td>Idarubicin</td>
<td>Combo therapy for acute myeloid leukemia</td>
</tr>
<tr>
<td>Valrubicin</td>
<td>Intravesical therapy for carcinoma in situ of the bladder</td>
</tr>
</tbody>
</table>

Serious ADRs: **Cardiotoxicity**, nausea/vomiting, red urine, **myelosuppression**, 2\textsuperscript{nd}ary **malignancies**, alopecia, anaphylaxis. Will cause nerve death if injected intrathecally and **tissue necrosis** if given IM/SQ. Must be administered by rapid IV injection or PO.

Table adapted from: *Focus on Nursing Pharmacology, 4th Ed.*, by AM Karch, Lippincott, Williams & Wilkins, 2008
Antineoplastic drugs

Natural Products: Antibiotics - anthracyclines

• **Doxorubicin** mechanism of action
  – Intercalates DNA
  – Inhibits topoisomerase II
  – Generates free radicals
    • Damage DNA, RNA and proteins
  – Liposomal doxorubicin
    • Encapsulation in liposomes made of egg phosphatidycholine and cholesterol
      – Prolongs exposure in the tumor cells due to selective uptake by the tumors

• **Max. cumulative dose = 550 mg/m²**
  – Add Dexrazoxane (Cardioxane®) after 300 mg/m² (55% max dose)
    • cardioprotective

Side effect = RED urine
## Antineoplastic drugs

### Natural Products: Antibiotics, streptomycins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bleomycin</strong> (Blenoxane)</td>
<td><em>Palliative</em> treatment of squamous cell carcinomas (cervix, head and neck, skin, vulva, penis and other soft tissues), testicular cancers (sarcomas), &amp; lymphomas (Hodgkin’s and non-Hodgkin’s). Treats malignant pleural effusion.</td>
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<td><strong>IV, IM, SC</strong></td>
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Antineoplastic drugs

Antibiotics streptomycins

• Bleomycin mechanism of action
  – Induces DNA strand breakage

Serious ADRs: nausea/vomiting, pneumonitis, pulmonary fibrosis, alopecia, dermatitis, chills, anaphylaxis and an idopathic reaction of hypotension, confusion, fever, chills & wheezing
Hormones and antagonists

- Adrenocortical suppressants
- Adrenocorticosteroids
- Progestins
- Estrogens
- Anti-estrogens
- Aromatase inhibitors
- Androgens
- Anti-androgen
- Gonadotropin-releasing hormone analog
## Antineoplastic drugs

### Female Homones & Hormone Modulators

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastrazole</td>
<td>Advanced breast cancer</td>
</tr>
<tr>
<td></td>
<td>Action: antiestrogen, blocks synthesis</td>
</tr>
<tr>
<td>Fulvestrant</td>
<td>Hormone receptor-positive breast cancer</td>
</tr>
<tr>
<td></td>
<td>Action: binds to/down regulates estrogen receptor</td>
</tr>
<tr>
<td>Tamoxifen (Nolvadex, Soltamox)</td>
<td>Adjuvant to treatment of: Breast cancer (receptor ⊕ tumors)</td>
</tr>
<tr>
<td></td>
<td>Action: competes for estrogen receptor (it is a non-steroidal antiestrogen)</td>
</tr>
</tbody>
</table>

PO
### Male Hormones & Hormone Modulators

#### Leuprolide (Lupron)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leuprolide</td>
<td>Advanced prostate cancer (hormone dependent)</td>
</tr>
<tr>
<td></td>
<td>Action: A super gonadotropin releasing hormone (GnRH) that in high levels,</td>
</tr>
<tr>
<td></td>
<td>blocks the release of gonadotropin hormones.</td>
</tr>
</tbody>
</table>

**IV, SC**

[Link](http://www.copewithcytokines.de/cope.cgi)
## Serious ADRs of Hormonal Modulators

<table>
<thead>
<tr>
<th>Drug</th>
<th>ADRs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoxifen</td>
<td>CVA/stroke, edema, hot flashes, thromboembolism, nausea/vomiting, diarrhea, <strong>endometrial cancer</strong> or <strong>uterine sarcoma</strong>, myelosuppression, hepatic necrosis, hypercalcemia, weight gain or loss, pulmonary <strong>embolism</strong> and skin changes</td>
</tr>
<tr>
<td>P450↓</td>
<td></td>
</tr>
<tr>
<td>Leuprolide</td>
<td>Dizziness, depression, myocardial infarction, peripheral edema, hot flashes, nausea/vomiting, weight gain or loss, impotence/amenorrhea, pulmonary fibrosis, gynecomastia or androgen-like effects</td>
</tr>
</tbody>
</table>
Antineoplastic drugs

**Others**

- Tyrosine kinase inhibitors
  - Erlotinib, Gefitinib, Imatinib (Gleevec)
- Hydroxyurea
- Monoclonal antibodies
  - Cetuximab (Erbitux), Panitumumab, Rituximab, Bevacizumab (Avastin), Gemtuzumab
- Photosensitizers
  - Aminolevulinic acid, Efaproxiral, Talaporfin, Verteporfin
- Unclassified
  - Retinoids, like Tretinoin (Vesanoid), Arsenic trioxide

Avastin sounds like Avastatin
End note: Thalidomide (Thalomid)

- Potent teratogen from the 1950’s
- Indications:
  - Multiple myeloma, erythema nodosum leprosum
- Mechanism:
  - Unknown
    - Immunomodulatory
      - \( \Theta \) chemotaxis & phagocytosis
    - Anti-inflammatory
      - \( \Theta \) production of tumor necrosis factor \( \alpha \)
    - Anti-angiogenesis
      - \( \Theta \) basic fibroblast growth factor & vascular endothelial growth factor
- ADRs
  - Peripheral sensory neuropathy
  - "Drowsiness", dizziness and constipation

ENL = immune-complex vasculitis caused by death of leprosy bacilli. Lesions usually present as nodules.

Must sport a “Do not get pregnant” sticker

PO