Management of the Hematological Manifestations of HIV Infection and AIDS

Kristin Kane Ownby, MPH, MSN, RN-CS, OCN

Hematological abnormalities, characterized by cytopenias, are a problem commonly encountered by persons with HIV or AIDS. Cytopenias can be multifactorial in their causation and potentially life threatening to this population. An understanding of the various causes of these cytopenias and the appropriate nursing care are tantamount to nursing practice and to ensure quality of life. Goals of medical and nursing care are directed at assessment, interventions, and patient education to prevent or minimize the complications of hematological abnormalities.

This article reviews current knowledge regarding the causes, pathophysiology, treatments, and nursing care of HIV/AIDS-related hematological abnormalities.

Key words: Hematological abnormalities, HIV/AIDS, medical/nursing management

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Seventy percent to 95% of persons with AIDS (PWAs) will experience some degree of anemia during the course of their disease (Brogan & Zell, 1990). Thrombocytopenia occurs in 3%-9% of persons infected with HIV (Glassman, 1989), and as the CD4+ count falls below 100 cells/mm³, the risk of developing granulocytopenia is increased. The differential diagnosis of hematological abnormalities can be multifactorial, including direct effects of the HIV virus on the hematological system, malignancies, opportunistic infections (OIs), and side effects of the various medications prescribed to treat the virus and OIs. Hematological abnormalities occur by three mechanisms: (a) decreased production of precursor cells in the bone marrow; (b) increased peripheral destruction of the differentiated cells; and (c) ineffective hematopoiesis.

Direct Effects of HIV on the Hematological System

HIV infection is associated with cytopenias. In vitro, the virus has been identified in myelomonocytic bone marrow precursor cells (CD34). This phenomenon suggests direct bone marrow invasion, resulting in abnormal growth of various progenitor cells (Folks et al., 1988). Defects in helper lymphocytic function may be associated with HIV-induced myelosuppression (Mitsuyasu, 1994). Mitsuyasu states that defects in mature granulocytes, monocytes, and lymphocytes have been identified. These defects may contribute to the increased incidence of infections and malignancies in HIV disease.

Cytokine production can be altered by the virus. For example, the cytokine tumor necrosis factor (TNF) can be stimulated by the virus, which can result in inhibition of erythrocyte production (Groopman, 1990). Hypergammaglobulinemia, associated with abnormal B-lymphocyte regulation and the development of autoantibodies that bind specifically to the membranes of myeloid cells, can induce cytopenias (Israel & Plaisance, 1991).
HIV-associated immune thrombocytopenia purpura (ITP), a syndrome characterized by increased peripheral platelet destruction, is an example of autoantibodies affecting platelets. Antibodies, primarily IgG, are deposited on the membrane surface of platelets, forming circulating immune complexes (Murphy et al., 1987). As the platelets travel through the spleen, phagocytic cells of the reticuloendothelial system recognize the Fc receptor of the immunoglobulin and destroy the platelets. Researchers hypothesize that antiplatelet antibodies recognize a specific antigen on the membrane of infected platelets. These antiplatelet antibodies will stimulate the complement to destroy platelets (Klaassen et al., 1990), thus resulting in a diminished number of platelets.

As the immune system becomes dysfunctional, the PWA is at risk for developing numerous opportunistic infections. Since HIV disease is a chronic infectious process, the anemia associated with the virus itself is categorized as an anemia of chronic disease. It is characterized by a normochromic, normocytic anemia, with hemoglobin concentrations ranging from 8–10g/dL. This anemia includes a modest reduction in red cell survival, decreased iron reutilization, and reduced levels of erythropoietin—an endogenous hormone that stimulates the production of erythrocytes.

Opportunistic Infections That Affect the Hematological System

As the immune system becomes dysfunctional, the PWA is at risk for developing numerous opportunistic infections; these infections can induce or exacerbate existing cytopenias. Direct invasion of the bone marrow is the mechanism by which certain obligate intracellular parasites cause suppression of marrow.

Mycobacterial infections—such as Mycobacterium avium complex and Mycobacterium tuberculosis—and fungal infections—including cryptococcus, histoplasmosis, and coccidiomycosis—have been implicated in cytopenias. Viruses, including varicella and cytomegalovirus, have been implicated in cytopenia induction, both by direct marrow invasion and by infecting peripheral monocytes (Baranski & Young, 1987).

The cytomegalovirus (CMV) also is capable of suppressing antigen presentation. Antigen presentation is necessary in the activation of specific immunity (Causey, 1991). Splenomegaly, caused by mycobacterial infections, also may lead to peripheral destruction of erythrocytes. The protozoal infection, toxoplasmosis, has been associated with thrombocytopenia. Salmonellosis can result in granulocytopenia.

Malignancies That Affect the Hematological System

Lymphoproliferative malignancies, particularly non-Hodgkin's lymphoma, are diagnosed in 3% of PWAs (Pluda, Yarchoan, & Broder, 1991). These malignancies invade the bone marrow and cause suppression of myeloid progenitors. Antineoplastic agents prescribed to treat neoplasms such as lymphomas and Kaposi's sarcoma (KS) cause myelosuppression. These chemotherapeutic agents include etoposide, doxorubicin, and cyclophosphamide. KS lesions, treated with radiation therapy, can result in myelosuppression if the radiation fields include significant marrow sites (e.g., long bones).

Medications That Affect the Hematological System

Many of the agents used for prophylaxis and treatment of OIs cause a drug-induced cytopenia. For example, sulfanamides such as sulfamethoxazole, sulfadiazine, and dapsone have a direct cytotoxic effect on precursor cells in the bone marrow.
Sulfonamide-induced cytopenias appear to be associated with hapten formation (Israel & Plaisance, 1991). Haptens are specific nonprotein substances that do not elicit antibody formation by themselves. However, when haptens are coupled with a carrier protein, they can elicit an immune response.

Folate antagonists—including trimetrexate, trimethoprim, and pyrimethamine—act as inhibitors of an enzyme needed for folate metabolism and block marrow maturation, resulting in ineffective hematopoiesis. Many OIs are treated with combination therapy using both a folate antagonist and a sulfonamide, thus compounding the problem of marrow suppression and hematopoiesis.

Combination therapy includes trimethoprim-sulfamethaxazole, used for prevention and treatment of *Pneumocystis carinii* pneumonia (PCP), and pyrimethamine-sulfadiazine, used for the treatment of toxoplasmosis. This combination of two cytopenic agents may result in the additive effect of bone marrow suppression.

Pentamidine, also used to treat PCP, can cause granulocytopenia. Although its direct mechanism of action is unknown, pentamidine is thought to be a folate antagonist.

Ganciclovir, effective in the treatment of CMV infections, can inhibit the maturation of progenitor cells and can lead to granulocytopenia and thrombocytopenia. Flucytosine, used in combination therapy with Amphotericin B for the treatment of fungal infections, can be deaminated by intestinal bacteria and converted to fluorouracil, a chemotherapeutic agent that causes suppression of bone marrow.

Alpha interferon, used to treat KS, can induce granulocytopenia. Zidovudine (ZVD), until recently the only drug approved by the United States Food and Drug Administration (FDA) to inhibit the proliferation of HIV, causes cytopenias—especially anemia. Zidovudine has been associated with a greater than 50% reduction of neutrophils in more than one-half of patients treated with this antiretroviral agent (Brogan & Zell, 1990). Researchers propose that the ZDV causes cytopenias through the suppression of bone marrow precursor cells.

Additional Factors

Poor nutritional intake and decreased, abnormal absorption of the GI tract can result in folate and vitamin B12 deficiencies. Although not solely implicated in the occurrence of certain cytopenias, these folate and B12 deficiencies can exacerbate an existing problem.

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In addition, blood loss can cause or worsen preexistent anemia. Blood loss in the PWA may occur because of one or more of the following problems: (a) Cytomegalovirus colitis can compromise the integrity of and erode the GI tract; (b) KS lesions in the GI tract can perforate; (c) frequent phlebotomy of hospitalized PWAs can have a cumulative and significant effect; and (d) coexistent marrow suppression can blunt the body’s ability to compensate for GI tract blood loss.

Management of Cytopenias

Identifying the underlying cause of the cytopenia is the first step in the medical management of myelosuppression. If the cytopenia is drug induced, the physician reduces the dose of the offending agent. If the cytopenia does not resolve, the therapy may have to be stopped in favor of an alternative therapy less likely to cause myelosuppression.

Red blood cell indices are used to diagnose the type of anemia the patient may be experiencing. When the absolute neutrophil count falls below 1000/mm$^3$, the patient is at high risk for developing an infection (Brager & Yasko, 1984). Platelet counts of less than 50,000/mm$^3$
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places the patient at increased risk for bleeding and requires frequent platelet counts (Brager & Yasko). Hemoglobin levels of 8g/dL or less or hematocrit levels of 23% or less need to be reported to a physician. Vitamin B12 and folate levels are drawn when deficiencies are suspected.

Epoetin (see Table 1) is a medication that stimulates the production of erythroid precursors. Epoetin is a genetically engineered derivative of an endogenous hormone, erythropoietin. It is effective in patients whose endogenous erythropoietin levels are less than 500mu/mL. However, the drug is not efficacious if the erythropoietin level is above 500mu/mL (Adamson & Eschbach, 1990). Epoetin is administered subcutaneously at doses of 300iu/kg, 3 times a week. Dose changes are dependent on the individual’s hematocrit. If the hematocrit rises more than four points over a 2-week period, or exceeds 36%, the dose should be reduced (Adamson & Eschbach).

Treatment of anemia may involve the transfusion of packed red blood cells. Transfusions generally are indicated if the hemoglobin falls below 8g/dL or if the hematocrit falls below 23%.

Supplemental vitamin B12 can be administered to correct a nutritional deficiency, a possible cofactor in cytophenias. Injections of B12 are administered on a monthly schedule.

The appropriate intervention for thrombocytopenia is to prevent bleeding by maintaining the integrity of the skin and mucous membranes and to prevent injury to the patient. Thrombocytopenia may present with easy bruising, petechiae, epistaxis, gingival and rectal bleeding, blood in the ejaculate, and mild splenomegaly—specifically seen in persons with idiopathic thrombocytopenia purpura (ITP).

Thrombocytopenia due to ITP generally does not result in excessive bleeding. Platelet transfusions are indicated rarely. Corticosteroids have been found to be effective for some patients with ITP. Prednisone is started at doses of 30mg–40mg daily for 1–2 weeks, then rapidly tapered to a maintenance dose of 10mg–15mg daily (Karpatin, 1990). Researchers hypothesize that prednisone modulates the reticuloendothelial system to clear circulating immune complexes. The potential side effects of steroid therapy, including hyperglycemia and fluid retention, should be monitored. The use of steroids in PWAs is a controversial treatment choice. Steroids are thought possibly to make the patient susceptible to the development of esophageal candidiasis or to promote herpes outbreaks.

A splenectomy is a treatment option for ITP (Karpatin, 1990). However, this procedure is associated with adverse effects, which include an increased incidence of infections by encapsulated organisms, such as pneumococci, and coagulopathies, which can be potentially life-threatening to hemophiliacs.

Table 1. Managing the Patient on Epoetin Therapy

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
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<tbody>
<tr>
<td>1.</td>
<td>Obtain an endogenous serum erythropoietin level before initiating therapy. Epoetin is indicated for patients whose levels are &lt; 500 mU/mL.</td>
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<td>2.</td>
<td>Evaluate iron stores, including transferrin saturation (at least 20%) and serum ferritin levels (at least 100ng/mL), before initiating therapy.</td>
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<tr>
<td>3.</td>
<td>Obtain and record a baseline blood pressure. Hypertension should be controlled before the therapy is initiated.</td>
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<td>4.</td>
<td>Start Epoetin at an initial dose of 100U/kg by SC or IV injection 3 times a week. Maintain this initial dose for at least 8 weeks.</td>
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<td>5.</td>
<td>Evaluate the efficacy of the therapy every 4 – 8 weeks by monitoring the patient’s hematocrit.</td>
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<tr>
<td>6.</td>
<td>Increase the initial dose by 50 to 100U/kg if the hematocrit has not increased after 8 weeks. Titrate to a maximum dose of 300U/kg 3 times a week.</td>
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<tr>
<td>7.</td>
<td>Discontinue the drug if the hematocrit exceeds 40%. Restart the drug when the hematocrit falls to 36%. Decrease the dose by 25% when the hematocrit drops below 36%.</td>
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<tr>
<td>8.</td>
<td>Teach the patient the elements of proper drug administration: drawing up the correct dose from a vial into a syringe; preparing the skin; injecting the drug subcutaneously; storing the drug; and disposing of syringes and needles.</td>
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Another treatment is immune gamma globulin (IgG), which has been demonstrated to provide transient relief of ITP by binding with the Fc portion of immunoglobulins (Glassman, 1989).

The risk of developing a bacterial infection is greatly increased as the person’s absolute neutrophil count falls below 1000/mm³. Infection is the most serious complication of granulocytopenia.

Colony-stimulating factors are drugs found to be effective in reversing granulocytopenia. Granulocyte-colony stimulating factor (G-CSF) is the first drug in this classification to be approved for the treatment of neutropenia. This drug enhances the migration of circulating neutrophils toward a site of infection or inflammation, increases phagocytic activity, and increases antibody-dependent cellular cytotoxicity (Scarffe & Kamthan, 1990). It is administered either intravenously or subcutaneously and is associated with mild-to-moderate bone pain.

Granulocyte macrophage-colony stimulating factor (GM-CSF) is another genetically engineered cytokine found to stimulate the proliferation and differentiation of granulocytes and macrophages. It enhances neutrophil chemotaxis and phagocytic and cytotoxic activity against bacteria and yeasts (Hardy, 1991). GM-CSF increases the survival of neutrophils and eosinophils. The side effects of GM-CSF include fever, myalgias, fatigue, gastrointestinal distress, rash, and bone pain.

Leucovorin may be prescribed with pyrimethamine and sulfadiazine and with trimetrexate to reduce the granulocytopenia caused by these agents. Its mechanism of action is to compete with the folate antagonist for the folate receptors of the cells.

### The Nurse’s Role

The nurse serves a vital role in the team approach when caring for the PWA. This role includes assessing for the manifestations of cytopenias, administering and monitoring the progress and effectiveness of prescribed medical treatments, and planning and implementing appropriate nursing interventions.

Assessment for cytopenias involves monitoring the patient’s complete blood count (CBC) for decreases in the white blood cell count and its differential, hemoglobin, hematocrit, and platelets. The nurse should observe for the clinical presentation of anemia, which includes fatigue, malaise, tachycardia, decrease in activities of daily living, diminished sexual function, shortness of breath, and/or pallor.

### The use of steroids in PWAs is a controversial treatment choice.

Nursing interventions for anemia include minimizing fatigue through planned periods of rest and activity, instituting measures to reduce shortness of breath, and administering blood transfusions or Epoetin as ordered. When a transfusion is medically indicated, the nurse should insure that the ABO blood type and Rh factor of the transfusion are compatible with the patient and monitor the patient for possible hemolytic reactions.

Because the possibility of multiple bleeding sites exists, the urine, stool, and emesis of thrombocytopenic patients should be tested for occult blood. In the menstruating patient, pad and/or tampon counts, along with the amount of saturation, need to be monitored and documented. Also, the assessment for blood loss requires examining the patient for tachycardia, hypotension, and tachypnea.

Intracranial bleeding is an emergency situation that can occur in the thrombocytopenic patient. The nurse should evaluate the patient for complaints of headaches and blurred vision, changes in personality, such as restlessness, and changes in the level of consciousness.

To prevent trauma to rectal tissue, the use of rectal thermometers should be avoided. Intramuscular injections should be contraindicated; and all venipuncture sites require firm pressure for a least 5 minutes. Extending the patient’s arm above the head after venipuncture helps to stop bleeding.
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The nurse should monitor the patient for signs and symptoms of infection. Problems of the respiratory tract signaling infection include changes in breath sounds, cough, and dyspnea. In the genitourinary tract, these problems include dysuria; cloudy, odorous urine; hematuria; and urinary frequency. Other potential sources of infection need to be assessed, such as intravenous infusion sites, indwelling catheters, body cavities, and skin folds. However, the nurse must be aware that the neutropenic patient may not have the usual signs and symptoms of inflammation—redness, swelling, heat, and discharge (pus).

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Patient Education

Patients need to learn about the potential and actual signs and symptoms of cytopenias, as well as the interventions that may prevent and/or alleviate the problems.

Fatigue is a common symptom of anemia. To preserve energy levels, the PWA should be taught to rest at intervals, pace activities, and seek assistance when physical tasks become difficult. Because sleep is vital to alleviating fatigue, the nurse should instruct the patient to follow usual bedtime habits, use relaxation techniques, and minimize distractions in the environment (Brager & Yasko, 1984).

Optimal nutritional intake is important to the PWA with hematological disorders; therefore, dietary counseling cannot be overlooked during educational interventions. The patient needs to know the key to proper nutrition is a diet high in carbohydrates and protein and low in fat.

Thrombocytopenia can result in life-threatening hemorrhage. Consequently, several strategies designed to decrease the possibility of bleeding should be taught to the PWA. For example, medications that might alter platelet production and function are harmful and should not be taken. These treatments include the familiar over-the-counter medicines—aspirin and nonsteroidal antiinflammatory drugs. Alcohol can inhibit platelet function and must be avoided. The mucous membranes in the oral cavity may be maintained by using a soft bristle toothbrush or sponge-tipped applicator. Gastrointestinal integrity may be preserved by promoting mobility and good fluid intake, as well as taking stool softeners, to prevent constipation. Enemas, harsh laxatives, and anal intercourse should be avoided. Prevention of physical injury is a priority; strenuous activity and bending from the waist is not recommended. For shaving, electric razors are safe.

The greatest risk to a neutropenic patient is infection. The PWA needs to be educated about exposure to potential sources of infection (see Table 2.). Vigorous hand-washing using friction is an important preventive measure for the individual when preparing or eating food, or after using the toilet. In addition, the patient should be taught to take his or her temperature twice daily at the same time each day and report to the physician any elevations (usually readings greater than 101°F).

The patient's first line of defense against invading pathogens is good personal hygiene, which maintains the integrity of the skin. A mild soap should be used to prevent skin drying and cracking. Consistent and thorough oral hygiene is necessary to prevent infections. The female patient should be taught the importance of perianal care, including front-to-back cleansing.

Finally, the nurse needs to shore up the patient's knowledge about the spread of diseases, placing emphasis on sexual hygiene, the use of condoms, and routine infection-control practices.

Summary

The causes of hematological abnormalities and myelosuppression in persons with AIDS are multifaceted and include treatment-induced cytopenias, malignancies, opportunistic infections, and the virus itself. Diligent
Table 2. Potential Sources of Infection

- Persons with transmittable diseases:
  - Herpes zoster
  - Colds
  - Influenza
  - Chicken pox
  - Measles
- Persons recently vaccinated with live or attenuated microbes
- Excrement from animals such as birds, cats, and dogs
- Fresh fruits, raw vegetables, raw eggs
- House plants, cut flowers, and stagnant water

Assessment is required to diagnose the problem and to identify the underlying causes of the cytopenias. The appropriate medical treatments, nursing interventions, and patient education may prevent the potentially life-threatening consequences of such abnormalities.

References


