Immune Globulin IV Therapy: Optimizing Care of Patients in the Oncology Setting

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Purpose/Objectives: To review major clinical applications of immune globulin IV (IGIV) therapy, properties of currently available IGIV preparations, procedures for dosing and administration, management of infusion-related adverse effects, and strategies for effective patient education.

Data Sources: Published articles, abstracts, and textbook chapters.

Data Synthesis: IGIV therapy supports immune function by providing immunoglobulin G antibodies for protection against pathogens and modulation of autoimmune and other potentially damaging host responses. Licensed uses include treatment of primary immune deficiencies and autoimmune conditions and prophylaxis against viral infection.

Conclusions: The safety and effectiveness of IGIV therapy depend on selection of an appropriate product, dosage, and infusion rate; patient comorbidities and other risk factors; and patient education and treatment adherence.

Implications for Nursing: Nurses have an essential role in the safe and effective use of IGIV, from educating patients about the rationale for and effects of therapy to administering the product and monitoring for adverse effects.

Key Points . . .

- All available immune globulin IV (IGIV) products display the same immune-supportive properties, but specific product differences can affect the volume of infusion, the rate of infusion, the product's suitability for peripheral or central infusion, and the need for a filter during administration.
- Patients usually receive initial infusions of IGIV in a hospital or ambulatory care setting, where nurses can provide close supervision and potential infusion complications can be managed safely.
- Before beginning infusions, nurses should verify physicians' orders, check for clinical contraindications to IGIV therapy, and assess patients' renal, hepatic, cardiovascular, respiratory, and neurologic functions.

Since its introduction in the early 1980s, immune globulin IV (IGIV) therapy has become an important means for treating a variety of disease states manifested by deficient production of immunoglobulins or by aberrant production of autoantibodies (autoimmune disorders). Among the conditions are primary immune deficiency (PID), idiopathic (or immune) thrombocytopenic purpura (ITP), Kawasaki disease, chronic lymphocytic leukemia (CLL), hematopoietic stem cell transplantation (HSCT), and HIV infection in children. This article discusses the medical indications for IGIV therapy, clinical implications of specific IGIV product properties and differences, and practical considerations in IGIV dosage and administration, nursing management, and patient education. Two case reports highlight nurses' role in administering IGIV therapy and monitoring patients for adverse effects.

Immune Function

The body has two major immune response systems: nonspecific and specific. Nonspecific immunity includes barriers (e.g., physical barriers such as skin, chemical barriers such as gastric acid) as well as immune responses such as granulocytic phagocytosis and complement protein activation. Nonspecific immunity is essential as the first line of defense against potentially invading pathogens. It is most important for inflammatory reactions and destruction of bacterial microbes.

Lymphocytes are the essential elements of the specific immune response, which targets unique antigenic structures, foreign proteins, viral particles, and transplanted tissue. The two arms of the specific immune system are cellular and humoral. Cytokines from T lymphocytes provide protein-specific cytotoxicity (i.e., cellular immunity). B lymphocytes provide targeted cell destruction (i.e., humoral immunity) through creation of antibodies, also known as immunoglobulins. The B cells that conduct the humoral immune response may be activated by a direct encounter with an antigen or by T-cell cytokines. In either case, activated B cells evolve into antibody-producing cells known as plasma cells. If a specific antigen particle or organism enters the body for a second or subsequent time, a

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humoral immune response may be conducted by plasma cells known as memory cells. The cells are familiar with the antigen from a previous encounter and therefore are directly equipped to produce antibodies to it immediately.

Immune deficiency states may be related to inadequate numbers of immunologic cells or to the dysfunction of the cells. Disorders of inadequate or inappropriate specific immune responses may be treated by IGIV therapy.

Nature of Immune Globulin IV

The first therapeutic use of human immunoglobulin G (IgG) occurred in 1952, when it was given by intramuscular injection to treat the genetic immune deficiency X-linked agammaglobulinemia (Pierce & Jain, 2003). Limitations of early preparations included difficulty providing adequate quantities of IgG via tissue injection as well as anaphylactic reactions from the formation of IgG aggregates with the route of administration. After nearly three decades, IGIV therapy became commercially available in 1981 for treating hypogammaglobulinemia, allowing for the administration of larger amounts of IgG and the achievement of higher plasma levels to meet clinical needs (Pierce & Jain).

Immune Globulin IV Composition

Each lot of IGIV is made from plasma pooled from 3,000–10,000 human donors. Donors and the donated plasma are screened for bloodborne pathogens (e.g., hepatitis viruses, HIV). The standard manufacturing process includes initial fractionation to isolate the IgG; subsequent production steps, which vary by manufacturer, are designed to purify and stabilize the product (Brown, 2003; Hall, 1993; Miller, Petteway, & Lee, 2001). How a product is stabilized (i.e., with the addition of sucrose, another sugar, or albumin) and other differences in the manufacturing process affect its properties and can have important clinical implications.

IGIV preparations provide intact IgG with an IgG subclass composition closely resembling that of normal human serum (Hall, 1993). Most IGIV products also contain trace amounts of IgA (Hall) and certain cytokines, as well as some other proteins found in serum. The clinical half-life of infused IGIV preparations ranges from 21–28 days (Gelfand, 2000).

Clinical Uses

IGIV therapy is used to augment, supplement, or replace deficient components of the immune system (Miller et al., 2001). It also modulates or downregulates the immune response in immune-mediated diseases (Bussel, Eldor, et al., 2004; Hall, 1993; Miller et al.). Table 1 summarizes the licensed U.S. Food and Drug Administration (FDA) indications for IGIV therapy. In addition to the FDA's indications, IGIV has been used in the management of a wide range of other disorders, including Guillain-Barré syndrome, myasthenia gravis (Hall), chronic inflammatory demyelinating polyneuropathy (Hall), and dermatomyositis (Dalakas, 1999; Hall), as seen in Table 2. In fact, 58% of IGIV use is for off-label purposes (Ratko, Burnett, Foulke, Matuszewski, & Sacher, 1995). An informal survey conducted at a symposium during the 2005 annual meeting of the Oncology Nursing Society indicated that oncology nurses care for patients receiving IGIV therapy primarily for ITP and oncology-related indications (CLL and post-transplant immune support), although off-label uses also are common (Griffin, 2005).

Properties of Currently Available Preparations

Table 3 lists currently available IGIV preparations. All contain 90%–98% IgG and provide a full complement of the four IgG subclasses, although the subclass percentages in different preparations may vary (Swenson, 2000). All available IGIV products display the same immune-supportive properties, but the unique composition of each product can affect the volume of infusion, the rate of infusion, the product's suitability for peripheral or central infusion, and the need for a filter during administration.

Immunoglobulin A content: The immunoglobulin A (IgA) content of IGIV products ranges from ≤ 2.2–720 µg/ml. Patients with selective IgA deficiency can develop autoantibodies to IgA, which places them at increased risk for severe, life-threatening hypersensitivity reactions, including anaphylaxis (Dalakas, 1999; Miller et al., 2001; Swenson, 2000). Such conditions are extremely rare, and the vast majority of IgA-deficient patients do not have the autoantibodies. Nonetheless, although anaphylactic reactions are extremely rare with IgA-containing IGIV products, caution should be used when administering IGIV to IgA-deficient patients.

Form: IGIV products are available as lyophilized powders or liquid formulations. Lyophilized products must be reconstituted in a diluent and thus require additional time for preparation, which may adversely affect some nurses' practices. Preparation of a lyophilized product may take 30–60 minutes, in contrast to 10 minutes for that of a liquid product (Davis et al., 2003). The additional up-front time required to prepare a lyophilized product commonly is balanced by using a lower infusion volume (i.e., reconstituting to a higher concentration) and shortening the infusion time. However, attempts to compensate in this manner for the time spent reconstituting lyophilized products need careful consideration, particularly when patients are at risk for renal or thromboembolic complications. Reconstitution in a smaller volume may increase the osmolarity of the solution. Hyperosmolarity could result in serious adverse events such as renal complications (e.g., acute tubular necrosis [ATN]) or thromboembolic events (Lemm, 2002). Likewise, an infusion rate higher than that recommended for a product has been associated with thromboembolic events (Grillo, Gorson, Ropper, Lewis, & Weinstein, 2001).

Osmolarity: An IGIV product's osmolarity is affected by its electrolyte (e.g., sodium) and sugar content. Physiologic osmolarity is 275–290 mOsm/kg. The osmolarity of IGIV preparations ranges from less than 200 to 1,000 or more mOsm/kg, a factor that should be considered when selecting an IGIV product for patients with compromised renal function or only peripheral access and patients who cannot tolerate a large osmotic load (Ratko et al., 1995). As noted previously, hyperosmolarity may lead to renal or thromboembolic adverse events (Lemm, 2002).

Sugar content: The sugar content of an IGIV product is an important factor for patients who have preexisting kidney disease and volume depletion, especially older adults and those with diabetes or poor hydration (Dalakas, 1999). Such patients may be at increased risk for developing acute renal failure with sugar-containing products. In such patients, sugar-free products are more appropriate. A disproportionately high frequency of renal failure, likely caused by osmotic injury to the proximal renal tubules, has been

Table 1. U.S. Food and Drug Administration Licensed Indications for IGIV Therapy

Primary Immunodeficiency[a]	Immune System Defect	Clinical Features	Treatment (Other Than IGIV)
Bruton's or X-linked agammaglobulinemia	• Decreased IgA, IgG, IgM • Complete absence of B cells	• Onset in infancy or childhood affects males. • Marked by repeated bacterial infections (e.g., sinuses, lungs, bones) and arthritis of large joints • Onset in adulthood affects both sexes.	Antibiotic therapy for infection
Common variable immunodeficiency	• Hypogammaglobulinemia • Presumed T-cell regulatory defects • Poor immune response to polysaccharide antigens	• Marked by repeated bacterial infections (e.g., bacterial sinusitis, pneumonia), malabsorption, diarrhea, giardiasis, and increased lymphoreticular malignancy	Prophylactic antibiotics
Severe combined immunodeficiency	• Complete loss of T cells or T-cell function • Variable loss of B cells • Severe hypogammaglobulinemia (IgG levels may be normal at birth as a consequence of transplacental transport of maternal IgG)	• Onset in infancy; without treatment, typically lethal during the first year of life • Marked by multiple severe infections (bacterial, fungal, and viral), GVHD, diarrhea, rash, and failure to thrive	Bone marrow transplantation early in life and protective isolation
Wiskott-Aldrich syndrome	• T- and B-cell deficiencies	• Affects males • Marked by thrombocytopenia with microplatelets, eczema, recurrent viral and bacterial infections, and increased incidence of lymphoreticular malignancy or autoimmunity	Bone marrow transplantation and antibiotics
Idiopathic thrombocytopenic purpura	• Massive destruction of platelets by autoantibodies	• Affects children and adults • Marked by severe hemorrhage, petechiae, and epistaxis • Symptoms correlate with the degree and severity of thrombocytopenia • Has rapid onset (acute form) in childhood but may resolve spontaneously; typically persists throughout life (chronic form) in adults	Corticosteroids, anti-D IGIV, and splenectomy
Kawasaki disease (Kawasaki syndrome)	• Massive activation of the immune system, resulting in autoantibodies and self-directed immune response at the coronary arteries • Characterized by increased numbers of macrophages and elevated serum cytokine levels of tumor necrosis factor	• May develop secondary to disease (e.g., HIV infection, systemic lupus erythematosus) • Typically affects infants and children younger than five years • Marked by fever, erythematous macular rash, conjunctivitis, and vasculitis of the coronary and other arteries	Aspirin
Chronic lymphocytic leukemia	• IgG deficiency	• Marked by lymphadenopathy, fatigue, anorexia, weight loss, and dyspnea on exertion • Predisposition to bacterial infection	Chlorambucil, fludarabine, rituximab, and alemtuzumab
Pediatric HIV infection[b]	• Severe CD4+ T lymphopenia and T-cell dysfunction; impaired antigen-specific immune responsiveness	• Failure to thrive • Recurrent bacterial and opportunistic infections • Splenomegaly and lymphadenopathy	Antiretroviral therapy, including nucleoside and nonnucleoside reverse transcriptase inhibitors
Bone marrow transplantation (allogeneic)[b]	• Severe immune dysfunction secondary to the toxic effects of the myeloablative or immunoablative preparative therapy	• Increased infection risk of activating viruses, including cytomegalovirus • Increased risk of bacterial infections • GVHD with skin rash and diarrhea	Prophylactic antifungal, antiviral, and antibacterial agents and immune suppression (e.g., with corticosteroids and cyclosporine) to prevent GVHD

[a] More than 100 primary immunodeficiency diseases exist; only the most common are listed here.

[b] Gamimune N, which is no longer manufactured, was the only IGIV product licensed for this indication.

GVHD—graft-versus-host disease; Ig—immunoglobulin; IGIV—immune globulin IV

Note. Based on information from Wright & Shelton, 1993.

Table 2. Selected Off-Label Uses for IGIV Therapy

Disease	Clinical Features	Treatment
Chronic inflammatory demyelinating polyneuropathy	• Acquired polyneuropathy resulting from destruction of the myelin sheath, perhaps resulting from autoantibody production • Typical onset from weeks to months • Marked by weakness, loss of reflexes, and impaired sensation	• Corticosteroids (first-line treatment) and plasmapheresis (to remove autoantibodies) • IGIV may block Fc receptors of macrophages, thereby preventing destruction of the autoantibody-coated myelin sheath.
Dermatomyositis	• Results from deposition of MAC (a complement cluster) on intramuscular capillaries • Marked by ischemia of the affected muscles, proximal muscle weakness, inflammation, and a purplish rash on the face, hands, and feet	• Corticosteroids (first-line treatment) • IGIV used for corticosteroid-resistant cases; may inhibit MAC deposition on capillaries
Guillain-Barré syndrome	• Autoantibody-mediated demyelinating disease • Causes severe weakness or paralysis of legs, arms, and possibly respiratory muscles • Reaches its peak manifestation within two weeks of onset	• Plasmapheresis (to remove autoantibodies) • IGIV (to neutralize autoantibodies)
Myasthenia gravis	• Induced by autoantibodies against ACh receptors on postsynaptic nerve terminals, which are essential for nerve-impulse transmission in cholinergic nerves	• Anticholinesterase drugs (to preserve ACh and ACh-mediated impulse transmission across the synaptic cleft) • Thymectomy (to retard cell-mediated attack on ACh receptors) • Immunosuppressive drugs (e.g., azathioprine and cyclosporine) • Plasmapheresis • IGIV (as effective as plasmapheresis but with fewer adverse effects)

ACh—acetylcholine; IGIV—immune globulin IV; MAC—membrane attack complex

Note. Based on information from Dalakas & Clark, 2003; Hall, 1993.

reported with sucrose-containing IGIV products (Centers for Disease Control and Prevention, 1999; Pierce & Jain, 2003). Maltose- or glucose-containing products also have been associated with renal failure but at a lower frequency compared with sucrose-containing products (Centers for Disease Control and Prevention). Additionally, nurses should be aware that, following infusion of maltose-containing IGIV products, blood glucose monitoring using dehydrogenase pyrroloquinolinequinone–based glucose monitoring systems may yield falsely elevated glucose readings (FDA, 2005). Inappropriate administration of insulin and consequent life-threatening or fatal hypoglycemia based on erroneous test results have been reported.

Table 4 summarizes important factors for consideration in the selection of an IGIV product for patients with specific risk factors. IGIV preparations also differ in their available package sizes. If a vial contains more than an individual dose, leftover product may be wasted. A disadvantage of reconstituted products is limited shelf-life after reconstitution. These variables may be considered in the selection of IGIV products for individual practices or institutions.

Administration

Setting

IGIV can be given safely in a variety of settings, including a hospital, physician's office, clinic, infusion center, or home. The choice of setting is based on the appropriate level of care that patients require. Initial infusions of IGIV usually are given in a hospital or ambulatory care setting, where close nursing supervision can be provided and potential infusion complications can be managed quickly and safely.

Patient Assessment

Before beginning IGIV treatment for patients, nurses must verify physicians' orders, check for clinical contraindications to therapy, and determine whether patients have a history of diabetes or infusion-related reactions to other medications administered via IV (see Figure 1). Renal, hepatic, cardiovascular, and neurologic function should be evaluated in adult and pediatric patients. Baseline laboratory tests typically include serum measurements of IgG, glucose, electrolytes, alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen (BUN), and creatinine as well as serum osmolality. Baseline vital signs, pretreatment height and weight (to verify accurate dosing), and fluid intake and output should be recorded, and breath sounds should be assessed. If a pretreatment assessment reveals risk factors for adverse reactions or evidence of renal impairment, adjusting the infusion rate or, in some cases, selecting a different product or product concentration may be necessary. Pretreatment assessments should be performed before each infusion. Although IGIV preparations are derived from human blood, the risk of viral transmission is extremely low, and obtaining signed informed consent is not necessary. However, it is critical to inform patients of any potential—albeit minimal—risk of infection before the initiation of IGIV infusion.

Setup

Equipment needed for IGIV infusion includes an IV administration set; an electronic infusion pump; an in-line filter set with a 15 micron filter, if it is required for the particular product being infused (see Table 3 for products that require a filter); and supplies for venipuncture or IV catheter or port access. Supplies and medications needed for managing a potential hypersensitivity reaction should be readily accessible. Institutional policy

Table 3. Comparing Currently Available IGV Preparations[a]

Characteristic	Carimune® NF[b]	Flebogamma® 5%	Gammagard Liquid	Gammagard S/D	Gamunex®[b]	Iveegam EN	Octagam®	Polygam® S/D
Manufacturer	ZLB Bioplasma, King of Prussia, PA	Instituto Grifols, Barcelona, Spain	Baxter Healthcare Corp., Deerfield, IL	Baxter Healthcare Corp., Deerfield, IL	Talecris Biotherapeutics, Inc., Research Triangle Park, NC	Baxter Healthcare Corp., Deerfield, IL	Octapharma Phamazeutika, Vienna, Austria	Baxter Healthcare Corp., Deerfield, IL
FDA-approved indications[c]	PID, ITP	PID	PID	PID, ITP, CLL, KS	PID, ITP	KS, PID	PID	PID, ITP, CLL, KS
Form	Lyophilized	Liquid	Liquid	Lyophilized	Liquid	Lyophilized	Liquid	Lyophilized
Available sizes	1, 3, 6, 12 g	0.5, 2.5, 5, 10 g	1, 2.5, 5, 10, 20 g	2.5, 5, 10 g	1, 2.5, 5, 10, 20 g	0.5, 1, 2.5, 5 g	1, 2.5, 5, 10 g	5, 10 g
Available concentrations	3%–12%	5%	10%	5%, 10%	10%	5%	5%	5%, 10%
Storage: refrigeration	No	No	Optional	No	Optional	Yes	Optional	No
Shelf life (months)	24	24	Refrigerated, 36; room temperature, 9[c]	24	Refrigerated, 36; room temperature, 5[d]	24	24	24
Reconstitution time	Several minutes	None	None	< 5 minutes at room temperature; > 20 minutes if cold	None	≤ 10 minutes at room temperature	None	Within minutes
pH (after reconstitution)	6.4–6.8	5–6	4.6–5.1	6.4–7.2	4.0–4.5	6.4–7.2	5.1–6.0	6.8
IgA content (mc/ml)	720	< 50	37	≤ 2.2 (5% concentration)	46	< 10	≤ 100	≤ 2.2 (5% solution)
Sugar content	Sucrose, 1.67 g per gram of protein	D-sorbitol, 50 mg/ml	None (stabilized with glycine)	Glucose, 20 mg/ml (5% concentration)	None (stabilized with glycine)	Glucose, 50 mg/ml	Maltose, 100 mg/ml	Glucose, 20 mg/ml (5% solution)
Sodium content	0% water; 0.9% saline	< 3.2 mEq/l (< 0.02%)	None	0.85%	Trace	3 mg/ml	< 30 mmol/l	0.85%
Osmolarity/osmolality[e]	mOsm/kg: in sterile water, 192 (3%), 384 (6%), 576 (9%), 768 (12%); in 0.9% NaCl, 498 (3%), 690 (6%), 882 (9%), 1074 (12%); in 5% dextrose, 444 (3%), 636 (6%), 828 (9%), 1020 (12%)	240–350 mOsm/l	240–300 mOsm/kg	636 mOsm/l (5%); 1,250 mOsm/l (10%)	258 mOsm/kg	≥ 240 mOsm/l	310–380 mOsm/kg	636 mOsm/l (5%); 1,250 mOsm/l (10%)
Filtration required	No	Optional	Optional	Yes	No	Yes	Optional	Yes
Initial infusion rate	Use 3% solution for PID patients. Start at 10–20 drops (0.5–1 ml) per minute.	0.01 ml/kg per minute (0.5 mg/kg per minute)	0.5 ml/kg per hour (0.8 mg/kg per minute)	0.5 ml/kg per hour of 5% solution	0.01 ml/kg per minute (1 mg/kg per minute)	1–2 ml per minute	30 mg/kg per hour (0.01 ml/kg per minute)	0.5 ml/kg per hour of 5% solution

[a] All IGIV preparations are contraindicated in patients with IgA deficiency.

[b] The manufacturing process for this product provides reasonable assurance that prions associated with transmissible spongiform encephalopathy would be removed if present in donated plasma.

[c] Within the first 24 months of the date of manufacture

[d] Any time during the 36-month shelf life

[e] Physiologic osmolarity is 275–290 mOsm/kg.

CLL—chronic lymphocytic leukemia; FDA—U.S. Food and Drug Administration; IgA—immunoglobulin A; IGIV—immune globulin IV; ITP—idiopathic thrombocytopenic purpura; KS—Kawasaki disease; PID—primary immunodeficiency disorder

Note. Based on information from Siegel, 2006.

Table 4. Matching IGIV Product Characteristics to the Patient Profile

	Immune Globulin IV Risk Factors					
Patient Risk Factors	**Volume Load**	**Sugar Content**	**Sodium Content**	**Osmolality**	**pH**	**IgA**
Cardiac impairment	•		•	•		
Renal dysfunction	•	•	•	•		
Anti-IgA antibodies						•
Thromboembolic risk	•		•	•		
(Pre) diabetes		•				
Advanced age	•	•	•	•		
Neonates or pediatrics	•		•	•	•	

IgA—immunoglobulin A; IGIV—immune globulin IV

or physicians' orders dictate the choice of medications, which may include diphenhydramine, acetaminophen, hydrocortisone, ranitidine or another histamine-2–receptor blocker, bronchodilator inhaler, antiemetics, epinephrine (1: 1,000), and at least 1 L of 0.9% saline for blood pressure support if needed. The management of hypersensitivity reactions to IGIV products is similar to that for managing allergic blood reactions (Labovich, 1997) and is discussed in Figure 2. As with blood transfusions, infusion reactions may occur with any IGIV infusion. Because IGIV products are made from plasma pooled from multiple donors, each infusion has its own unique risk for inducing a hypersensitivity reaction.

Patient Education

Patient education is an essential component of effective IGIV therapy. Educating patients before initiating infusion is important for decreasing anxiety and improving compliance with future treatment. Patients should be asked whether they know why they are receiving IGIV therapy and what they have heard about such therapy. If necessary, nurses should explain the specific effects of patients' illness and the reasons for and benefits of IGIV therapy. Patients who need repeated IGIV therapy should be informed about the schedule of infusions, the need for ongoing monitoring in the months ahead, and the preferred setting for the infusions.

Patients' fears of contracting infection from human plasma products should be allayed with explanations of IGIV therapy's excellent safety record for more than a decade and, if necessary, descriptions of the procedures that manufacturers use to make IGIV products safe. If, for example, a patient relates a story of someone who has had an adverse experience with a blood or blood-product transfusion, nurses can explain that IGIV products are processed and tested extensively before use.

Nurses should tell patients that an IGIV infusion will take several hours and that it will start at a slow rate and then increase. They should assure patients that respiratory rate, heart rate, and other vital functions will be recorded at short intervals and that a nurse will be close at hand throughout most of the infusion. Explaining what may happen during an infusion and describing clearly all sensations that may indicate adverse effects are essential. Many patients report feeling a lump in the throat, the need to clear the throat, or a sensation of warmth as early indicators of hypersensitivity reactions. Patients should be asked to report any such sensations immediately.

Nurses also can teach family members about IGIV therapy, with a specific focus on its benefits for patients' particular conditions and families' important role in supporting patients during treatment. Insurance reimbursement should be confirmed prior to therapy, and referral to financial counselors or social services staff may be provided as required. Patients should be informed that reimbursement policies for IGIV differ among various insurance carriers. Additionally, insurance coverage may vary by setting (e.g., hospital inpatient or outpatient, physician office, home healthcare setting). If necessary, nurses can arrange appointments for patients, family members, or both to meet with the social services department to address their needs further.

Patient Assessment

Patient history
- Diabetes
- Renal dysfunction
- Cardiovascular diseases
- Infusion-related reactions
- Selective immunoglobulin A deficiency
- Concomitant nephrotoxic drug use

Monitor function
- Renal
- Cardiovascular
- Hepatic
- Neurologic

Baseline Measurements

Physical
- Height
- Weight
- Urinary output

Baseline Measurements (continued)

Vital signs
- Blood pressure
- Pulse
- Breath sounds

Laboratory
- Immunoglobulin G
- Glucose
- Electrolytes
- Alanine aminotransferase
- Aspartate aminotransferase
- Blood urea nitrogen
- Creatinine
- Osmolality
- Viscosity
- Complete blood count

Premedication

Patients at risk for infusion reaction
- Acetaminophen
- Diphenhydramine
- Hydrocortisone via IV 1–2 mg/kg, 30 minutes prior to immune globulin IV infusion for high-risk patients

Figure 1. Assessment of Patients Receiving Immune Globulin IV

Premedication

Premedication with acetaminophen and diphenhydramine usually is prescribed for patients receiving IGIV infusion. If a patient is at high risk for an infusion reaction, the physician may choose to add a corticosteroid, such as hydrocortisone. Premedications are given 30 minutes before the start of IGIV infusion. If a patient is febrile or has evidence of infection, postponing infusion should be considered so that symptoms are not recorded erroneously as being associated with IGIV infusion.

At the first sign of a reaction to IGIV infusion,

- Stop the infusion and notify the physician.
- Do not leave the patient if the reaction is severe; use the call system to request help.
- Administer normal saline to maintain vein patency, systolic blood pressure > 100 mmHg, and urine output > 100 ml per hour, if necessary.
- Monitor the patient's vital signs; assess for fever, chills, rash, hives, hypotension, dyspnea, pulmonary edema, wheezing, decreased urine output, and change in urine color.
- Administer appropriate medications ordered by the physician, which may include
  - Acetaminophen for fever
  - Antihistamines for effects of histamines (e.g., flushing, itching)
  - Corticosteroids for inhibition of vasoconstriction, bronchospasm, and increased vascular permeability
  - Epinephrine for anxiety, generalized urticaria, wheezing, and cardiovascular collapse
  - Diuretic (e.g., furosemide, mannitol) for maintenance of urine output > 100 ml per hour.
- Be prepared to call the emergency code team if signs of respiratory or circulatory collapse are present.
- Continue assessment and documentation of status every 5–15 minutes, as warranted, until the patient's condition stabilizes.
- Use appropriate monitoring equipment (e.g., pulse oximeter, cardiac monitor) to facilitate assessment.

Figure 2. Managing Hypersensitivity Reactions to Immune Globulin IV (IGIV) Infusion

Note. From "Transfusion Therapy: Nursing Implications," by T.M. Labovich, 1997, *Clinical Journal of Oncology Nursing, 1,* p.70. Copyright 1997 by the Oncology Nursing Society. Adapted with permission.

Administration

As for chemotherapy, in most circumstances two nurses validate IGIV infusion doses, checking independently to ensure accurate calculation of dose and infusion rate. If a single infusion calls for multiple vials of IGIV products, a nurse should use vials with the same lot numbers and document the lot numbers. Whenever possible, IGIV infusions should be scheduled when other nursing responsibilities do not require immediate or repeated attention and—for initial infusions or high-risk patients—at times when a physician will be directly available if needed.

IGIV products can be administered through peripheral venous access started by a nurse or through a central venous access device, such as an implanted port or catheter (tunneled or nontunneled). If a lyophilized IGIV product is used, a nurse should reconstitute it in 0.9% saline, 5% dextrose in water, or sterile water, depending on the product. The prescribing information for each IGIV product specifies the initial rate for the infusion and increments for titration. Nurses should not inject any other medications into the IGIV infusion line because precipitation or inactivation may occur. Typically, nurses monitor patients' vital signs and infusion flow rate at 15- to 30-minute intervals during the first hour and then with each rate titration or at least hourly throughout the remaining course of infusion.

IGIV dose and rate of infusion vary with the condition being treated, the product in use, and patients' weight and toleration of the infusion. Volume load is a particular concern for infants and young children because of their relatively lower renal clearance and for adults at risk for renal dysfunction or heart failure. Regular monitoring of patients' fluid intake and output or central venous pressure can help prevent fluid overload, as well as using an IGIV solution of greater concentration to reduce total infusion volume.

IGIV infusion typically lasts two to four hours and is determined by the infusion rate and patients' tolerance of any adverse effects. Saving one hour of infusion time could be perceived by patients to be an important advantage and may be achieved more easily with second or third courses of IGIV therapy for patients who already have tolerated earlier courses, especially if products from the same lot numbers, indicative of a common donor pool, are used. This reinforces the value of documenting the lot numbers of IGIV products. A recent, randomized study of eight patients with ITP found that administering IGIV therapy at a rate of 0.14 ml/kg per minute instead of 0.08 ml/kg per minute, as recommended by the manufacturer, could save approximately 48 minutes of infusion time, with greater convenience for caregivers and patients (Bussel, Hanna, & the IGIV Study Group, 2004).

Nurses should discard partly used vials of IGIV products and should not freeze IGIV solution. Avoidance of waste in the administration of IGIV is, however, an important economic consideration. Therefore, nurses should use the smallest package size of a product that will meet the immediate needs for a particular patient and infusion.

Adverse Events

IGIV products vary with regard to incidence and types of adverse events (see Table 5). The incidence of adverse events also increases with higher doses of IGIV products. Severe adverse reactions to IGIV therapy during infusion occur in fewer than 10% of patients and often are self-limiting (Dalakas, 1999; Swenson, 2000). Other adverse events, including headache, fever, chills, chest tightness, dyspnea, back pain, and a reaction at the infusion site, may be more common (Dalakas; Swenson). Nurses should record all adverse events accompanying IGIV therapy, whatever their nature, in patients' charts.

Serious adverse events associated with IGIV therapy include aseptic meningitis, renal failure, thromboembolic events, and anaphylaxis. Aseptic meningitis syndrome may occur within a few hours to two days following the initiation of IGIV therapy (Bussel, Eldor, et al., 2004; Dalakas, 1999; Kazatchkine & Kaveri, 2001; Pierce & Jain, 2003; Swenson, 2000); is marked by severe headache, neck stiffness, fever, drowsiness, photophobia, pain with ocular movement, nausea, and vomiting; and may occur more often with the relatively high IGIV dose of 2 g/kg or with rapid infusion. With cessation of IGIV infusion, the condition usually resolves within several days (Miller et al., 2001; Swenson). Antimigraine medications, nonsteroidal anti-inflammatory agents, analgesics, and corticosteroids also may be helpful for symptom management. Changing the infusion rate, extending the infusion period, or using an alternative IGIV product may help prevent recurrences. However, despite these measures, recurrences of aseptic meningitis have been reported (Pierce & Jain).

Anaphylaxis typically occurs within 30–60 minutes after the beginning of an IGIV infusion and, in some cases, has been attributed to a reaction of anti-IgA antibodies in recipients' serum with the small amounts of IgA contained in IGIV preparations (Dalakas, 1999; Miller et al., 2001; Swenson, 2000). Anaphylaxis has been reported in hypogammaglobulinemic patients with IgA deficiency and anti-IgA antibodies (Miller et al.; Swenson). The risk of anaphylaxis may be reduced by

assessing a prospective IGIV recipient's anti-IgA antibody level before beginning therapy and using an IGIV preparation with a low level of IgA (Dalakas). However, the National Institutes of Health Consensus Development Conference statement on IGIV therapy did not recommend screening for anti-IgA antibodies before initiating IGIV therapy because such reactions are rare ("NIH Consensus Conference," 1990). An informal survey at a symposium during the 2005 annual meeting of the Oncology Nursing Society indicated that 42% of nurses consider the risk of hypersensitivity reactions to be the most challenging nursing concern associated with IGIV administration (Shelton, 2005). A "tickle" in the throat accompanied by a cough or a lump in

Table 5. Management of Adverse Events With IGIV Therapy

Common, Nonserious Adverse Event	Management	Prevention
Pyrogenic reactions • Fever • Shaking	Stop infusion; administer methylprednisolone, diphenhydramine, and a sufficient dose of IV narcotic analgesics. Once reactions are controlled, the infusion may be continued.	Pretreat prior to subsequent infusions or use a different IGIV product, but the first few infusions should be administered slowly and patients should be monitored carefully.
Minor systemic reactions • Headache, dizziness, lightheadedness • Chills • Nausea, vomiting • Generalized myalgia • Intense back or hip pain and leg pain	Stop infusion; after reactions subside (usually within 30 minutes), restart infusion at half the previous rate, then gradually increase to the recommended rate.	Premedicate with acetaminophen or diphenhydramine about one hour prior to the infusion; add hydrocortisone via IV (1–2 mg/kg 30 minutes prior to infusion) to the premedication regimen if patients continue to have reactions. For longer infusions, remedicate four hours into the infusion.
Vasomotor symptoms with or without additional cardiac manifestations • Hypotension • Hypertension • Flushing • Tachycardia	Stop infusion and monitor patient closely; after reactions subside, restart infusion at half the previous rate, then gradually increase to the recommended rate.	–
Postinfusion reactions • Headache • Low-grade fever • Nausea • Arthralgias • Generalized malaise • Flu-like symptoms	Manage with over-the-counter analgesics, antihistamines, and low-dose systemic steroids.	–
Serious Adverse Event	**Management**	**Prevention**
Aseptic meningitis Symptoms include • Severe headache • Neck stiffness • Fever • Drowsiness • Photophobia • Pain with ocular movement • Nausea and vomiting.	Usually resolves within several days of stopping infusion; antimigraine medications, nonsteroidal anti-inflammatory agents, analgesics, and corticosteroids may ease symptoms.	Change infusion rate, extend infusion period, or use an alternative IGIV product.
Renal adverse events Risk factors include • Preexisting renal insufficiency • Diabetes mellitus • Age older than 65 years • Volume depletion • Sepsis • Paraproteinemia • Concomitant nephrotoxic drugs.	Dilute IGIV solution (if lyophilized product is being used), reduce infusion rate, and avoid sucrose-containing products.	Pretreatment renal function assessment and repeated evaluation of renal function during IGIV infusion
Thromboembolic events Risk factors include • History of atherosclerosis • Multiple cardiovascular risk factors • Advanced age • Impaired cardiac output • Known or suspected hyperviscosity (cryoglobulins, fasting chylomicronemia or markedly high triglycerides, or monoclonal gammopathies).	Reduce infusion rate; use IGIV products of lower concentration (low sodium or osmolarity).	Baseline assessment of blood viscosity
Anaphylactic reactions (see Figure 2)	–	–

IGIV—Immune globulin IV

the throat may indicate laryngospasm preceding bronchoconstriction with chest tightness and wheezing. These symptoms of anaphylaxis require immediate cessation of the infusion and administration of antihistamines, corticosteroids, and epinephrine until the symptom resolves.

IGIV-associated renal dysfunction has been reported in the literature (Dalakas, 1999; Pierce & Jain, 2003), sometimes has required dialysis (Centers for Disease Control and Prevention, 1999; Dalakas; Pierce & Jain), and occasionally has been associated with mortality (Centers for Disease Control and Prevention; Davis et al., 2003; Swenson, 2000). ATN can occur in patients with volume depletion, especially those who are older or have a history of poor hydration or diabetes (Dalakas). Also at increased risk for ATN are patients who have sepsis or paraproteinemia and patients who are taking nephrotoxic drugs concomitantly. ATN usually is marked by an increase in the serum creatinine level occurring 1–10 days after the beginning of IGIV therapy and has been associated with use of IGIV products containing high sucrose concentrations (Centers for Disease Control and Prevention; Davis et al.; Swenson). Pretreatment assessment of patients' renal function (with BUN and serum creatinine levels) and repeated evaluation of renal function during IGIV treatment are important for preventing IGIV-associated renal dysfunction (Centers for Disease Control and Prevention; Pierce & Jain). Dilution of the IGIV infusion solution (if a lyophilized product is being used), reduction of the infusion rate, and avoidance of sucrose-containing products may reduce the risk of renal dysfunction (Centers for Disease Control and Prevention; Dalakas; Pierce & Jain).

Thromboembolic events, including deep vein thrombosis, pulmonary embolism, stroke, transfusion-related acute lung injury, and myocardial infarction, also have been reported with IGIV therapy (Caress, Cartwright, Donofrio, & Peacock, 2003; Dalakas & Clark, 2003; Go & Call, 2000; Gottlieb, 2002; Katz et al., 2003). A number of factors have been implicated collectively in IGIV-induced thromboembolic events. Most IGIV products contain factor XI, a prothrombotic factor (Go & Call). In addition, all IGIV products increase plasma viscosity when administered. A faster infusion rate and product-specific factors, such as sodium content and osmolality, also likely play a role. Patients at risk for thromboembolic events may include those with a history of atherosclerosis, multiple cardiovascular risk factors (e.g., hypertension, hyperlipidemia, obesity, diabetes), advanced age, impaired cardiac output, known or suspected hyperviscosity, and hypovolemia (Dalakas & Clark). Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia or markedly high triglycerides, or monoclonal gammopathies.

Minor systemic adverse events are common to all IGIV products. Headache, dizziness, or lightheadedness occurring during infusion usually is caused by a rapid infusion rate. Temporarily discontinuing the infusion and then slowing the infusion rate usually diminish the symptoms (Bussel, Eldor, et al., 2004; Miller et al., 2001; Pierce & Jain, 2003). Patients who continue to have reactions despite decreased rate and volume of an infusion may be given premedication with acetaminophen and diphenhydramine or hydrocortisone. Flu-like symptoms sometimes occur several hours or days after IGIV therapy and can be managed with nonsteroidal anti-inflammatory agents, although caution should be used in patients with low platelet counts because of a risk of bleeding (Schleis, 2000). Antihistamines and low-dose systemic steroids also may be used. Blood pressure either can increase or decrease with IGIV infusion, and changes may be accompanied by flushing or tachycardia. Patients experiencing such reactions may report shortness of breath or tightness in the chest. Again, reducing the rate of infusion may diminish these adverse events (Schleis). Diarrhea accompanying IGIV infusion may be managed with a parasympatholytic antidiarrheal agent (e.g., atropine sulfate–diphenoxylate hydrochloride). Dermatologic effects of IGIV therapy are rare but can include eczema, erythema, urticaria, and a maculopapular rash.

Immune Globulin IV Product Pathogenic Contamination Risk

In 1994, an outbreak of hepatitis C was traced to a commercial IGIV preparation. The preparation was temporarily withdrawn from the market and reintroduced after the implementation of newer antiviral production methods (Bussel, Eldor, et al., 2004; Miller et al., 2001). Antiviral production processes also have been included in the manufacturing of other IGIV products, and no episode of IGIV-related viral or other pathogenic infection has been reported since (Dalakas, 1999; Miller et al.; Swenson, 2000). Even so, the FDA requires that labels of plasma-derived products warn users of the potential risk of pathogenic infection (Miller et al.).

Although it has never been associated with IGIV therapy, Creutzfeldt-Jakob disease, a fatal encephalopathy thought to be caused by protein particles known as prions, has been the subject of an FDA "guidance" advisory applying to all plasma- and other animal-derived therapeutic products (Miller et al., 2001; Pierce & Jain, 2003).

Case Studies of Nursing Care in Immune Globulin IV Therapy

Two case studies illustrate nurses' important role in administering IGIV therapy.

Case 1

A 34-year-old man with acute myelogenous leukemia who had tested negative for cytomegalovirus (CMV) received HSCT from a human leukocyte antigen–matched sibling who was CMV-positive. In accordance with clinical guidelines, the patient received ganciclovir and foscarnet for CMV prophylaxis. The patient became antigen-positive for CMV on day 24 post-HSCT and subsequently developed respiratory symptoms. The patient's dosage of ganciclovir was increased on day 37. By day 39, he developed respiratory distress syndrome, requiring oxygen by face mask, and bronchoalveolar culture was positive for CMV antigen. Also at that time, his serum aspartate aminotransferase level increased dramatically. Therapy with IGIV at 500 mg/kg weekly was begun to treat the documented CMV infection.

Because the patient already had a central venous catheter in place, he did not require peripheral venous catheterization for IGIV therapy. His weight, fluid intake and output, vital signs, and central venous pressure were recorded, and he received electrolytes and plasma several hours before IGIV infusion to avoid any risk of product interaction or difficulty determining the etiology of a reaction. To minimize the risk of headache, the patient's room was darkened and he was given hard candy

to counteract the sensation of a metallic taste that sometimes accompanies IGIV therapy.

IGIV infusion was begun at a rate of 30 ml per hour; the infusion rate was increased after 30 minutes to 45 ml per hour, and after another 30 minutes to 60 ml per hour. However, the patient soon complained of a severe frontal headache and a sensation of "jitteriness," and he appeared flushed. The infusion was stopped for 20 minutes, and his symptoms eased. The infusion was resumed, but toward the end of the three-hour infusion period, the patient developed dyspnea and respiratory examination revealed anterior chest "crackles." Believing the patient was experiencing volume overload, the physician ordered and the nurse administered 20 mg of furosemide via IV, but the patient did not void. When a second, 40 mg dose of furosemide also failed to prompt voiding, the dose was increased to 80 mg. The patient excreted 1,200 ml of urine, and his respiratory symptoms improved. The IGIV infusion was completed without further incident. Subsequent IGIV infusions during the following three weeks were administered with furosemide and planned fluid restrictions. The patient tolerated the infusions well and did not develop additional respiratory symptoms.

After a prolonged course of respiratory and hepatic compromise, the patient's condition was stabilized, and he was discharged. Although CMV antigenemia resolved within two months, he continued to have chronic restrictive pulmonary disease. He has had no further acute exacerbation of CMV infection.

Case 2

A 44-year-old man presented with CD20-positive follicular lymphoma of recent onset. He had experienced a viral infection four years earlier and developed persistent lymphadenopathy, followed by chronic idiopathic ITP. Serologic testing showed no antibodies to Epstein-Barr virus or HIV. Following a short period of observation, the patient was treated with IGIV therapy at 400 mg/kg in courses of five days each after his platelet count fell below 5,000/µl. During the previous year, the frequency of his IGIV infusions had been increased from once every three months to once every two months and, most recently, monthly. During the previous year, he had experienced an episode of candidal infection and intermittent bouts of infection with *clostridium difficile*.

The patient was admitted to the oncology unit. Physical and laboratory findings included temperature, 38.6°C; heart rate, 124 beats per minute; respiratory rate, 32 breaths per minute; blood pressure, 100/42 mmHg; arterial oxygen saturation, 90% on room air; and platelet count, 12,000/µl. The patient also had dermal bruising, bleeding gums, abdominal distension with an enlarged liver presenting as a palpable mass in the right upper quadrant, muscle cramping, bilateral adenopathy in the groin, and an occasional irregular pulse. His renal function was borderline normal, with a creatinine clearance of 52 ml per minute, a serum lactate dehydrogenase level of 878 IU/l, and a rising serum uric acid level.

The dilemma for the patient's physician was determining which condition merited treatment priority: lymphoma or ITP. Because of the patient's infection history, a peripheral line was preferred over a central venous catheter. Ultimately, chemotherapy for lymphoma was given priority over IGIV therapy for ITP. The chemotherapy regimen included corticosteroids, which caused considerable short-term hyperglycemia. Clinicians decided to replace the IGIV product the patient had been receiving with another product that was less likely to cause renal toxicity or exacerbate hyperglycemia and that also could be administered via the established peripheral venous access.

IGIV therapy was begun two days after administration of chemotherapy. The patient developed nausea and vomited during the first hour of infusion. The infusion was stopped, and he was given a serotonin antagonist, which eased nausea and emesis. The patient experienced an episode of paroxysmal supraventricular tachycardia toward the end of the first day of treatment that was identified as atrial fibrillation. Coincident with the IGIV infusion, he also appeared to develop tumor lysis syndrome, as reflected by an increase in serum levels of potassium (6.0 mEq/l), phosphorus (8.1 mg/dl), and creatinine.

The patient ultimately required continuous renal replacement therapy, which was interrupted during IGIV infusions. Continuous renal replacement therapy with temporary discontinuation for IGIV therapy provides 24-hour blood filtration and yields greater clinical stability in cases of tumor lysis syndrome. The patient's platelet count stabilized without further need for IGIV therapy. Hyperglycemia resulting from physiologic stress and corticosteroid administration was managed with a short course of continuous insulin therapy, and his lymphoma went into short-term remission, a pattern often observed with lymphoproliferative disease following an autoimmune process.

Summary

In more than two decades of use, IGIV therapy has proven its value in the management of PID, ITP, CLL, and various other conditions. Selection of an appropriate IGIV product should take into consideration specific patient characteristics, such as a history of cardiovascular or renal disease or diabetes. Nurses have an essential role in the safe and efficient use of IGIV, from educating patients about the rationale for and effects of therapy to administering the product and monitoring for adverse effects.

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References

Brown, P. (2003). Raising nurses' awareness of primary immune deficiency. *Nursing New Zealand, 9,* 26–27.

Bussel, J.B., Eldor, A., Kelton, J.G., Varon, D., Brenner, B., Gillis, S., et al. (2004). IGIV-C, a novel intravenous immunoglobulin: Evaluation of safety, efficacy, mechanisms of action, and impact on quality of life. *Thrombosis and Haemostasis, 91,* 771–778.

Bussel, J.B., Hanna, K., & the IGIV Study Group. (2004). Intravenous immunoglobulin manufactured using a novel caprylate and chromatography-based method (IGIV-C, Gamunex®) was safe and well tolerated when administered at an increased maximum rate in patients with idiopathic thrombocytopenic purpura (ITP). *Blood, 104,* a632.

Caress, J.B., Cartwright, M.S., Donofrio, P.D., & Peacock, J.E., Jr. (2003). The clinical features of 16 cases of stroke associated with administration of IVIg. *Neurology, 60,* 1822–1824.

Centers for Disease Control and Prevention. (1999, June). Renal insufficiency and failure associated with immune globulin intravenous

therapy—United States, 1985–1998. *MMWR: Morbidity and Mortality Weekly Report, 48,* 518–521.

Dalakas, M.C. (1999). Intravenous immunoglobulin in the treatment of autoimmune neuromuscular diseases: Present status and practical therapeutic guidelines. *Muscle and Nerve, 22,* 1479–1497.

Dalakas, M.C., & Clark, W.M. (2003). Strokes, thromboembolic events, and IVIg: Rare incidents blemish an excellent safety record. *Neurology, 60,* 1736–1737.

Davis, J., Duff, K., Ganio, S., Garrow-Harris, L., Gomez, J., MacPherson, P., et al. (2003, March). *Criteria for selecting an IGIV preparation: The infusion nurse's perspective.* Paper presented at the 60th annual meeting of the American Academy of Allergy, Asthma, and Immunology, Denver, CO.

Gelfand, E.W. (2000). The clinical use of intravenous immunoglobulin in immunodeficiency and allergic disorders. *Journal of Intravenous Nursing, 23*(5, Suppl.), S14–S17.

Go, R.S., & Call, T.G. (2000). Deep venous thrombosis of the arm after intravenous immunoglobulin infusion: Case report and literature review of intravenous immunoglobulin-related thrombotic complications. *Mayo Clinic Proceedings, 75,* 83–85.

Gottlieb, S. (2002). Intravenous immunoglobulin increases risk of thrombotic events. *BMJ, 324,* 1056.

Griffin, J.M. (2005, April). *Defining IGIV therapy: Clinical usage.* Paper presented at IGIV Therapy: Optimizing Care of Patients in the Oncology Setting, Orlando, FL.

Grillo, J.A., Gorson, K.C., Ropper, A.H., Lewis, J., & Weinstein, R. (2001). Rapid infusion of intravenous immune globulin in patients with neuromuscular disorders. *Neurology, 57,* 1699–1701.

Hall, P.D. (1993). Immunomodulation with intravenous immunoglobulin. *Pharmacotherapy, 13,* 564–573.

Katz, K.A., Hivnor, C.M., Geist, D.E., Shapiro, M., Ming, M.E., & Werth, V.P. (2003). Stroke and deep venous thrombosis complicating intravenous immunoglobulin infusions. *Archives of Dermatology, 139,* 991–993.

Kazatchkine, M.D., & Kaveri, S.V. (2001). Immunomodulation of autoimmune and inflammatory diseases with intravenous immune globulin. *New England Journal of Medicine, 345,* 747–755.

Labovich, T.M. (1997). Transfusion therapy: Nursing implications. *Clinical Journal of Oncology Nursing, 1,* 61–72.

Lemm, G. (2002). Composition and properties of IVIg preparations that affect tolerability and therapeutic efficacy. *Neurology, 59*(12, Suppl. 6), S28–S32.

Miller, J.L., Petteway, S.R., Jr., & Lee, D.C. (2001). Ensuring the pathogen safety of intravenous immunoglobulin and other human plasma-derived therapeutic proteins. *Journal of Allergy and Clinical Immunology, 108*(4, Suppl.), S91–S94.

NIH consensus conference. Intravenous immunoglobulin: Prevention and treatment of disease. (1990). *JAMA, 264,* 3189–3193.

Pierce, L.R., & Jain, N. (2003). Risks associated with the use of intravenous immunoglobulin. *Transfusion Medicine Reviews, 17,* 241–251.

Ratko, T.A., Burnett, D.A., Foulke, G.E., Matuszewski, K.A., & Sacher, R.A. (1995). Recommendations for off-label use of intravenously administered immunoglobulin preparations. University Hospital Consortium Expert Panel for Off-Label Use of Polyvalent Intravenously Administered Immunoglobulin Preparations. *JAMA, 273,* 1865–1870.

Schleis, T.G. (2000). The financial, operational and clinical management of intravenous immunoglobulin administration. *Journal of Intravenous Nursing, 23*(5, Suppl.), S23–S31.

Shelton, B.K. (2005, April). *Focus on use of IGIV therapy in the oncology setting.* Paper presented at IGIV Therapy: Optimizing Care of Patients in the Oncology Setting, Orlando, FL.

Siegel, J. (2006, January). Immune globulins: Therapeutic, pharmaceutical, and cost considerations. *Pharmacy Practice News,* 19–23.

Swenson, M.R. (2000). Autoimmunity and immunotherapy. *Journal of Intravenous Nursing, 23*(5, Suppl.), S8–S13.

U.S. Food and Drug Administration. (2005). Important safety information on interference with blood glucose measurement following use of parenteral maltose/parenteral galactose/oral xylose-containing products. Retrieved June 26, 2006, from http://www.primaryimmune.org/pubs/ImportantSafetyAlert-MaltoseGalactoseOralXylose.pdf

Wright, J.E., & Shelton, B.K. (1993). The hematologic and immune systems. In *Desk reference for critical care nursing* (pp. 1073–1247). Sudbury, MA: Jones and Bartlett.