Granulocyte Macrophage Colony-Stimulating Factor: Current Practice and Novel Approaches

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Endogenous colony-stimulating factors (CSFs) are a class of glycoproteins that act on hematopoietic cells by binding to specific cell surface receptors to stimulate proliferation, differentiation, commitment, and on-cell function activity (Dereskinski & Kempster, 1998). Until recently, CSFs have been found only in humans, but development of recombinant DNA techniques have allowed these agents to be mass produced and studied in a variety of applications. Two major endogenous myeloid CSFs exist: granulocyte macrophage CSF (GM-CSF) and granulocyte CSF (G-CSF).

GM-CSF has broad activity in the proliferation and differentiation of myeloid lineage progenitor cells, whereas G-CSF acts selectively on cells of the granulocyte lineage. Clinical trials suggest that GM-CSF has clinical benefits beyond enhancing neutrophil recovery, including shortening the duration of mucositis and diarrhea, stimulating dendritic cells, preventing infection, acting as an adjuvant vaccine agent, and facilitating antitumor activity.

Endogenous myeloid colony-stimulating factors (CSFs) have demonstrated the ability to enhance the clinical management of immunosuppressed patients with cancer. These agents are associated with significant decreases in chemotherapy-associated infections, antibiotic use, length of hospital stays, and mortality. Two major endogenous recombinant myeloid CSFs currently are being manufactured: granulocyte macrophage CSF (GM-CSF) (sargramostim, Leukine®, Immunex Corporation, Seattle, WA) has broad activity in the proliferation and differentiation of myeloid lineage progenitor cells, whereas granulocyte CSF (filgrastim, Neupogen®, Amgen, Inc., Thousand Oaks, CA) acts selectively on cells of the granulocyte lineage. Clinical trials suggest that GM-CSF can prevent or diminish the clinical properties of yeast-derived GM-CSF to bacteria-derived GM-CSF.

GM-CSF is a recombinant CSF that “turns on” the immune system by stimulating production of the myeloid progenitor stem cells of neutrophils, monocytes, macrophages, eosinophils, and dendritic cells. It also has a role in functional cell activities, such as T cell activation. Increased monocyte activity generates macrophages and allows for increased phagocytosis that may prevent or diminish the

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The modular sequence of endogenous human GM-CSF was identified in 1985. Three types of recombinant GM-CSF were manufactured: yeast-derived GM-CSF from Saccharomyces cerevisiae (sargramostim), bacteria-derived GM-CSF from E. coli (molgramostim), and mammalian-derived GM-CSF from Chinese hamster ovary cells (regramostim) (Armitage, 1998). Early clinical studies in GM-CSF were conducted using E. coli-derived agents; however, only yeast-derived GM-CSF is available in the United States. Present misconceptions that yeast-derived GM-CSF has a similar side profile to those occurring from E. coli-derived GM-CSF are common because early clinical trials in the United States used bacteria-derived GM-CSF. The latter product is no longer available in the United States. Table 1 compares the clinical properties of yeast-derived GM-CSF to bacteria-derived GM-CSF.

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occurrence of life-threatening bacterial and fungal infections, such as Staphylococcus aureus, Torulopsis, Candida albicans, Histoplasma capsulatum, and Cryptococcus neoformans. Dendritic cells, the major antigen-presenting cells, also are stimulated by GM-CSF and may enhance the body’s antitumor and immune activity. These unique actions extend the role of GM-CSF beyond fighting infection (DeMeyer & Barr, 2000; Gabrilove et al., 1988; Gabrilovich, Corak, Ciermik, Kavanaugh, & Carbone, 1997).

Dendritic cells are capable of recognizing neoplasms as altered forms of self, resulting in their activation against cancer. Patients with cancer have defective T cell function and a decrease in the number and function of dendritic cells. GM-CSF may hold potential antitumor effects by stimulating the dendritic cells to combat neoplastic growth (DeMeyer & Barr, 2000). GM-CSF enhances the proliferation, maturation, and function of dendritic cells. Dendritic cells seek out foreign or abnormal self-antigens, engulf and break them down, and move the antigens to the cell surface. The dendritic cells then migrate to the lymph nodes, where the CD4+ T cell (helper T cell) recognizes the antigen and provides support and direction for the development of either a B cell (antibody, humoral) or CD8+ (killer T cell, cytotoxic) response (Armitage, 1998). When stimulated by GM-CSF, these cells offer enhanced antitumor activity (see Figure 1).

### Cell Cycling

CSF-stimulated cells have cycles of rapid division and a resting or quiescent phase. The timing of CSF administration is critical to ensure that rapidly dividing progenitor cells are not attacked by myelotoxic chemotherapy, thereby causing life-threatening neutropenia (Aglietta et al., 1989; de Wit et al., 1996). Kinetic studies confirm that on discontinuation of GM-CSF, progenitor cells enter the resting phase in 24 hours, whereas G-CSF-stimulated progenitor cells continue to cycle for an additional 48–72 hours (Aglietta et al.; Broxmeyer, Benninger, Patel, Benjamin, & Vadhan-Ray, 1994; Broxmeyer, Hangoc, & Cooper, 1992; de Wit et al.). Vadhan-Ray et al. (1992) found that GM-CSF administered in concert with optimal cell cycling diminished the myelosuppressive effects of cyclophosphamide, doxorubicin, and dacarbazine and concluded that a safe interval between cycles of chemotherapy is necessary to protect CSF-stimulated progenitor cells from chemotherapy-induced neutropenia. These studies support that GM-CSF, with its comparatively short resting phase, can play an important role in the design of novel approaches to dose escalation clinical trials and allow higher doses of cell cycle-specific chemotherapy to be given in shorter periods of time. These studies also suggest that the guidelines established by the American Society of Clinical Oncology (1994) for CSF administration be revised to acknowledge the differences in the cycle cell kinetics of endogenous CSF.

### Indications

GM-CSF is approved by the U.S. Food and Drug Administration for use following induction chemotherapy in older adults (≥55 years of age) with acute myelogenous leukemia (AML) to shorten time to neutrophil recovery (Rowe et al., 1995). Other indications include mobilization of hematopoietic progenitor cells into peripheral blood for collection by leukopheresis and following transplant of these cells, myeloid reconstitution after autologous bone marrow transplant (BMT), myeloid recovery after allogeneic BMT, and treatment of BMT failure or engraftment delay (PDR: Physician’s Desk Reference [PDR], 2002).

Although the current indications are based on GM-CSF’s ability to shorten time to neutrophil recovery thereby reducing the incidence of life-threatening infections and increasing survival rates, other areas are under investigation. GM-CSF’s role in antitumor activity and its use as an adjuvant vaccine, supportive agent in HIV treatment, fungal infection treatment, wound healing, as well as its effectiveness in decreasing mucositis, stomatitis, and diarrhea, currently are under investigation (Armitage, 1998) (see Figure 2).

### Administration

The recommended dose of GM-GSF is 250 mcg/m² IV or subcutaneous (SC) daily.
beginning 24 hours after chemotherapy and continuing until an absolute neutrophil count (ANC) greater than or equal to 1,500 for three consecutive days is achieved (PDR, 2002). An ANC of 1,500 cells/mm$^3$ is the critical level for neutrophils because an ANC greater than 1,500 cells/mm$^3$ offers no further decrease in the incidence of infection. Rather, the longer the duration of granulocytopenia, the more severe the infection will be (Bodey, Buckley, Sathe, & Freireich, 1996). Studies in patients receiving GM-CSF indicate sustained therapeutic ANC's after drug cessation (PDR).

Patients with chemotherapy-induced neutropenia commonly receive GM-CSF at a “flat dose” of 500 mcg. Five to seven injections usually are required to obtain an ANC of 1,500 cells/mm$^3$ (after nadir), at which time it is safe to discontinue therapy because of sustained ANC blood levels. For patients with AML and those who have undergone hematopoietic transplant, 10 days of GM-CSFs, on average, is indicated (Beveridge & Miller, 1993).

GM-CSF is supplied in a solution or a lyophilized powder. The liquid is formulated as a sterile, preserved (1.1% benzyl alcohol) solution (500 mcg/ml) supplied in a vial. The lyophilized powder (250 mcg) requires reconstitution, usually is reserved for the pediatric population, and must be refrigerated (PDR, 2002). Once the GM-CSF liquid vial has been entered, it is stable up to 20 days at 36$^\circ$–46$^\circ$ F. Preparations containing benzyl alcohol are to be avoided in the neonate population because of their inability to detoxify benzyl alcohol and its metabolites. Some neonates have been reported to manifest “gassing syndrome” as a result of receiving solutions containing benzyl alcohol. “Gassing syndrome” is characterized by extended periods of deep “all or none” breaths accompanied by a slow respiratory rate. This condition often is fatal in neonates (Boss, 1994).

### Side Effects

Yeast-derived GM-CSF generally is well tolerated, and side effects are manageable (PDR, 2002). Similar to other biologic agents, the most commonly seen side effects include injection site reactions, bone pain, fever, and flu-like symptoms (PDR). Table 2 illustrates common complications, nursing interventions, and patient-education strategies. Nursing management of patients receiving GM-CSF often is based on adverse effects experienced from injection of E. coli-derived GM-CSF (Houston, 1997). These formulas must be distinguished from one another because variation in the pharmacokinetics, biologic activity, and immuno- nogenicity lead to a variation of clinical toxicities. Dorr (1993) reviewed 32 clinical trials to determine the relative frequency of adverse reactions in patients treated with bacteria-derived GM-CSF versus that expressed in yeast. Leukine® (Immunex, Seattle, WA) was associated with a more favorable toxicity profile than was Leucomax® (Schering Plough and Sandoz, East Hanover, NJ). Although overlaps were found in the frequency ranges, the median frequencies of fluid retention, dyspnea, fever, myalgias, and bone and joint pain were consistently higher in patients treated with Leucomax, the bacteria-derived product. The frequency of all complications, except the rash, was about two times greater in patients treated with Leucomax.

In a randomized trial comparing yeast-derived GM-CSF and G-CSF in patients receiving myelosuppressive chemotherapy, both GM-CSF and G-CSF were well tolerated with similar safety profiles. The incidence and severity of local systemic adverse events were similar in both groups, except that more patients receiving GM-CSF developed a fever of grade 0 or 1 (37.1$^\circ$–38.0$^\circ$ C). No grade 4 toxicities were reported, and no patients were removed from the trial secondary to toxicity. No clinically significant differences were observed between patients receiving yeast-derived GM-CSF and G-CSF (Beveridge et al., 1997, 1998). Regan (2000) reported similar findings.

Pain occurring immediately after injection reportedly has been less severe with GM-CSF than G-CSF. In a randomized, double-blind, cross-over trial of healthy volunteers, less pain was reported with GM-CSF injection compared to G-CSF (Immunex, 2001) (see Figure 3). GM-CSF 500 mcg liquid vials contain the preservative benzyl alcohol, which is a known anesthetic that diminishes SC pain on injection (St. Peter, Lewis, & Macres, 1998; Williams & Howe, 1994).

### Beyond Neutrophil Recovery

The ability of GM-CSF to stimulate multiple lineages of the hematopoietic cascade is the basis for current studies exploring the immunomodulating and cytotoxic effects of GM-CSF on solid and hematologic tumors, such as malignant melanoma, breast cancer, prostate cancer, AML, and chronic myelogenous leukemia. Studies have shown that tumor cells can escape detection from the immune system on different levels. Some tumors do not present antigens on their surface; therefore, they are poorly immunogenic, whereas other tumor cells excrete vascular endothelial growth factor, a chemical that inactivates dendritic cells and results in a loss of antigen presentation to T lymphocytes (Gabrilovich et al., 1997). Researchers have found that patients with advanced breast cancer had a decreased number and potency of dendritic cells and possessed a defective T cell response. Data also suggest that when dendritic cells are stimulated from precursors, the T cell response returns to normal (Gabrilovich et al.). Additionally, tumor cells may down-regulate the major histocompatibility complex, which is necessary to distinguish self from nonself and to attract T cells and activate a T cell cytotoxic response (Shu, Plautz, Krauss, & Chang, 1997). Antitumor immunotherapy mediated by GM-CSF may bypass these tumor escapes by initiating or augmenting an immune response to tumor antigens resulting in cytotoxicity.

### Cancer Treatment

Melanoma has been a focus of studies using GM-CSF as an immunomodulatory treatment. Spitzer et al. (2000) conducted a study of patients with stage 3 and 4 surgically resected melanoma to evaluate disease-free and overall survival rates, and toxicity. After surgery, the patients were given GM-CSF $125$ mcg/m$^2$ daily for 14 days, followed by 14 days of rest. The GM-CSF was continued for one year or until disease progression occurred. Median disease-free survival was 37.5 months for those treated with GM-CSF versus 12.2 months for matched historical controls.

Another study examined the induction of systemic antitumor immunity in patients with melanoma primed with interferon al- pha for enhancement of antigen expression, followed by myelosuppressive chemotherapy for tumor eradication with dose immundulatory GM-CSF (O’Day et al., 1999). Patients experienced acceptable
Bone pain: Caused by stimulation of white cell activity in marrow cavities, such as iliac crest, sternal, and long bones, or the release of tumor necrosis factor or gamma interferon

Mild grade 1 or 2 rash: Caused by possible yeast sensitivity

Transient low-grade fevers: Caused by the release of interleukin (IL) and endogenous pyrogens or by immune system stimulation

First dose reactions: Caused by the sequestering of granulocytes in the pulmonary circulation

Fluid retention, capillary leak syndrome, pleural and pericardial effusion: Caused by cytokine IL-2 receptor-positive cells and CD8 positive lymphocytes

Site reactions (localized transient cutaneous erythematous rash occasionally accompanied by mild tenderness, burning, pain, or itching): Caused by local immune response or macrophage stimulation with GM-CSF

Adverse Effect and Cause | Nursing Interventions | Patient Teaching
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Bone pain: Caused by stimulation of white cell activity in marrow cavities, such as iliac crest, sternal, and long bones, or the release of tumor necrosis factor or gamma interferon | Administer drug in evening to minimize patient discomfort. Administer acetaminophen 20–30 minutes prior to injection and continue every four hours as needed. Opioids rarely are required. Ensure patient compliance. | Discuss the mechanism of granulocyte macrophage colony-stimulating factor (GM-CSF) and possible side effects. Discuss the mechanism dose and frequency of acetaminophen in pain control. Reassure the patient that the need for opioid support is rare. Instruct the patient to report relief measures to the clinical staff. |
Mild grade 1 or 2 rash: Caused by possible yeast sensitivity | Assess for allergies. Administer diphenhydramine to decrease allergic response. Assure patient that condition usually is mild and GM-CSF treatment usually is not discontinued. | Instruct the patient to report all allergies. Review diphenhydramine’s dosage and schedule. Instruct the patient to report all cutaneous symptoms. |
Transient low-grade fevers: Caused by the release of interleukin (IL) and endogenous pyrogens or by immune system stimulation | Administer acetaminophen prior to injection. Repeat every four hours if necessary. | Give the patient an easy-to-read thermometer; instruct the patient on its use. Instruct the patient to report a temperature of 100.5°F (38°C) or per institutional guidelines. Remind the patient to take acetaminophen 20–30 minutes before GM-CSF injection as ordered. If chilling occurs, patients should apply warm blankets. |
First dose reactions: Caused by the sequestering of granulocytes in the pulmonary circulation | Monitor the patient for hypoxia, flushing, hypotension, syncope, and tachycardia for about 20 minutes after first injection. Administer first dose in clinical setting. Monitor the patient for one hour for dyspnea: warm, red skin; dizziness; syncope; and tachycardia. Administer oxygen, methylprednisolone, and diphenhydramine if indicated. | Prepare the patient for the possibility of a first-dose reaction. Review the symptoms of a first-dose reaction. |
Fluid retention, capillary leak syndrome, pleural and pericardial effusion: Caused by cytokine IL-2 receptor-positive cells and CD8 positive lymphocytes | Monitor the patient for edema and weight gain, which are seen more with IV versus subcutaneous GM-CSF administration. Administer methylprednisolone, if ordered. | Instruct the patient to report difficulty breathing, weight gain, or any swelling. |
Site reactions (localized transient cutaneous erythematous rash occasionally accompanied by mild tenderness, burning, pain, or itching): Caused by local immune response or macrophage stimulation with GM-CSF | Allow vial or previously drawn up GM-CSF to reach room temperature prior to administration. Maintain volume injectate to less than 2 ml. Use a 25 or 27 gauge, 5/8” needle. Rotate injection sites among abdomen, thigh, and upper arm. Apply ice prior to and after injection. Avoid pinching of skin, if possible. Administer injection slowly. Avoid intermuscular injections. Do not rub area after medication is given. | Instruct the patient to assess the injection site daily and report symptoms of a localized reaction. |

Note. Based on information from Immunex, 2002.

Toxicity with a relatively high response rate and an increase in the number of durable responses. Tumor vaccines and injections of GM-CSF directly into tumors have been studied in the treatment of melanoma with varying results (DeMeyer & Barr, 2000). The results of all trials suggest that GM-CSF mediates an immunomodulatory/tumoridal effect on melanoma that warrants further study. Prospective trials currently are being conducted.

GM-CSF is being studied to improve response rates for patients with breast cancer. Researchers believe that the release of necrotic cells and the abundance of apoptotic bodies resulting from chemotherapy may provide appropriate danger signals to trigger maturation and activation of dendritic cells (DeMeyer & Barr, 2000). Pinedo and Bulter (2000) found improved clinical response and survival rates among patients with locally advanced breast cancer treated with prolonged neoadjuvant chemotherapy plus GM-CSF. Patients had a 98% response rate and a complete response rate of 50%. Although the response rate was independent of the number of cycles, the disease-free and
Overall survival rates appeared to improve with the increasing number of cycles. Preliminary studies evaluating GM-CSF in patients with prostate cancer have been reported. Two sequential studies were conducted to evaluate the efficacy of GM-CSF in patients with hormone refractory progressive prostate cancer. In the first study cohort, 23 men were given GM-CSF at a dose of 250 mcg/m² daily for 14 days of a 28-day cycle (Small et al., 1999). After oscillating, prostate-specific antigen (PSA) responses were observed in this first cohort, a second study cohort was studied in which patients (N = 13) received maintenance GM-CSF at 250 mcg/m² three times weekly after the first 14 days of daily GM-CSF (Small et al.). Maintenance therapy continued until disease progression. All but one patient experienced a decline in PSA levels, with a median response duration of 3.5 months. One patient experienced a decline in his PSA greater than 99% and an improvement in his bone scan that lasted for 14 months. These data suggest that GM-CSF may have biologic activity in prostate cancer (Small et al.). Further studies need to be conducted on patients with less heavily treated, smaller tumor burdens to identify the mechanism of action, effectiveness, and relevance of GM-CSF in the treatment of prostate cancer.

Anti-CD20 monoclonal antibody (rituximab, Rituxan®, Genentech, South San Francisco, CA, and IDEC Pharmaceuticals, San Diego, CA) is an approved treatment for low-grade non-Hodgkin’s lymphoma (NHL). When combined with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy, the response rate is 100% (Venugopal et al., 2000). However, the durability of this response rate still has to be determined. The CD20 antigen is expressed in more than 90% of patients with indolent NHL. The activity of the anti-CD20 monoclonal antibody on the CD20+ tumor cells depends on its ability to bind with the cell and cause cell death (Coleman, Chodakewitz, Bartiss, & Mellors, 1998). One of the important factors that determine the binding of the antibody to the cell is the intensity of the expression of the CD20 antigen on the surface of the tumor cell. Up regulation of the CD20 antigen has been observed with interleukin-4 (IL-4), tumor necrosis factor, and GM-CSF. Studies now are being conducted to determine the durability of remissions with CHOP and Rituxan, as well as the influence of cytokine priming (Venugopal et al.). In these incidents, GM-CSF dosing is similar to infection management in the immunosuppressed patient with cancer. Antibody dependent cellular cytotoxicity may play a role in increasing efficacy of monoclonal antibodies (Venugopal et al.).

GM-CSF currently is being studied to enhance the functional effects of tumor vaccines on monocytes, macrophages, and dendritic cells (DeMeyer & Barr, 2000). Leukine has been studied as an enhancement for tumor cell vaccines, recombinant peptide tumor vaccines, and autologous idioype keyhole limpet hemocyanin tumor vaccines (Armitage, 1998).

Dendritic cell vaccines are developed ex vivo in a number of ways. One type of tumor vaccine is developed by isolating CD34+ progenitor cells and cryopreserving them until needed. When the progenitor cells are thawed, GM-CSF, IL-4, and IL-12 cytokines are added to cultivate dendritic cells. The stem cells then are exposed to tumor antigens and administered to the patient. This type of vaccine can be developed into a general cancer vaccine and primed with a common antigen found in most cancers or can be developed into an autologous vaccine that is primed with a sample of the patient’s own tumor (DeMeyer & Barr, 2000). The optimal dose, schedule, and administration still have to be determined; therefore, further studies need to be conducted.

Wound Healing

Wound healing is another area in which GM-CSF may be beneficial. Research has shown that GM-CSF enhances the migration and proliferation of endothelial cells and promotes keratinocyte growth (Bussolino, Camussi, & Baglioni, 1988; Hancock, Kaplan, & Cohn, 1988). Studies of animal models documented that local application of GM-CSF to wounds resulted in increased formation of granulation tissue and increased breaking strength of incisional wounds, and reversal of wound contraction in infected wounds resulted in faster wound healing time (Kucukcelebi, Carp, & Haywood, 1992; Vyalov, Desmouliere, & Gabbiani, 1993).

Studies of wound healing conducted in humans offer promising results. Chronic leg ulcers have been treated with GM-CSF in various methods: (a) as a topical application, (b) injected in the periphery of the wound, and (c) in GM-CSF-incubated skin grafts that resulted in patients experiencing complete or partial healing (Braunstein et al., 1994; Kaplan et al., 1992; Marques da Costa, Jesus, Aniceto, & Mendes, 1997). In a double-blind, placebo-controlled study to establish efficacy of GM-CSF on wound healing, 40 patients either received 400 mcg of GM-CSF or a similar volume of saline. The study was unblinded and terminated prematurely because the wounds treated with GM-CSF healed significantly more rapidly than wounds treated with the placebo (Marques da Costa et al.).

Clinicians have reported that other off-study use has resulted in promising outcomes. Ulitin, Guden, Dedé, and Pak (2000) compared G-CSF and GM-CSF administered at a dose of 400 mcg/m² SC in the treatment of two chemotherapy extravasation ulcers. GM-CSF healed one ulcer, whereas the ulcer treated with G-CSF was unaffected (Ulitin et al.). Other researchers have found that SC injection of 10 mcg/cm² GM-CSF in healing chronic refractory wounds is safe and effective (Malik et al.,...
Mucositis and Diarrhea

The gastrointestinal tract is a major target of myelosuppressive therapy, and symptoms include painful mucositis, stomatitis, diarrhea, and secondary infections. Symptom management may require the need for intensive supportive care and result in economic burdens. The cost of managing mucositis in BMT recipients has been about $42,000 more compared to recipients who do not experience this disorder (Sonis et al., 2001). Early research found that BMT recipients who received GM-CSF experienced less mucositis than those who did not receive GM-CSF (Nemunaitis et al., 1995). Interest has been renewed in the use of CSFs in reducing mucositis because of the increase in dose intensive chemotherapy and stem cell transplantation (Stiff, 2001). Investigators studied the effect of GM-CSF administration in pediatric recipients of stem cell transplants (N = 13) and found that GM-CSF reduced the duration but not the severity of oral mucositis and time to systemic infection. However, parenteral nutrition and pain control measures were reduced significantly in those receiving GM-CSF (Gordon et al., 1994). Rosso, Blasi, Gherlone, and Rosso (1997) found similar effects in patients with head and neck cancers treated with chemotherapy.

Two phase I trials of GM-CSF in combination with leucovorin (LV) 500 mg/m² and escalating doses of 5-fluourouracil (5-FU) in patients with colorectal cancer resulted in decreased rates of diarrhea compared to historical controls (Grem et al., 1994). Meropol, Youcef, Creaven, Blumenson, and Frank (1999) explored the hypothesis that myeloid CSFs can serve as mucosal protectants in dose-limiting chemotherapy secondary to mucositis. The objective of the study was to determine the maximum tolerated dose of weekly 5-FU when administered with GM-CSF and high-dose LV. The researchers found that the maximally tolerated dose of 5-FU was higher than previously reported without GM-CSF, suggesting that GM-CSF may be a mucosal protectant. Randomized trials comparing weekly 5-FU plus LV with and without GM-CSF are needed and currently are under way (Masucci, 1996).

Summary

GM-CSF stimulates and enhances the production of multiple hematopoietic progenitor cells in the myeloid lineage and activates many functional activities of neutrophils, monocytes, macrophages, and dendritic cells. Use of this agent as an adjuvant to standard infection measures has enhanced protection of the host against a broad spectrum of bacterial and fungal organisms, thereby lessening the use of antibiotics, shortening hospital stays, and extending survival in a large number of patients. Clinical trials are evaluating the use of GM-CSF in shortening the course of mucositis and diarrhea, as a vaccine adjuvant against infectious diseases and malignancies, and as immunotherapy in the treatment of malignancies, including melanoma, breast cancer, and neuroblastoma. Additionally, this agent shows promise in those with compromised wound healing and ulcerations. As cancer chemotherapy regimens become dose intensive and longer in duration, or shorter in time to the next dose, GM-CSFs will have an even more important role. To ensure optimal patient care, nurses practicing in all healthcare settings must be aware of current and future applications and management of GM-CSF in a wide range of patients.

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References


Granulocyte Macrophage Colony-Stimulating Factor: Current Practice and Novel Approaches

- Granulocyte macrophage colony-stimulating factor (GM-CSF) is a glycoprotein that shortens time to neutrophil recovery following chemotherapy administration.
- Current research suggests that GM-CSF may decrease the course of chemotherapy-induced mucositis, stimulate dendritic cells, and possess immunologic tumor control capabilities.
- Commonly observed side effects associated with GM-CSF include bone pain, mild rash, transient low-grade fevers, and injection site reactions.
- GM-CSF has been found to enhance proliferation of endothelial cells and keratinocyte growth and may have a role in promoting wound healing.
- Clinical trials are evaluating the use of GM-CSF as a vaccine adjuvant against infectious diseases and malignancies and as immunotherapy in the treatment of various malignancies, such as melanoma, breast cancer, and neuroblastoma.