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Introduction to Clinical Pharmacology

Chapter 48
Immunostimulants and Modulators

Learning Objectives

1. Describe how immunity related cells communicate to each other in the body.
2. Explain how interferons are used to treat multiple sclerosis.
3. Describe the function of the different types of blood cells.
4. List the drugs used in the treatment of anemia and bleeding and prevention of infection.
5. Explain the actions, uses, general adverse reactions, contraindications, precautions, and interactions of the agents used in the treatment of anemia and bleeding and prevention of infection.

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Learning Objectives (continued)

6. Distinguish important preadministration and ongoing assessment activities the nurse should perform on a client receiving an agent used in the treatment of anemia and bleeding and prevention of infection.
7. Identify nursing diagnoses particular to a client receiving an agent used in the treatment of anemia and bleeding and prevention of infection.
8. Examine ways to promote an optimal response to therapy and important points to keep in mind when educating clients about the use of an agent used in the treatment of anemia and bleeding and prevention of infection.

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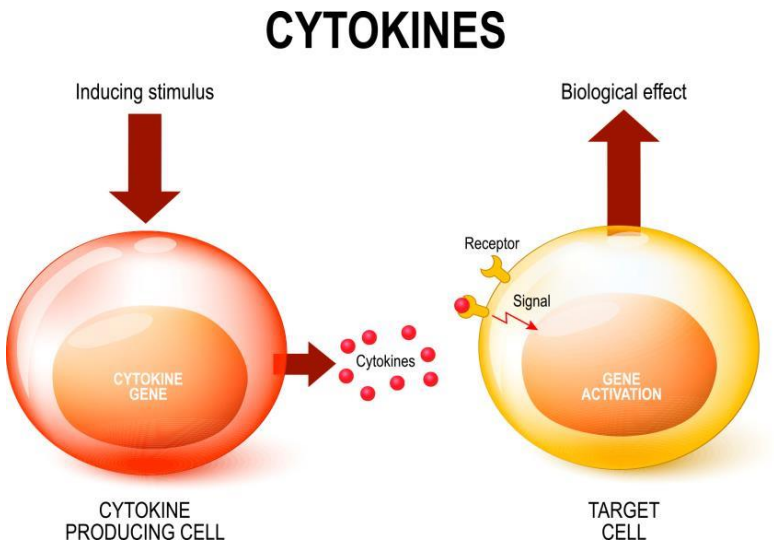
Cytokines

Cytokines are a broad group of proteins involved in cell-to-cell communication

- Respond to disease
- Convey messages to modulate the immune system
- Three types
  - Interferons
  - Colony-stimulating factors
  - Interleukins



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Immunostimulants and Modulators Drug Classes

- Interferons and Interleukin
- Immunostimulants for Bleeding and Infection
  - Colony-stimulating factors
  - Thrombopoietin receptor agonists
- Hematopoietic Factors for Anemia
  - Erythropoiesis-stimulating agents
  - Iron preparations
  - Folic acid
  - Vitamin B_{12}

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Interferons—Actions

- Interferon actions: cytokine antiviral agents which get their name from the ability to “interfere” with viral replication inside a cell
  - Prevent virus from replicating inside of host cells
  - Stimulate specific receptors on other, healthy cells to prevent viral invasion
  - Inhibit tumors, stimulate T-cells, and enhance the inflammatory response
  - Stimulate phagocytes to be more aggressive
  - Act as anti-infective to some bacterial and parasitic infections
- Interleukin actions: cytokine that targets white blood cells

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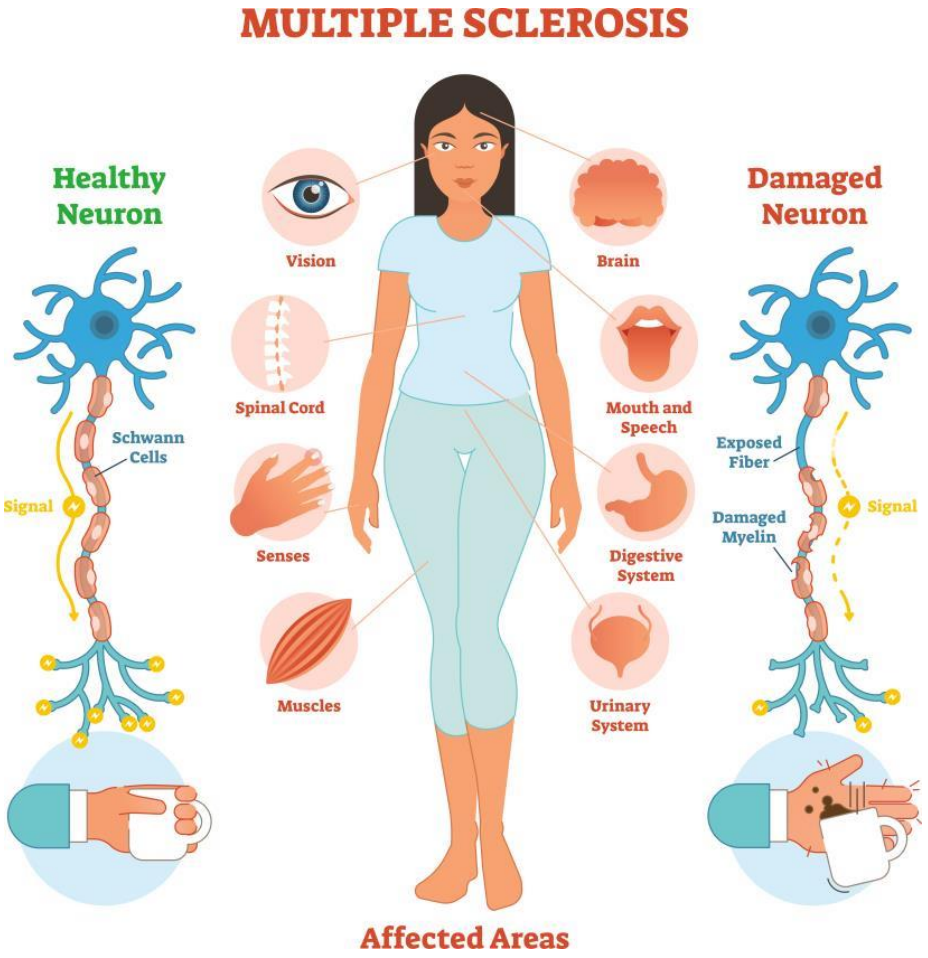
Interferons—Uses

- Interferons are identified as alpha, beta, gamma, and peginterferons
- Used to treat:
  - Select group of cancers
  - Multiple sclerosis
  - Skin Issues
  - Hepatitis B and C



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Interferons—Adverse Reactions #1

- Most Common Adverse Reactions are “Flu-Like” Symptoms:
  - Chills
  - Cough
  - Fever
  - Headache
  - Malaise

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Interferons—Adverse Reactions #2

- Other Common Generalized Reactions:
  - Nausea
  - Muscle aches
  - Fatigue
  - Sore throat
  - Reduced appetite
  - Diarrhea
  - Skin rashes, injection pain, edema in the extremities
  - Antibody development

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Interferons—Contraindications and Precautions

- Interferons are contraindicated in clients with:
  - hypersensitivity to the drug or drug components
  - pregnancy and lactation

- Clients taking interferons should not receive live-attenuated vaccines

- Use cautiously in clients with:
  - habitual alcohol consumption
  - cardiac or liver disease
  - a history of seizure disorder
  - thyroid problems

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Interferons—Interactions

Interacting Drug	Common Use	Effect of Interaction
Cladribine	Chemotherapy	Increased lymphopenia, adverse interferon reactions
Zidovudine	HIV antiretroviral	Increased adverse reactions of zidovudine
Levodopa and methyldopa	Treatment of Parkinson disease	Decreased effect of antiparkinsonism medication
Ascorbic acid	Vitamin supplement	Increased absorption of iron

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Pharmacology in Practice Exercise #1

Interferons bolster the immune system by which of the following methods?

a) Direct attack on bacteria and virus

b) As an antifungal agent

c) Stimulate healthy cells as viral protection

d) Stimulating B cells and the inflammatory response

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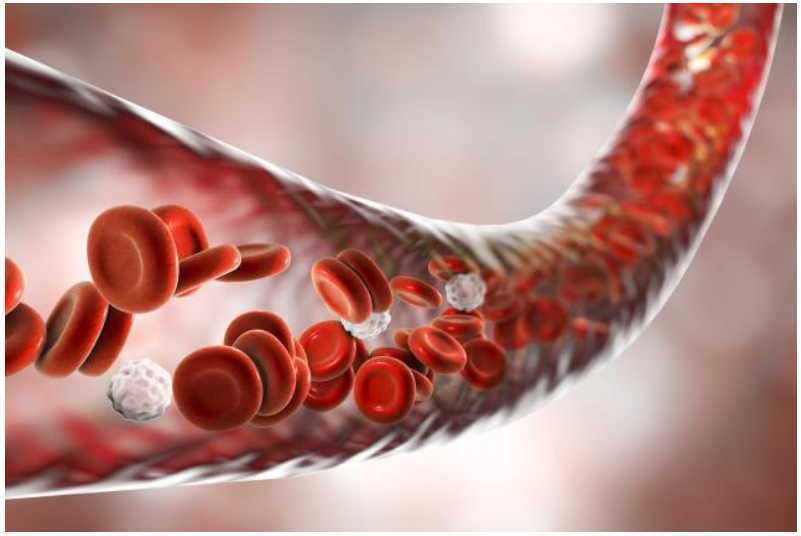
Types and Functions of Blood Cells

- Red blood cells (erythrocytes): supply oxygen to cells and tissues
- White blood cells (leukocytes): protect against microorganisms
- Platelets (megakaryocytes): control bleeding



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Immunostimulants for Bleeding and Infection

- Stimulating Neutrophils—Colony-stimulating factors (glycoproteins)
- Stimulating Platelet Development—Colony-stimulating factors (thrombopoietin)

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Stimulating Neutrophils—Colony-Stimulating Factors: Actions and Uses

- Actions: Colony-stimulating factors (CSF)—glycoproteins act on hematopoietic cells to stimulate proliferation, differentiation, and maturation of white blood cells
- CSF: used to prevent infection from
  - Chemotherapy-induced neutropenia during solid tumor cancer treatment
  - Neutropenia during bone marrow transplantation
  - Production of stem cells for harvest before bone marrow transplant
  - Neutropenia in those susceptible to symptomatic chronic infection

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Stimulating Neutrophils—Colony-Stimulating Factors: Actions and Uses (continued)

- Filgrastim: used after a cycle of chemotherapy
- Pegfilgrastim: used as single dose between chemotherapy cycle
- Sargramostim: used following BMT and induction chemotherapy used with leukemia, and to stimulate stem cells for harvest

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Stimulating Neutrophils—Colony-Stimulating Factors: Adverse Reactions

- General System Reactions:
  - Bone pain
  - Hypertension
  - Nausea and vomiting
  - Alopecia
  - Hypersensitivity or allergic reactions

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Stimulating Neutrophils—Colony-Stimulating Factors: Contraindications, Precautions, and Interactions

- Contraindications:
  - Hypersensitivity to the drug or any of the drug components

- Precautions:
  - Pregnancy category C, caution when breastfeeding
  - Filgrastim: caution with hypothyroid disease
  - Pegfilgrastim: causes sickle cell crisis
  - Can stimulate cancer cell growth

- Interactions

  Increase in neutrophil count can occur when these drugs are taken with lithium

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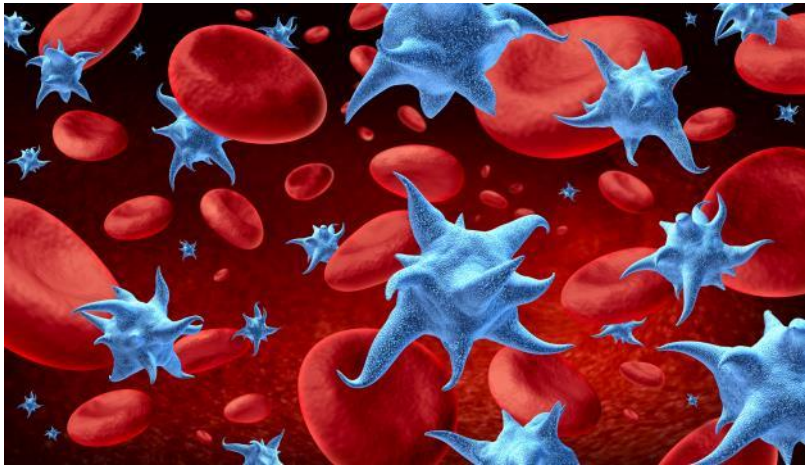
Stimulating Platelet Development—Colony-Stimulating Factors—Actions and Uses #1

- Action: thrombopoietin receptor agonists stimulate megakaryocyte production resulting in more platelets

- Uses
  - Reduces need for multiple platelet transfusions
  - Used to treat or prevent thrombocytopenia



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Stimulating Platelet Development—Colony-Stimulating Factors—Adverse Reactions

- General System Reactions:
  - Headache
  - Fatigue
  - Muscle aches
  - Fever
  - Allergic reactions

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Stimulating Platelet Development—Colony-Stimulating Factors—Actions and Uses #2

- Cardiovascular System Reactions:
  - Peripheral edema
  - Palpations
  - Atrial fibrillation
  - Emboli resulting in stroke and pulmonary edema
  - Capillary leak syndrome

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Stimulating Platelet Development—Colony-Stimulating Factors—Contraindications, Precautions, and Interactions

- Thrombopoietin drugs are contraindicated in clients:
  - with hypersensitivity to the drug or any component of the drug
- Use cautiously in clients with
  - Renal or liver failure
  - Pregnancy category C; use effective contraception; stop breastfeeding
- Low platelet counts can occur when discontinuing eltrombopag or romiplostim

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Hematopoietic Factors for Anemia

- Stimulating red blood cell development—Colony-stimulating factors
    - Erythropoiesis-stimulating agents
- Drugs used in treating specific anemias

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Stimulating Red Blood Cell Development—Colony-Stimulating Factors—Actions and Uses

- Epoetin alfa actions: drug that stimulates erythropoiesis
  - Used to treat anemia associated with chronic renal failure; chemotherapy for cancer treatment; zidovudine therapy for human immunodeficiency virus; postsurgical blood replacement in place of allogeneic transfusions
- Darbepoetin alfa and methoxy polyethylene-epoetin β actions: erythropoiesis-stimulating proteins
  - Used to treat anemia associated with kidney disease in clients with or without dialysis
- These drugs elevate or maintain RBC levels and decrease the need for infusions

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Stimulating Red Blood Cell Development—Colony-Stimulating Factors—Adverse Reactions

- Most Common Adverse Reactions:
  - Hypertension
  - Headache
  - Nausea, vomiting, diarrhea
  - Rashes
  - Fatigue
  - Arthralgia and skin reaction at the injection site

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Stimulating Red Blood Cell Development—Colony-Stimulating Factors—Contraindications and Precautions

- Epoetin alfa is contraindicated in clients with:
  - uncontrolled hypertension; those needing emergency transfusion; those with hypersensitivity to human albumin
- Darbepoetin alpha is contraindicated in clients with:
  - uncontrolled hypertension, those allergic to drug
- Use cautiously in clients with
  - hypertension; heart disease; congestive heart failure; history of seizures; pregnancy (pregnancy category C); and lactation

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Pharmacology in Practice Exercise #2

A client is prescribed epoetin alfa for the treatment of anemia associated with chronic renal failure. With which of the following hemoglobin counts is epoetin alfa contraindicated?

a) 2 g/dL

b) 6 g/dL

c) 11 g/dL

d) 17 g/dL

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Drugs for Iron Deficiency Anemia—Actions and Uses

- Iron preparations:
  - Act by elevating serum iron concentration, which replenishes hemoglobin and depleted iron stores
  - Used during pregnancy and lactation and for dietary supplantation if iron in diet is not sufficient
- Parenteral iron:
  - Used when client cannot take oral drugs or when client experiences gastrointestinal intolerance to oral iron administration; treating iron deficiency anemia

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Drugs for Iron Deficiency Anemia—Adverse Reactions #1

- Gastrointestinal System Reaction:
  - GI irritation
  - Nausea and vomiting
  - Constipation, diarrhea
  - Darker, black stools

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Drugs for Iron Deficiency Anemia—Adverse Reactions #2

- Generalized System Reaction:
  - Headache
  - Backache
  - Allergic Reactions
- When given parenterally:
  - Soreness, inflammation and sterile abscess at IM injection site; phlebitis if given IV; anaphylaxis

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Drugs for Iron Deficiency Anemia—Contraindications and Precautions

- Iron supplements: contraindicated in clients with known hypersensitivity to drug or any component of the drug

- Iron compounds
  - Contraindicated in clients with hemochromatosis or hemolytic anemia
  - Used cautiously in clients with hypersensitivity to aspirin

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Drugs for Iron Deficiency Anemia—Interactions

Interacting Drug	Common Use	Effect of Interaction
Antibiotics	Fight infection	Decreased GI absorption of the antibiotic
Levothyroxine	Treatment of hypothyroidism	Decreased absorption of levothyroxine
Levodopa and methyldopa	Treatment of Parkinson disease	Decreased effect of antiparkinsonism medication
Ascorbic acid	Vitamin supplement	Increased absorption of iron

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Drugs for Folic Acid Deficiency Anemia—Actions, Uses, and Adverse Reactions

- Folic acid: used in treating megaloblastic anemia; for women of childbearing age to decrease incidence of neural tube defects
- Leucovorin: derivative of folic acid used to diminish hematologic effects after the administration of methotrexate, which is used in treating certain types of cancer (leucovorin rescue); used if a client cannot take the oral form of folic acid
- Adverse reactions are rare: parenteral administration may cause allergic hypersensitivity

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Drugs for Folic Acid Deficiency Anemia—Contraindications and Precautions

- Contraindications:
  - Folic acid, leucovorin: contraindicated for treating pernicious anemia, other anemias in which vitamin B_{12} is deficient

- Use cautiously with:
  - Pregnancy (pregnancy category A) and lactation; generally considered safe; follow RDA guidelines of folate during pregnancy

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Drugs for Folic Acid Deficiency Anemia—Interactions

Interacting Drug	Common Use	Effect of Interaction
Sulfasalazine	DMARD antirheumatic	Signs of folate deficiency
Hydantoins	Anticonvulsant	Increase in seizure activity

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Drugs for Vitamin B_{12} Anemia—Actions and Uses

- Vitamin B_{12} used to treat clients with a vitamin B_{12} deficiency; also used to perform the Schilling test for pernicious anemia
- Clients at risk for vitamin B_{12} deficiency have:
  - A strict vegetarian lifestyle
  - Total gastrectomy or subtotal gastric resection
  - Intestinal diseases such as ulcerative colitis or sprue
  - Gastric carcinoma
  - Congenital decrease in the number of gastric cells that secrete intrinsic factor

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Drugs for Vitamin B12 Anemia—Adverse Reactions #1

- Adverse Reactions:
  - Mild diarrhea
  - Itching
  - Increase in RBC production
  - Acne
  - Peripheral vascular thrombosis
  - CHF
  - Pulmonary edema

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Drugs for Vitamin B12 Anemia—Adverse Reactions #2

- Generalized System Reaction:
  - Headache
  - Backache
  - Allergic Reactions
- When given parenterally:
  - Soreness, inflammation and sterile abscess at IM injection site; phlebitis if given IV; anaphylaxis

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Drugs for Vitamin B_{12} Anemia—Contraindications and Precautions

- Contraindicated in clients allergic to cyanocobalamin

- Used cautiously:
  - during pregnancy (pregnancy category A orally and pregnancy category C parenterally)
  - in clients with pulmonary disease or anemia

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Drugs for Vitamin B_{12} Anemia—Interactions

Interacting Drug	Common Use	Effect of Interaction
Alcohol	Social drinking, relaxation	Decrease the absorption of oral vitamin B_{12}
Neomycin	Anti-infective	
Colchicine	Treats gout	

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #1

Preadministration Assessment

- **Objective** Data
  - Vital signs
  - General appearance
  - Specific signs for anemia
  - Inspect physical appearance, note skin color, temperature, lesions, differences bilaterally
  - Lab tests: baseline blood counts and organ function
  - Weight for drug calculation

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #2

Preadministration Assessment

- **Subjective** Data
  - Description of type and intensity of symptoms
  - Reported ability to carry out activities of daily living
  - History of bowel issues and habits
  - History of other current nonmalignant disease or disorder (e.g., autoimmune, diabetes)
  - History of travel to areas of infectious diseases or contraction of infectious disease

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #3

Ongoing Assessment

- Monitor client's vital signs for signs of low RBCs; monitor for bleeding and infection in first few days of CSF therapy
- Monitor client for adverse reactions; report any occurrence of adverse reactions to primary healthcare provider before next dose is due
- Inform client that color of stool will become darker or black (iron supplement)
- Assess client for relief/improvement of symptoms of anemia
- For parenteral iron, teach client to monitor injection sights daily for inflammation, swelling, or abscess

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Pharmacology in Practice Exercise #3

A nurse administers the CSF filgrastim following chemotherapy. During the ongoing assessment, which of the following data points would the nurse call the primary healthcare provider with the intent to discontinue daily injections?

a) Complaints of sore throat

b) Hemoglobin lab value of 12 g/dL

c) Neutrophil count of 30,000/mm3

d) Petechiae on the torso

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #4

Nursing Diagnosis

- Fatigue related to dilutional anemia caused by fluid retention
- Malnutrition related to lack of iron, folic acid, other (specify) in the diet
- Constipation related to adverse reaction to iron therapy

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #5

Planning

- Expected client outcomes depend on the reason for administration of the drug but include
  - Optimal response to therapy
  - Management of adverse drug reactions
  - Confidence in an understanding of the prescribed medication regimen

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #6

Implementation

- Promoting an Optimal Response to Therapy
  - Thrombopoietin receptor agonists: should be taken 2 hours before or 4 hours after meals high in calcium; antacids, or supplements; do not reuse oral syringes; take missed doses immediately but do not double up on doses
  - Epoetin alfa: monitor blood pressure closely; report any rise of 20 mm Hg or more in systolic, diastolic pressure to primary healthcare provider; mix the drug gently during preparation; single-dose vial; report increase of hemoglobin over 11 g/dL or increase in hematocrit of 4 points within a 2-week period

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #7

Implementation

- Promoting an Optimal Response to Therapy (continued)
  - Iron: give between meals with water unless the client has trouble tolerating; check with hospital pharmacist regarding simultaneous administration of iron salts with other drugs; if iron dextran is being administered, test dose may be administered at a gradual rate over a period of at least 30 seconds
  - Vitamin B_{12}: clients with vitamin B_{12} anemia are treated with vitamin administered by parenteral route weekly

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #8

Implementation

- Monitoring and Managing Client Needs
  - **Fatigue**
    - Explain to the client that they are experiencing fatigue from dilutional anemia that can occur during administration of CSF drugs
    - Give the client permission to feel tired
    - Teach the client and family energy-saving skills to maintain activities of daily living

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #9

Implementation

- Monitoring and Managing Client Needs
  - **Malnutrition**
    - Recommend balanced diet with emphasis on foods that are high in iron, folic acid, or vitamin B_{12}
    - Monitor amount of food eaten at meals
    - Vegetarian client: dietitian should be consulted to provide menus with appropriate iron-rich foods
    - Provide small portions of food and a pleasant atmosphere for eating

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #10

Implementation

- Monitoring and Managing Client Needs
  - **Constipation**
    - Instruct client to increase fluid intake to 10 to 12 glasses of water daily
    - Eat a diet high in fiber, and increase activity

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #11

Implementation—Educating the Client and Family

- Explain medical regimen thoroughly to client and family
  - Emphasize importance of following the prescribed treatment regimen

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #12

Implementation—Educating the Client and Family

- Hematopoietic Factors
  - Instruct client to keep all appointments with healthcare provider appointments
  - If hypertensive to strictly follow antihypertensive drug therapy during epoetin alpha therapy
  - Educate client about adverse reactions and when to report them
  - If the client is self-administering injections, teach the client proper administration and disposal

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #13

Implementation—Educating the Client and Family

- Iron
  - Take this drug with water on empty stomach; liquid preparation should be mixed with water or taken through a straw to avoid staining teeth
  - If gastrointestinal upset occurs, take drug with food or meals
  - Educate client that iron should not be taken at the same time or within 2 hours of taking antacids, tetracyclines, penicillamine, or fluoroquinolones
  - Inform client that the drug can cause darkening of stools

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #14

Implementation—Educating the Client and Family

- Folic Acid
  - Avoid use of multivitamin preparations unless such use has been approved by the primary healthcare provider
  - Follow diet recommended by primary healthcare provider because diet and drug are necessary to correct a folic acid deficiency

- Leucovorin
  - Megaloblastic anemia: adhere to diet prescribed by the primary healthcare provider
  - If purchase of foods high in protein becomes a problem, discuss this with primary healthcare provider

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #15

Implementation—Educating the Client and Family

- Vitamin B_{12}
  - Nutritional deficiency of vitamin B_{12}: eat a balanced diet that includes seafood, eggs, meats, and dairy products
  - Pernicious anemia: lifetime therapy is necessary, avoid contact with infections, report any signs of infection to primary healthcare provider immediately
  - Instruct the client to adhere to the treatment regimen and encourage them to keep all appointments at the clinic or with provider

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Nursing Process—Client Receiving an Immunomodulating Drug Used in the Treatment of Anemia, Bleeding, or Infection #16

Evaluation

- Was the therapeutic effect achieved?
- Were adverse reactions: identified, reported, and managed?
  - Client reports fatigue is manageable
  - Client maintains adequate nutrition status
  - Client reports adequate bowel movements
- Did client and family express confidence and demonstrate understanding of drug regimen?

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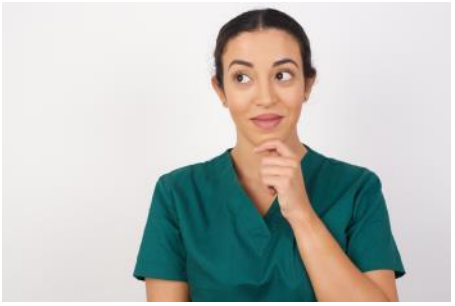
Turn and Talk—Case Study #1

A client recently diagnosed with carcinoma is receiving chemotherapy which is making them severely neutropenic. The physician orders filgrastim (Neupogen) 5 mcg/kg/day IV until ANC is adequate.

1. If the client weighs 61 kilograms, what will today's dose of filgrastim be for the treatment?
2. Filgrastim comes in a 300 mcg and a 480 mcg vial, which one should the nurse select to draw up the medication for this client?



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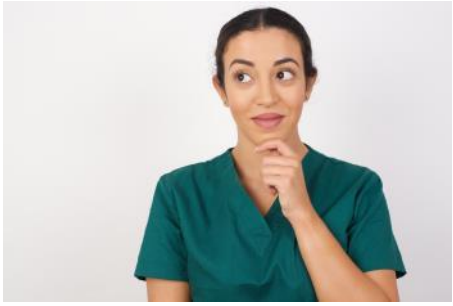
Turn and Talk—Case Study #2

A client recently diagnosed with carcinoma is receiving chemotherapy which is making them severely neutropenic. The physician orders filgrastim (Neupogen) 5 mcg/kg/day IV until ANC is adequate.

3. Filgrastim is what type of immunostimulant drug, and what is its mechanism of action?



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