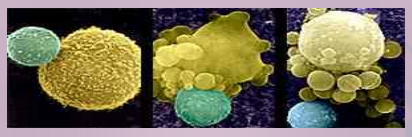
Drugs Affecting the Immune System: Biologic Response Modifiers



Maritess F. Najera, MSN, RN, CCN

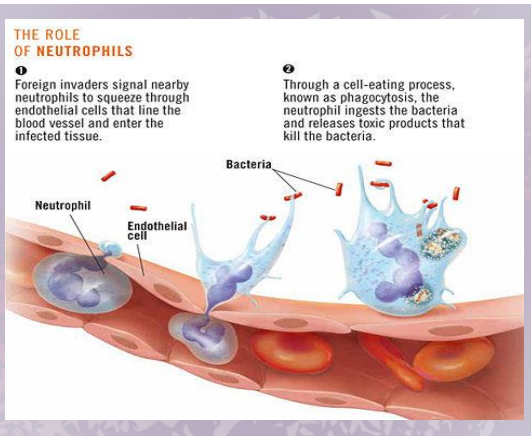
Los Angeles County

College of Nursing and Allied Health

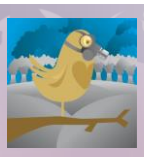
mnajera@dhs.lacounty.gov

Objectives

- Terminology
- Lab Monitoring
- Herbal Precautions
- Biologic Response Modifiers
- Nursing Process
- Client Teaching
- Vitamins & Minerals
- Sociocultural Considerations

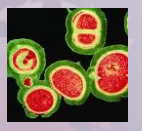


Terminology



- Neutropenia
  - ↓ number of neutrophils in the blood
  - Absolute neutrophil count (ANC) < 1800mm3
  - Normal ANC: 1.5 to 8.0 (1,500 to 8,000/mm3)
- Leukopenia
  - ↓ number of WBCs in the blood

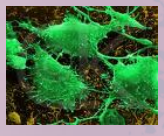
Terminology



- Thrombocytopenia
  - ↓ number of platelets in the blood
  - Normal: 150,000 – 400,000
- Anemia
  - ↓ number of RBCs in the blood
- Female: 11.5-16 mg/dl
- Male: 14-18 mg/dl

Lab Monitoring

- ANC determines the effectiveness of Epogen
- The WBC consists of the following (differential):
  Lymphocytes: 20-40%
  Neutrophils: 50-60%
  Basophils: 0.5-2%
  Eosinophils: 1-4%
  Monocytes: 2-9%



- **ANC** = Total WBC x (% "Segs" + % "Bands")
  Equivalent to: WBC x percentage of mature & nearly mature neutrophil

Terminology

- Hematinics
  - Agents that ⇧ the **Hgb** level & **Erythrocytes**
- Hematopoiesis
  - Formation of **blood** cellular components in response to body demands
- Granulocytes
  - WBCs characterized with granules in their cytoplasm: Neutrophils, eosinophils, & basophils

Terminology

- Granulocytes
  - WBCs characterized with granules in their cytoplasm: Neutrophils, eosinophils, & basophils
- Erythrocytes
  - Mature red blood cells (RBCs)
- Reticulocytes
  - Immature red blood cells (RBCs)

Herbal Alert

- **Echinacea, Elderberry, Ginseng, Goldseal & Green Tea**
  - Act to stimulate the immune system
    - Cause untoward effects
- Not recommended in combination with BRMs
- **Table 6-2**: Summary of Selected Herbs

Biologic Response Modifier
(Immunomodulator)
Functions

1. Enhance client immunologic functions
   - Immunomodulation
2. Destroy or interfere with tumor activities
   - Cytotoxic/Cytostatic effects
3. Promote differentiation of stem cells
   - Examples: Interferons, Interleukins, Colony-stimulating Factors, & Monoclonal Antibodies

Interferons (IFN)

- **Naturally occurring proteins**
  - **Type I**
    - Alpha & Beta
    - Bind selectively to effector cells
  - **Type II**
    - Gamma
    - Binds to a different cell surface receptor

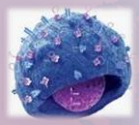
Actions of Interferons

1. **Aid immune system to resist invading microorganisms**
2. **Decrease cell proliferation**

When germ relationships go bad

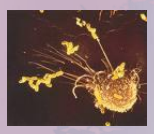
When would you want to slow cell proliferation?

Interferon Alpha



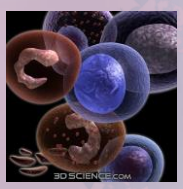
- Produced by B cells, T cells, macrophages, & null cells
- Antiviral, Antiproliferative, & Immunomodulatory effects
  - Inhibits intracellular replication of viral DNA
  - Interferes with tumor cell growth
  - Enhances natural killer (NK) cell activity

IFN Alpha Pharmocokinetics



- 80% absorbed by body
  - Metabolized & excreted by liver & kidneys
- Peak: 4-8 hrs
- Route: subQ, IM, & IV
  - subQ: Platelet count < 50,000

IFN Alpha Side Effects/Adverse Reactions



- Flu-like syndrome
  - Chills, fever, myalgias, & **fatigue**
- Gastrointestinal
  - N/V/D, **anorexia**, & xerostomia

IFN Alpha
Side Effects/Adverse Reactions

- Neurological (70%)
  - Somnolence, mild confusion, poor concentration, irritability, seizures, transient aphasia, & hallucinations
  - **Depression, suicidal ideation (SI), & suicide attempts**
  - **→ DC immediately**
  - **Reversible after DC'd**

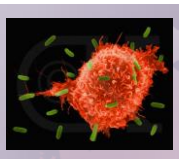
IFN Alpha
Side Effects/Adverse Reactions

- Cardiopulmonary
  - **Tachycardia, tachypnea, pallor, EKG changes, orthostatic hypotension, & MI**

- Renal & Hepatic
  - **Increased BUN/Cr, proteinuria, & elevated transaminases**

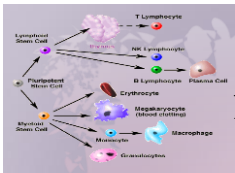
IFN Alpha
Side Effects/Adverse Reactions

- Hematologic (**Reversible**)
  - **Neutropenia & thrombocytopenia**
- Dermatologic
  - Maculopapular rash, pruritus, injection site irritation, & alopecia
- Hydration minimizes side effects



Interferon Nursing Implications

- Administer cautiously in:
  - Severe cardiac, renal, & hepatic disease
  - Seizures & CNS dysfunction
- 18 & older
- Use 2nd form of Contraceptive



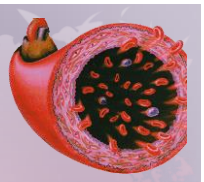
Interferon Nursing Implications

- Baseline & periodic CBC & LFTs
- Minimum 6 months of tx
- Dose reductions

Roferon-A Uses

1. Hairy Cell Leukemia (18 & ⇧)
2. Chronic Myelogenous Leukemia
3. Condylomata acuminata
4. AIDS-related Kaposi's sarcoma

Intron A Uses

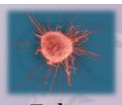


1. Malignant Melanoma
2. Hairy Cell Leukemia
3. Follicular non-Hodgkin's lymphoma
4. AIDS-related Kaposi Sarcoma
5. Condylomata Acuminata
6. Chronic Hepatitis B & Non-A Hepatitis

Interferon Beta

1. Enhances activity of suppressor T cells
2. Reduces production of proinflammatory cytokines
3. Reduces antigen-presentation
4. Inhibits movement of lymphocytes in the Central Nervous System (CNS)

- **Tx:** Multiple Sclerosis



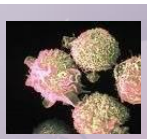
Interferon Gamma-1b

1. Enhances oxidative metabolism of macrophages
2. Enhances antibody-dependent cell toxicity
3. Activates natural killer cells
4. Enhances Fc receptors & major histocompatibility antigens

- **Tx:** Severe Malignant Osteopetrosis
  Chronic Granulomatous disease
  Chronic Myelogenous Leukemia
  Renal Cell Carcinoma

Colony-stimulating Factors (CSF)

- Proteins that stimulate or regulate the growth, maturation, & differentiation of bone marrow stem cells
- Not directly tumoricidal
- Used in Cancer tx



Colony-stimulating Factors

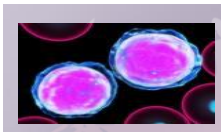
1. Decreases length of post-treatment neutropenia
   - Reduces incidence & duration of infection
2. Permits delivery of higher doses
   - Minimizes myelosuppression toxicity

Colony-stimulating Factors

3. Reduces bone marrow recovery time after bone marrow transplantation
4. Enhances macrophage or granulocyte tumor-, virus-, & fungus-destroying ability
5. Prevents severe thrombocytopenia after myelosuppressive chemotherapy

Colony-stimulating Factors

- Treatment
  - Neutropenia secondary to disease or treatment
  - subQ or IV
- FDA approved:
  - Erythropoietic stimulating agents, granulocyte colony stimulating factor, granulocyte macrophage colony stimulating factor, & thrombopoietic growth factor

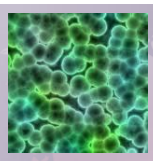


Erythropoietin

- Glycoprotein produced by the kidneys
  - Stimulates RBC production in response to hypoxia
  - Stimulates division & differentiation of committed RBC progenitors in the bone marrow

Erythropoietin Stimulating Agents (ESAs)

- **Epoetin Alfa (Procrit)**
  - Anemia secondary to CRF
  - AZT-treated HIV infections
  - Cancer Chemotherapy
  - Anemic clients to undergo surgery
- Reduce dose 25% if Hgb is:
  - 12 g/dl or increases > than 1 g/dl in any 2 wks
- Hold if > 12 g/dl, resume once < 11 g/dl



Erythropoietin Stimulating Agents

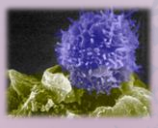
- **Darbepoetin Alfa (Aranesp)**
  - Anemia secondary to CRF
  - Chemotherapy tx for Nonmyeloid Malignancies

ESA Side Effects/Adverse Reactions

- DO NOT administer if Hgb > 12 g/dl
  - Closely monitor for target Hgb
  - Risks of death, serious CV events, & tumor progression

- **HTN, HA**, arthralgias, N/V/D, fatigue, chest pain, asthenia, dizziness, seizures, & thrombosis

ESA Contraindications



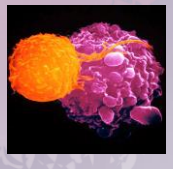
- Uncontrolled HTN
- Hypersensitivity to:
  - Mammalian Cell-derived products
  - Human Albumin or Polysorbate
- Evaluate iron stores
  - Transferrin sat. (min. 20%) & Ferritin (100ng/ml)
  - Iron supplements to enhance erythropoiesis

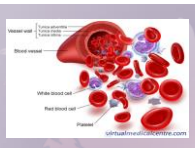
ESA Nursing Implications

- Do not shake vial
- Single use vial
- Warm to room temperature: subQ
- 1 ml or less/injection
- Ice injection site
- Change needle for injection

Granulocyte CSF (G-CSF)

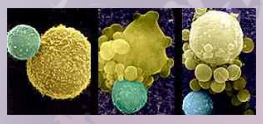
- A glycoprotein produced by
  - Monocytes, fibroblasts, & endothelial cells
- Regulates the production of neutrophils in the bone marrow
- FDA approved:
  - Filgrastim (Neupogen)
  - Pegfilgrastam (Neulasta)





Granulocyte CSF

- ↓ the incidence of infections in clients:
  1. Receiving myelosuppressive cancer chemo
  2. Receiving induction or consolidation chemo for Acute Myeloid Leukemia
  3. Receiving bone marrow transplantation for cancer

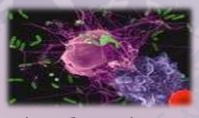


Granulocyte CSF

- ⇩ the incidence of infections in clients:

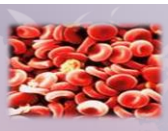
4. Undergoing peripheral blood progenitor cell collection & therapy
5. Severe, chronic neutropenia

Neupogen (Filgrastim): Side Effects



- N/V/D, **bone pain**, skeletal pain, alopecia, neutropenia, fever, mucositis, fatigue, anorexia, dyspnea, headache, cough, skin rash, chest pain, generalized weakness, sore throat, stomatitis, constipation & pain
- Bone pain ~ Tx: Nonopioid analgesia
- Occurs in pts receiving higher IV doses
- Splenic rupture: LUQ abd/shoulder tip pain

Neupogen (Filgrastim): Nursing Implications



- Do not administer 24 hrs before or after chemo
- Dosing: ANC dependent
- Contraindicated with hypersensitivity to E. coli derivant proteins
- Single use vials (no preservatives)
- Do not freeze or shake vials/syringes

Neulasta (Pegfilgrastim): Nursing Implications

- **Similar to Neupogen**
- Do not administer **14 days before & 24 hrs** after cytotoxic chemo
- Dosing: ANC dependent
- Contraindicated with hypersensitivity to E. coli derivant proteins
- Single use vials (no preservatives)
- Do not freeze or shake vials/syringes

Granulocyte-macrophage colony-stimulating factor (GM-CSF)

- Sargramostim (Leukine)

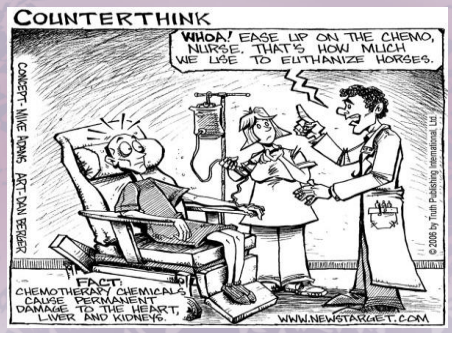
1. Support survival
2. Clonal expression
3. Differentiation (maturation) of hematopoietic progenitor cells

Sargramostim: Side Effects/Adverse Reactions

- Fever, malaise, sepsis, N/V/D, asthenia, **liver damage**, alopecia, peripheral edema, rash, peripheral edema, **dyspnea**, blood dyscrasias, **renal** dysfunction, CNS disorder

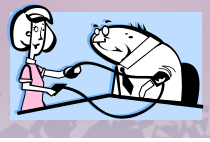
- Pleural or pericardial effusions
  - Causes increased fluid retention

Does the benefit outweigh the risk?



Sargramostim: Side Effects/Adverse Reactions

- Underlying pulmonary disease
  - Reduce by ½ or DC if dyspnea
- Supraventricular dysrhythmia
- Labs: Serum Cr, bilirubin, & LFTs



Sargramostim: Contraindications

1. Excessive leukemia myeloid blast cells in the bone marrow or peripheral blood
2. Known hypersensitivity to:
   - GM-CSF or any component of the product
   - Yeast-derived products

Sargramostim: Nursing Implications

- Do not administer:
  1. 24 hrs before or after chemo
  2. Within 12 hrs before or after radiation
- Reconstitute for injection
- May be stored up to 20 days

Thrombopoietic Growth Factor

- Oprelvekin (Neumega)
  - Recombinant human interleukin-11
  - A platelet growth factor
- Prevents recurrent severe chemo-induced thrombocytopenia
  - Stimulates megakaryocyte & thrombocyte production → normal circulating platelets

Neumega Uses

- High risk nonmyeloid malignancy clients
  - Prevents severe thrombocytopenia
  - Reduces need for platelet transfusion following myelosuppressive chemo
  - Platelet count increases in 5-9 days
- Efficacy: following chemo cycle

Neumega: Side Effects/Adverse Reactions

1. Serious fluid retention
   - **Peripheral edema, exertional dyspnea**, worsening pleural effusions, & ascites
   - Reversible after dc'd ~ several days
2. Cardiovascular events
   - A. Fib & A. Flutter ~ 10%
   - Ventricular arrhythmias

Neumega: Side Effects/Adverse Reactions

3. Opthalmologic events
   - Papilledema & transient visual blurring (1.5%)
4. Hypersensitivity reactions
   - Including Anaphylaxis
   - DC if symptomatic bronchospasms or anaphylaxis occurs

Neumega Drug Interactions

Diuretics:

1. ↑ risk of hypokalemia
2. ↓ in Hgb & serum proteins
3. ↑ in plasma fibrinogen

Neumega : Nursing Implications

- Dose reduction in renal dysfunction
- Platelet count determines tx duration
- Single use reconstituted vial
- Do not rub injection site

Interleukin-2 (IL-2)

- Aldesleukin (Proleukin)
- A group of proteins produced by lymphocytes
- FDA approved for tx of:
  - Metastatic renal cell carcinoma
  - Metastatic melanoma

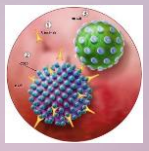
IL-2 Side Effects/Adverse Reactions

- **Only used in clients with normal cardiac & pulmonary functioning**
  - **Capillary leak syndrome**
- **Infection**
  - Sepsis & bacterial endocarditis
- **Hypotension**, sinus tachycardia, arrythmias, N/V/D, stomatitis, anorexia**, GI bleed**, & ALOC, oliguria/anuria, anemia, thrombocytopenia, fever, chills, dyspnea, pain at injection site, fatigue, weakness, malaise, & elevated LFTs.

Keratinocyte Growth Factor

- Palifermin (Kepivance)
- Initiates proliferation, differentiation, & migration of epithelial cells → thicker buccal mucosa
  - Decreases the incidence & duration of severe oral mucositis
  - Decreases opioid use for oral mucositis in transplant clients

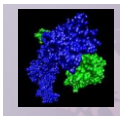
Kepivance: Side Effects/Adverse Reactions



- Skin toxicities
- Oral toxicities
- HTN
- Transient ↑ in serum lipase & amylase
- Tumor stimulation
  - Only use in Hematologic malignancies treated with myelotoxic chemo with stem cell support

Kepivance: Nursing Implications

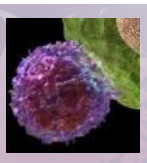
- Contraindicated with hypersensitivity to E. Coli-derived therapy or Palifermin
- Flush central line containing Heparin
  - Kepivance binds to Heparin
- Do not administer within 24 hrs of myelotoxic chemo
- Reconstitute → stable up to 24 hrs refrigerated → administer at room temp



Monoclonal Antibodies

- Human epidermal growth factor receptor (EGFR)
- Targets antigens & receptors on Cancer cells "Targeted therapy"
  - EGFR1 & EGFR2: Receptors that are "turned on" in Cancer

EGFR1

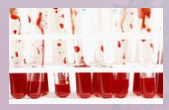


1. Increased cell proliferation
2. Avoidance of programmed cell death (apoptosis)
3. Increased cell invasiveness leading to metastasis
4. Release of vascular endothelial growth factor (VEGF)

Nursing Process: Assessment

- Herb & drug history
- Physical status
  - Head-to-toe/ labs/VS/ I&O /ADL / cardiopulmonary & skin assessment/ nutrition status/ presence or absence of underlying symptoms of disease, & use of current or past medication and treatment.
- Filgrastim, Pegfilgrastim, Sargramostim, & Oprelvekin:
  - Assess CBC before therapy & biweekly
  - Rationale: Avoid leukocytosis & thrombocytosis

Nursing Process: Assessment



- Renal & hepatic dysfunction
  - LFTs, BUN, & serum Cr
- Erythropoietin Stimulating Agents
  - Hct & Hgb, serum ferritin (>100), & serum iron transferring saturation (>20%)
  - Most pts will require iron supplements
  - Assess BP before start of and, especially, early in therapy.

Nursing Process: Assessment

- Psychosocial status
  - Preferred learning, support system, coping strategies, self-care abilities & emotional difficulties
- Signs/Symptoms of BRMs
  - Fatigue, edema, cardiac conditions, capillary leak syndrome, & respiratory distress
- Family
  - subQ injection & understanding of treatment

Nursing Process: Diagnosis

1. Imbalanced nutrition, less than body requirements, r/t side effects of BRM therapy
2. Risk for infection r/t side effects of chemo & disease condition
3. Impaired oral mucous membrane, skin integrity r/t side effects of chemo & disease condition
4. Fatigue r/t side effects of BRM therapy

Nursing Process: Diagnosis

4. Anxiety r/t cancer diagnosis & the unknown outcomes of tx

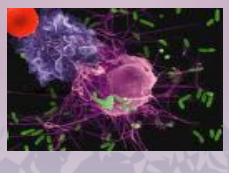
5. Fear r/t the cancer diagnosis
6. Risk for caregiver role strain r/t the cancer dx, tx, & care responsibilities
7. Risk for deficient fluid volume r/t side effects of cancer therapy.

Nursing Process: Planning/Goals

1. Client & family will verbalize an understanding of reporting BRM-related side effects.
2. Client & family will demonstrate correct & safe BRM administration.
3. Client & family will identify strategies to deal with BRM-related side effects.

Nursing Process: Planning /Goals

4. Client will remain free of infection (Filgrastim & Sargramostim).
5. Client will remain free of hemorrhage.



Nursing Process: Nursing Interventions

1. Monitor temp. @ onset of chills
2. Administer Meperidine 25-50 mg IVP to decrease rigors
3. Premedicate with Tylenol to ⇩ chills & fever; Benadryl to ⇩ nausea
4. Encourage > **2 L/day** to promote excretion of cell breakdown

Nursing Process: Nursing Interventions

5. Administer antiemetic **ATC** after BRM administration to prevent N/V
6. Administer BRM **@ bedtime** to ⇩ fatigue
7. Sargramostim: Single use dose/vial, **do not shake vial**
   - **Use within 6 hrs once reconstituted**

Nursing Process: Nursing Interventions

8. Filgrastim: same as Sargramostim
9. Oprelvekin: Single use vial
   - **Use refrigerated dose within 3 hrs**
   - **Don't shake vial**
10. Palifermin binds with **Heparin**
    - Central line: **Flush with NS** prior to and after adminstration of Palifermin

Client Teaching

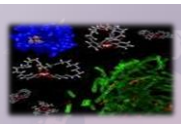
1. Explain rationale of BRM therapy
2. Explain frequency & rationale for studies & procedures
3. Teach that most BRM side effects disappear within 72-96 hrs after DC of tx

Client Teaching

4. Instruct client to use contraceptives during tx until 2 yrs after completion
5. Provide info on effects of BRM-related fatigue on ADLs & sexuality
6. Explain that herbal products with BRM therapy is not recommended

Client Teaching

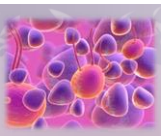
- Report difficulty in concentration, confusion, or somnolence
- **Report weight loss**
- Report dyspnea, palpitations, & **s/s of infection or bleeding**
- Demonstrate subQ techniques
- Provide written or video instructions



Nursing Process: Evaluation

1. Ask client & family about the potential effects of BRM on the quality of life
2. Self-administration technique
3. Client & family's management of BRM side effects

Nursing Process: Evaluation



4. There will be a ↓ incidence of infection in clients after autologous bone marrow transplant
5. There will be a ↓ incidence of thrombocytopenia in clients after chemo

Principles of Drug Therapy

- Inpatient
  - Concurrent with chemo
- Outpatient
  - Upon follow-up appointments

Vitamins & Minerals: Beneficial to cellular membranes & regenerates & oxygenates RBCs

- **Iron**
  - Manufactures hemoglobin & transfers to tissues
- **Vitamin B12, B6, & Folic acid**
  - Production of RBCs
- **Copper**
  - Enzyme function: blood formation, bone metabolism, & immune system
- **Vitamin C**
  - Wound healing

Sociocultural & Religious Considerations: Erythropoietin

- **Jehovah's Witness:**
  - Induction of hematopoiesis
  - Cellular protection in hypoxic conditions
- Leviticus: "As for any man who eats any sort of blood, I shall certainly set my face against the soul that is eating the blood, and I shall indeed cut him off from among his people."

BRM Study Guide