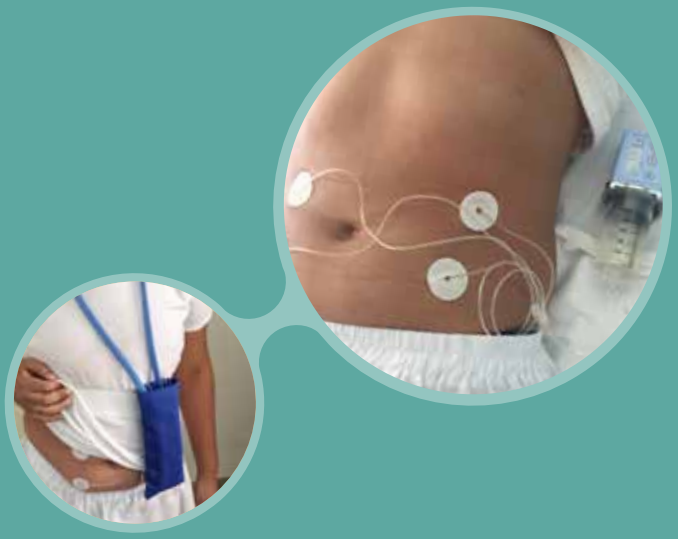

IDF Guide for Nurses

Immunoglobulin Therapy for Primary Immunodeficiency Diseases

Immune Deficiency Foundation

مؤسسة حمد الطبية
Hamad Medical Corporation
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IDF GUIDE FOR NURSES

Immunoglobulin Therapy for Primary Immunodeficiency Diseases

THIRD EDITION

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Thank you for taking a copy of IDF Guide for Nurses, Immunoglobulin Therapy for Primary Immunodeficiency Diseases. This booklet is a part of the Allergy and Immunology Awareness Program at Hamad Medical Corporation. It is intended to provide information to the nursing staff and the families of patients about the Immunoglobulin replacement therapy, which is replacing the deficient antibodies in the patient by giving them either intravenously or subcutaneously.

Since this therapy has been proven to be an effective treatment, we have been keen to translate this booklet and our goal is to guide the nurses and families to the appropriate way of giving it, possible risks and how to avoid and treat them.

We hope this booklet is sufficient to serve the intended purpose. If you have any questions or suggestions please don't hesitate to contact us. We would appreciate your valuable feedback in this regard.

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About the Immune Deficiency Foundation

Immune Deficiency Foundation

The Immune Deficiency Foundation (IDF) is the national nonprofit patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research. IDF was founded in 1980 by parents of children with primary immunodeficiencies and their physicians. At that time, there were few treatments available for primary immunodeficiency diseases, almost no educational materials for patients, no public advocacy initiatives, and little research being done. In the past thirty years, IDF has pursued an aggressive agenda to remediate these problems and has made tremendous strides in the following areas:

- Helping the patient and professional communities gain a broader understanding of primary immunodeficiency diseases through comprehensive education and outreach efforts;
- Promoting, participating in, funding, and supporting research that has helped characterize primary immunodeficiency diseases and given healthcare providers substantially improved treatment options for the care of patients with primary immunodeficiency diseases;
- Addressing patient needs through public policy programs on local, national and international levels by focusing on issues such as insurance reimbursement, patient confidentiality, SCID newborn screening, preventing genetic discrimination, ensuring the safety and availability of immunoglobulin therapy, and maintaining and enhancing patient access to a full range of treatment options;
- Establishing supportive networks of patients and professionals to ensure that the needs of patients with primary immunodeficiency diseases are recognized and addressed.

Primary immunodeficiency diseases represent a group of more than 150 rare disorders. In the United States, approximately 250,000 people are diagnosed with primary immunodeficiency diseases. Thousands more go undetected.

These individuals live throughout the country and experience a number of problems which have been documented by IDF. These patient problems include:

- Difficulty in finding specialized healthcare by immunologists or care providers knowledgeable about immunodeficiency
- An inordinate delay in reaching proper diagnoses
- Problems with availability of appropriate treatment
- Difficulties financing healthcare and treatment
- Finding instructional materials about the specific diseases
- Educating the community and those with whom they come in contact about their disease and particular needs
- Lack of peer support and connection to others with whom they can share experiences

The goal of IDF is to address these issues and help affected individuals to overcome these difficulties, thereby enabling them to live healthy and productive lives.

IDF Nurse Advisory Committee

A Resource for Nurses and Patients

The Immune Deficiency Foundation established the Nurse Advisory Committee in 1999. The committee is comprised of nurse experts who have many years of managing and providing care for patients with primary immunodeficiency diseases. The goal of the committee is, first and foremost, to improve the quality of healthcare received by patients with primary immunodeficiency diseases. This goal is primarily achieved by educating and providing resources for patients' caregivers. The Nurse Advisory Committee also increases awareness of primary immunodeficiency diseases through professional education and outreach on local, national and international levels. The Committee is instrumental in increasing educational and peer support opportunities for individuals and families affected by primary immunodeficiency diseases.

The Nurse Advisory Committee is available as a resource for nurses providing therapy for or treating patients with primary immunodeficiency diseases. The committee is also available for patients requiring assistance. Members can be reached by contacting IDF at 800 296 4433 or idf@primaryimmune.org.

Immunoglobulin replacement therapy is indicated for a significant number of patients with primary immunodeficiency diseases.

The IDF Nurse Advisory Committee is proud to offer this guide to help nurses to administer this therapy, safely and effectively. By doing so, nurses are in a unique position to improve the treatment experiences and provide a better quality of life for patients living with primary immunodeficiency diseases.

Introduction To Primary Immunodeficiency Diseases

The World Health Organization recognizes more than 150 primary immunodeficiency diseases – some are relatively common, others are quite rare. Some affect a single cell within the immune system; others may concern one or more components of the system. These diseases are classified according to the part of the immune system involved, either the adaptive or innate immune system. Immunodeficiencies involving adaptive immune responses are characterized by impaired antibody production or function. Problems with innate immunity are those which involve natural killer lymphocytes, neutrophils, monocytes, macrophages, or the complement system.

Regardless of whether the problem is with the adaptive or innate system, patients affected with primary immunodeficiency are at risk for infection with virtually any pathogen. Even organisms which are not pathogenic in immunocompetent hosts can be pathogenic for people with immunodeficiencies. These infections can be unusually severe or recurrent and they can sometimes be difficult to treat with conventional therapy. For the most part, primary immunodeficiencies are rare and, because of this, may go unrecognized. Often patients experience many years of recurrent infections before they are appropriately diagnosed.

Some primary immunodeficiencies are caused by a problem with a single gene, whilst others are caused by defects in multiple genes. There can be a clear inheritance pattern, such as with those immunodeficiencies that are x-linked diseases; for other diseases the inheritance pattern is less clear. It is believed that some primary immunodeficiencies develop over time and may be the result of a combination of genetic and environmental factors. Therefore, primary immunodeficiencies may present and be diagnosed at any age. Similarly, there can be tremendous phenotypic and immunologic variability among individuals with the same diagnosis.

Many patients with primary immunodeficiencies have significant co-morbidities. Some of these co-morbidities may be related to the immunodeficiency itself. For example, a

patient with recurrent pneumonias may have irreversible lung damage (bronchiectasis) because of the infections. It is also known that patients with primary immunodeficiency diseases may have a predisposition to autoimmune diseases including problems such as; autoimmune cytopenias, inflammatory bowel disease, or rheumatoid arthritis. Sometimes the immunodeficiency is diagnosed after a presentation of autoimmune disease. Some immunodeficient patients may also have a greater risk for lymphoreticular cancers, such as lymphocytic leukemia, multiple myeloma or lymphoma, compared to the risk of the general population.

Patients with antibody disorders are the largest group of people with primary immunodeficiencies. These include patients with selective IgA deficiency, by far the most common primary immunodeficiency disease; patients with hypogammaglobulinemia and impaired antibody responses; and patients with combined B and T cell problems. For some of these diagnoses, but not all, immunoglobulin replacement therapy is the standard care. This therapy provides antibodies from thousands of plasma donors to those who do not have and/or cannot make protective levels of antibody.

Clinical Uses for Immunoglobulin Replacement Therapy

Concentrated human immune globulin preparations first became widely available during World War II and were used for prophylaxis against infectious diseases such as hepatitis, measles and polio. The use of immunoglobulin as replacement therapy for primary immunodeficiency was described by Dr. Ogden Bruton in 1952. Dr. Bruton treated a boy diagnosed with X-linked agammaglobulinemia with subcutaneous injections of immunoglobulin from immunocompetent human plasma donors.

Initially, immunoglobulin was given predominantly by intramuscular injections. These injections were painful, and the maximum doses that could be given were limited because of the volumes involved. In the early 1980s, preparations that could be safely given by the intravenous route were first licensed in the U.S. Intravenous immunoglobulin replacement therapy or IVIG, also referred to as IGIV, was generally well tolerated by most patients and became the standard care for treatment of patients with primary immunodeficiencies with antibody deficiencies. Larger doses of immunoglobulin could be given via this route, more closely mimicking the body's own production of antibodies. Better infection prophylaxis was achieved, resulting in significant improvements in the patients' conditions and outcomes.

In 2006, the first commercial preparations for subcutaneous immunoglobulin replacement therapy (SCIG) were approved by the United States Food and Drug Administration (FDA). These preparations, given in smaller doses and more frequently than IVIG provide very stable, consistent levels of IgG as opposed to the peaks and troughs associated with the intravenous route.

For some patients, this is an important consideration.
All immunoglobulin preparations currently available in the U.S. are manufactured using donor pools from 10,000 to 60,000 units of donated human plasma. They contain IgG antibodies against a broad spectrum of vaccine antigens and infectious agents. All preparations contain ≥ 96% IgG. Most also contain some IgA and trace amounts of other plasma proteins. There are differences in the manufacturing processes and in the stabilizing agents used for each manufacturer's products.

Immunoglobulin (Ig) therapy is indicated as replacement therapy for primary and secondary immunodeficiencies for patients who do not make sufficient amounts of specific antibodies to adequately protect themselves from infectious diseases, those whose antibodies do not function correctly, and those with poor immunologic memory.

Two examples of primary immunodeficiency conditions requiring replacement therapy are agammaglobulinemia (either x-linked or autosomal) and common variable immunodeficiency (CVID). Examples of secondary immunodeficiencies include hypogammaglobulinemia, caused by chemotherapy, monoclonal antibody therapy, and immunosuppressive therapies.

In addition to antibody replacement, immunoglobulin also has anti-inflammatory and/or immunomodulatory effects. As such, it is sometimes used to treat patients with a variety of conditions other than primary immunodeficiency diseases. Immunoglobulin therapy has been demonstrated to be efficacious in the treatment of such diseases as idiopathic thrombocytopenia purpura (ITP), Kawasaki disease and some neuromuscular diseases. However, some of these other uses are experimental and/or "off-label", which means that the FDA has not approved the use of immunoglobulin for those particular conditions.

Table 1: FDA Approved Uses of Immunoglobulin (Ig)

Clinical Condition	Clinical Case
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	Improve neurological symptoms
Primary Humoral Immunodeficiency	Antibody replacement therapy
Kawasaki Disease	Prevent coronary artery aneurysms
Idiopathic Thrombocytopenia Purpura (ITP)	Increase platelets counts to prevent and control bleeding
B-cell Chronic Lymphocytic Leukemia	Prevent recurrent bacterial infections

Table 2: Immunodeficiencies that ALWAYS Require Ig Replacement Therapy

Agammaglobulinemia (X-linked, autosomal, or acquired)
Common Variable Immunodeficiency
Hyper IgM Syndrome
Severe Combined Immunodeficiency (SCID) - before and sometimes after bone marrow transplant

Table 3: Immunodeficiencies that MAY Require Ig Replacement Therapy

Severe Cases of Transient Hypogammaglobulinemia of Infancy
Selective Antibody Disorder
Wiskott Aldrich Syndrome
DiGeorge (22q11 deletion) Syndrome
Ataxia Telangiectasia
Pediatric HIV

Product Selection and Characteristics

There are several different brands of immunoglobulin and hyperimmune products currently licensed for use in the United States. The U.S. Food and Drug Administration (FDA) has mandated that all immunoglobulin administered in the U.S. must be manufactured from plasma donated in the country. All manufacturing must be done in FDA approved facilities.

Immunoglobulin is a plasma product. Thousands of carefully screened and tested donors provide plasma for a single lot of product. It is produced via a multifaceted manufacturing process designed to remove and/or inactivate bacterial and viral pathogens. These processes vary from manufacturer to manufacturer but include steps such as cold alcohol fractionation, low pH incubation, nanofiltration, chromatography, and solvent/detergent treatment. While the immunoglobulin manufactured in the U.S. is a very safe product, the possibility of transmission of existing or emerging pathogens cannot be completely ruled out.

All immunoglobulin products are mostly IgG (> 96%). They also contain trace amounts of IgM and IgA. The remainder of the products is made up of stabilizing agents. Products vary in concentration, pH, stabilizing agents, osmolarity and osmolality, as well as sugar and sodium content. There is variability in administration factors as well, including the form of the drug (lyophilized or liquid), shelf life, approved means of administration (intravenous and/or subcutaneous) and prescribed infusion time. All of these factors need to be carefully considered when choosing a product for a particular patient. (See Table 4)

Table 4 : Examples of Factors to Consider in Choosing a Immunoglobulin Product

Potential Patient Risk Factors	Potential Immunoglobulin Risk Factors					
	Volume Load	Sugar Content	Sodium Content	Osmolality	Volume Load	Volume Load
Cardiac Impairment	■			■	■	
Renal Dysfunction	■	■	■			
Anti IgA Antibodies						■
Thromboembolic Risk	■		■	■		
(Pre) Diabetes		■				
Elderly Patients	■	■	■	■		
Infants/Children	■		■	■	■	

Preparations

Immunoglobulin products are supplied as liquids or lyophilized powders (freeze dried powder that requires reconstitution). Some liquids require refrigeration, whilst others are stored at room temperature. It is important to follow the manufacturer's specifications regarding storage. Any liquid which has been frozen should be discarded. Refrigerated products should be allowed to warm to room temperature before administration, as adverse effects can be associated with the administration of products that are too cold.

Lyophilized products can be stored at room temperature before reconstitution. It is possible for these products to be prepared at more than one concentration depending on the amount of diluent added. Possibilities for different concentrations are specified in the manufacturer's prescribing data. Nurses may be asked to reconstitute lyophilized products in the home or infusion clinic. It is critically important to be aware of and to follow manufacturer's guidelines, prescriber's orders and aseptic technique, when reconstituting these products.

Stabilizers

Stabilizers include different sugars and/or amino acids that are added to immunoglobulin products to stabilize the IgG molecules and prevent them from aggregating. These stabilizing agents may pose a risk for some patients. For example, products containing glucose should be used cautiously in patients with diabetes. Similarly, some sucrose containing lyophilized products have been implicated in causing or exacerbating renal disease.

IgA Levels

There are small amounts of IgA in all immunoglobulin products. If a patient has an absence of IgA they may have anti-IgA antibodies, then that patient could be at risk to anaphylaxis. Unfortunately, there is no commercial assay available for measuring IgE antibodies to anti-IgA. Fortunately, antibody deficient patients are rarely able to mount IgE responses, so this is not a widely prevalent problem. Patients with low or undetectable levels of IgA may be able to tolerate all immunoglobulin without problems;

however, these patients (particularly the CVID patients) should be carefully monitored. The first infusion should always be administered in a controlled setting where emergency treatment can be administered immediately should problems occur. If the infusion is tolerated, the patient is not likely to have subsequent problems with IgA containing products.

Product Integrity

All products should be carefully inspected before administration.The packaging should be inspected for tampering, as should the vials and their closures. Any evidence of tampering should be reported to the supplier and/or manufacturer and the product should not be used.

Reconstituted and liquid products should not be given if there is particulate matter, precipitate crystals, or fibers in it. Products that have been frozen should not be given. For the most part, immunoglobulin should be clear, although there can be a slight amount of cloudiness at times. The manufacturer's package insert will provide information about the range of color as this can vary from one product to another. If the nurse or patient has any doubts about the integrity of the product at all, it should not be administered.

Documentation

All IVIG infusions should be carefully documented.

Documentation should include:

- The patient's current health status and any changes in this status in the period between infusions
- The name and dose of the product, AND the lot numbers of the product used
- Any pre medications that were given
- How long it took for the infusion and specific rate titrations that were made
- Any problems the patient experienced during the infusion and what the response to these problems was
- How long the infusion took

Similar documentation is important for SCIG infusions. Documentation of SCIG infusions should also include patient teaching interventions and documentation of the patients' ability to administer their own infusions.

Delivery of Immunoglobulin Replacementtherapy

Nursing Responsibilities

Whether the nurse is administering an intravenous infusion or teaching patients to administer their own subcutaneous infusion, safety should always be the first priority. The prescriber's orders should be carefully followed and any problems with the orders should be addressed and resolved before the infusion.

Communication of potential issues and problems so that they can be proactively addressed is critical. The following are broad guidelines for nursing interventions prior, during, and after administration of immunoglobulin replacement therapy. These guidelines are offered to help infusion nurses minimize problems and adverse effects, and safely provide a successful infusion experience for the patient.

Key Pre-infusion Assessments

- Assess that the immunoglobulin product ordered is appropriate for the patient. Communicate potential problems to the prescriber. It is important to be aware of the differences between the various products available. As previously discussed, the qualities of a particular product may affect the tolerability and success of an infusion. Remember, not all immunoglobulin products are the same and consequently are NOT interchangeable. The first dose of any product should be administered in a controlled setting, where emergency equipment and treatment is readily available. The transition to home infusions can take place after it has been demonstrated that a particular product is tolerated. Should it be necessary to change products, the first infusion of the new product should, again, be in a controlled setting.
- Assess product integrity. If the protective seals are not intact, the dispensing pharmacy should be notified immediately and the product should not be given.
- Assess product temperature. The immunoglobulin should be at room temperature before the infusion. Solutions should be allowed to come to room temperature naturally. Product integrity may be compromised (denatured)

by freezing or heating. NEVER put the product into the microwave for warming.

- Assess the level of patient's understanding of therapy.
- Assess the patient's general health and hydration status. It is important to document and inform the prescriber of any new health problems that have arisen since the last infusion and/or any new medications the patient is taking as these may have an impact on prescribed therapy. If the patient is poorly hydrated, consideration should be given to the possibility of providing some hydration, either enterally or parenterally, before the infusion.
- Assess for any weight loss or gain. Immunoglobulin replacement therapy is prescribed based on weight. Any significant change (greater or less than 10%) may indicate a need for dosage increase or (less likely) reduction.
- Assess heart rate and respiratory status. Patients with congestive heart failure or who are at risk of fluid overload, especially, should be assessed carefully before beginning the infusion. Both the volume of fluid infused and the characteristics of the fluid (osmolality, sodium content) could exacerbate these problems. Patients should be reassessed frequently during the infusion to be sure that there is no change in respiratory status, which could indicate fluid overload. Diuretics may be prescribed before, during or after the infusion to prevent or relieve respiratory distress and/or complications associated with fluid overload in these patients.
- Assess for fever prior to the start of infusion. If fever is present, the prescriber should be notified directions for proceeding with or deferring the infusion. If the patient has an acute febrile illness or other indications of an infection are present, the infusion may need to be postponed until the patient is treated with antibiotics and/or the fever subsides. Administration of intravenous immunoglobulin when the patient has an acute infection may lead to adverse effects due to the formation of immune complexes.
- Assess the need for premedication. Although the patient should have communicated any adverse events associated with previous infusions to the prescriber, this may not have happened. It is important to establish that the patient tolerated his/her previous infusion without problems. If problems did occur, then the prescriber should be notified and asked if premedication should

be given. Premedications may be indicated to diminish the risk of infusion-related adverse events. Examples of premedications include systemic corticosteroids, antihistamines, antiemetics, acetaminophen and/or NSAIDs.

- Assess the need for localized anesthesia and obtain an order as necessary. Children, especially, may prefer to have topical anesthesia applied in advance of needle insertion to numb the sites at which needles or intravenous catheters will be placed.
- Assess preparedness for emergency situations. Emergency equipment should be readily available during the infusion. Emergency medications, including epinephrine, diphenhydramine and parenteral fluids, should be checked to ensure that they have not expired. The nurse should ensure that he/she is prepared to respond to an emergency and that orders are in place for this response. A phone, to call 911, should always be available. A protocol for communicating with the prescriber for both routine and emergency issues should be in place.
- Assess the need for laboratory blood work before the start of infusion. For patients receiving intravenous immunoglobulin, trough levels of IgG are an important monitoring tool. These levels need to be drawn immediately before beginning an infusion. The nurse should review the results of previous lab work with the patient and communicate with the prescriber to ensure that routine monitoring labs are done as ordered.
- Assess the patients experience with previous infusions. It is important for the nurse to listen to the patient and ensure that established routines are followed to avoid causing undue stress. Children, in particular, may have routines in place to assist them in dealing with both the physical and psychological impacts of infusions.

Key Intra-infusion Assessments

- Assess the patient to ensure that the infusion is being tolerated. The nurse should listen carefully to any complaints and be sensitive to any alterations in the patient's baseline status. Vital signs should be assessed as ordered and as indicated.

Key Post-infusion Assessments

- Assess for any problems occurring after the infusion which may be infusion related. These can include headaches, myalgias, fever, arthralgias, rashes or a subjective feeling of general "unwellness." If these problems are postulated to be infusion related, alterations to the infusion protocol may be necessary.
- Assess the need for premedications for future infusions and ensure that the premedications will be available for the next infusion.
- Assess the patient for his/her knowledge about the next infusion. It is important for the patient to know when the next infusion is due and what his/her responsibilities regarding this infusion are.

Routes of Administration

Immunoglobulin replacement therapy can be administered intravenously (IVIG) or subcutaneously (SCIG). There are multiple factors to consider when choosing the route of administration; careful consideration of these factors and their relationship to the individual patient is critical to ensuring success. The patient's wishes and whether these factors represent a "pro" or a "con" to the patient should be considered.

Factors and questions to consider include:

- Efficacy of Therapy: IVIG is usually given every three to four weeks. There is a peak in the level of IgG when the infusion is given and then the level declines to a trough before the next infusion, so there is a predictable rise and fall in levels. With SCIG infusions, the drug is slowly absorbed and is given more frequently, usually weekly. Once a steady state is reached, the level of IgG is remarkably consistent. This consistency of level may be important for patients with conditions such as protein losing enteropathies or for patients on IVIG who have frequent breakthrough infections.
- Time Factor: IVIG infusions generally require three to four hours a month in a single sitting. SCIG infusions require less time but are given weekly, at least.
- Adverse reactions: There is a greater risk for systemic reactions with IVIG; local reactions are more common

with SCIG. Patients who experience adverse reactions with IVIG and need premedication for their infusions may not experience these problems with SCIG.

- Cost of Therapy: In addition to the cost of drugs, there is an additional cost for nursing and/or overhead administration (infusion suite) with IVIG infusions. These costs are not uniform; the patient's insurance benefits and out-of-pocket costs need to be investigated.
- Patient Compliance: What is the patient's level of commitment? Will the patient do unsupervised home infusions of SCIG and follow up with appointments and lab work or is closer management/supervision required?
- Comorbidities: Does the patient have another illness which will be affected by therapy? For example, patients with cardiac disease may do better with the smaller amounts of fluid used in SCIG. Conversely, some patients may need a higher peak of IgG than can be achieved with SCIG and consequently IVIG may be a better choice for them.
- IV Access Issues: Is monthly IV access difficult? The American Academy of Allergy, Asthma and Immunology strongly discourages the use of permanent indwelling ports or central venous lines in antibody deficient patients due to the risk of infection and thrombotic events. If peripheral access is consistently difficult, SCIG may be a viable option.
- Availability of Nursing Resources: Home infusion nursing services are not always available in every area of the country and patients may not live close to infusion centers, making self-infusion a desirable alternative.

Intravenous Immunoglobulin Therapy

Intravenous immunoglobulin replacement therapy (IVIG) is generally given every three to four weeks at a dose of approximately 400-500 mg/kg/dose. It is well tolerated by the majority of patients, but it is important to note that, just as each patient may require a different immunoglobulin product, each may also require an individualized infusion regimen in order to achieve the desired therapeutic response. Once a successful regimen has been developed, it should be carefully followed with every infusion. This includes not only the rate of the infusion and necessary premedications, but the specific product, as well.

Administration

Different products vary in their compatibility with normal saline, sterile water or D5W, and manufacturer's guidelines should be followed carefully. Administration of concomitant medications through the same IV line should be avoided. Should medications be required prior to or during an infusion, it is recommended to flush the line with at least 5-10 ml of compatible fluid prior to administering the medication. Some medications will precipitate when in contact with IVIG, especially furosemide or diazepam. No medications should be directly administered into the same line simultaneously with the IVIG. If multiple medications are required, a second IV line should be placed so as not to interfere with the infusion. Another option is to piggyback the IVIG into the closest port in a line where a compatible fluid is already running. The compatible fluid can then be used as a flush if necessary.

Intra-infusion Assessments

- Assess the rate of infusion. Prescriber's orders and manufacturer's recommended rates of infusion should determine length of time for an infusion to take. Generally, a ramp-up procedure is used for IVIG rates of infusion. The infusion is started slowly and the rate increased incrementally approximately every 15 to 30 minutes, as tolerated, until the patient's maximum rate of infusion is reached. Although there is some literature reporting the tolerability of higher infusion rates, a general guideline to follow would be not to exceed the manufacturer's

recommended maximum rate. If a product change is necessary, the process for assessment of tolerability and potential rate increases must again be taken slowly.

- Assess the vital signs prior to each rate change to ensure that the infusion is being tolerated. Hyper or hypotension, increased heart rate, increased respiratory rate or effort, and fever could all be signs of problems. It is important to assess the clinical relevance of any alterations in vital signs. For example, if a comfortable patient falls asleep, his/her blood pressure, heart rate and respiratory rate may decrease and may not represent a pathologic concern. Similar findings in another patient may be signs of significant problems with the infusion.
- Assess the need for comfort measures during the infusion, particularly if side effects occur. Both pharmacologic and non-pharmacologic interventions (supplying blankets or pillows, heating pads and encouraging the use of relaxation techniques) may be indicated.
- Assess for signs of anaphylaxis. Although true IgE medicated anaphylaxis in antibody deficient patients is rare, if a patient has difficulty breathing, signs of tongue or throat swelling, a feeling that the throat is closing, stridor, wheezing and/or chest tightness, generalized urticaria, or extreme anxiety, the infusion should be stopped and immediate emergency treatment, including calling 911, should be initiated.

Adverse Reactions

Although most patients do well with IVIG, there is the potential for adverse reactions. It is estimated that 15-30% of patients experience some kind of reaction to their IVIG infusions. These reactions can range from mild to severe; however, most reactions occur during the initial 30 to 60 minutes of the infusion and are mild and self-limited. These reactions include anaphylactoid problems such as; headaches, chills and rigors; allergic reactions like urticaria and, potentially, anaphylaxis; and other problems such as aseptic meningitis. The most common problems are related to the rate of the infusion and the temperature of the product. Reactions are more frequent with patients who are therapy naïve, when therapy is given with a different product than the patient has previously been used to receiving, and/or in those who are not truly antibody deficient or those who have been

off of therapy for a period of time. It is important to note that most reactions occur during the initial 30 to 60 minutes of the infusion and are mild and self-limited. Regardless of the severity of a reaction, managing these problems requires timely interventions on the nurse's part. A nursing policy and orders must be in place for dealing with these issues.

There are risk factors that may identify persons at greater risk for having a reaction to IVIG. It is advisable to read the specific package insert for the IVIG product used, as the incidence and types of adverse events varies from product to product.

Types of Adverse Reactions

- Pyogenic Reactions: These reactions are marked by a significant rise in temperature and are usually accompanied by other systemic symptoms. Fever is the most common side effect in children. Management of acute pyogenic reactions includes the use of antipyretic medications such as acetaminophen or ibuprofen. Persons who repeatedly experience temperature elevations during administration of IVIG may benefit from premedication with an antipyretic/anti-inflammatory, such as acetaminophen, 30 to 60 minutes prior to initiation of the infusion.
- Allergic Reactions: True IgE mediated allergic reactions are rare in antibody deficient patients; however they can occur. In some cases, reactions to IVIG mimic those of true IgE mediated allergy but are actually due to activation of complement or other mediator systems by the IVIG. Allergic reactions can lead to acute anaphylaxis and shock. If these reactions occur, future use of IVIG is not precluded but, of course, must be closely monitored in a controlled environment (NOT in the patient's home). These reactions often begin with a generalized nonspecific feeling of unease. Patients may describe an uncomfortable feeling, such as a tightening around the neck, chest or abdomen. There may be difficulty swallowing, a choking sensation or difficulty breathing. Other symptoms may include wheezing, flushing, hives, rapid or weak pulse, hypotension, sweating or an upset stomach with or without nausea, vomiting or diarrhea.
- Vasomotor Symptoms: These can occur with or without additional cardiac manifestations. Blood pressure can

either increase or decrease, and may be accompanied by flushing or tachycardia. Patients experiencing such reactions may report shortness of breath or tightness in the chest.

- Anaphylactoid Reactions: These reactions most commonly include headache, dizziness or lightheadedness. Patients can also experience chills sometimes progressing to rigors, nausea and/or vomiting, back or hip pain, malaise, myalgias and arthralgias. Frequently the patient reports anxiety and in some cases "a sense of impending doom." The most frequent cause of these reactions is infusion at an excessively rapid rate or infusion of a drug which is colder than room temperature. Often, the patient will have elevated blood pressure rather than hypotension.

Table 5: Potential Nursing Interventions for Dealing with Adverse Reactions to IVIG

Reaction	Nursing Interventions
Chills/Rigors	• Stop infusion. • Administer prescribed medications. • When symptoms resolve, restart the infusion at the rate the patient was tolerating before the symptoms occurred
Headache	• Administer acetaminophen or NSAID as prescribed. • The patient's hydration status may affect the development of headaches; the patient should make sure he/she is adequately hydrated on the day of the infusion.
Migraine Headache *(patients with a history of and under treatment for headache problems)*	**Pharmacologic:** • Administer prescribed anti-migraine medications as soon as the first signs of a migraine occur. • Oral or IV steroids may help decrease the intensity of the headache and should be given if ordered. **Non-pharmacologic:** • Include comfort measures such as reducing auditory and visual stimuli, and applying cold compresses to the head or back of the neck.
Malaise/Flu-like Symptoms	• Resting after an infusion may help to minimize muscle aches or pain and to decrease excessive fatigue. • Acetaminophen or NSAIDS and ensuring adequate pre-infusion hydration may help with this problem.

Reaction	Nursing Interventions
Urticaria	• Stop the infusion. • Contact the prescriber. • Administer prescribed antihistamines and/or steroids. • Observe for signs of true anaphylaxis; if they occur administer epinephrine and activate the emergency response system (911).
Vasomotor Symptoms *(Hypotension, Hypertension, Flushing or Tachycardia)*	• Stop infusion. • Follow the prescriber's order for fluid bolus, diuretics or other interventions or administer fluid with hypotension, based on prescriber order. Administer diuretics on prescriber's order if fluid overload is likely.
Nausea/Vomiting	• Stop the infusion. • Administer prescribed antiemetic medications. • Provide comfort measures.
Back Pain/Hip Pain/Arthralgias/ Myalgias	• Stop or slow the infusion. • Administer acetaminophen or NSAIDS for the discomfort. • The use of a heating pad may be beneficial.

Potential Post-infusion Reactions

Post-infusion reactions can occur immediately or as long as 72 hours following the infusion. Symptoms associated with post-infusion reactions are usually less severe in nature but can interfere with a patient's quality of life. Common post-infusion reactions may include headache, low-grade fever, nausea, arthralgias and generalized malaise. Often patients describe a "flu-like" feeling. These reactions are generally managed with over-the-counter analgesics, antihistamines and may require a short course of corticosteroids.

Headaches are more frequent in patients who have a history of migraine or cluster headaches. Some patients, particularly those with histories of migraines, may have severe headaches and/or typical migraines up to 72 hours after their infusion. Over-the-counter analgesics are usually effective in treating these headaches, but they sometimes require the addition of oral steroids. Severe, persistent posterior occipital headaches may be a sign of aseptic meningitis, which have been reported in some patients after IVIG infusion.

Table 5 presents common adverse reactions and potential nursing interventions. It is important to follow the prescriber's orders when dealing with any infusion reaction. The prescriber should always be notified that a reaction has occurred and may wish to change immunoglobulin products or order premedications for future infusions. Reactions to IVIG can diminish with subsequent infusions, so the need for premedications needs to be reassessed periodically.

Complications Associated with IVIG

- Transmission of Bloodborne Pathogens: IVIG products are manufactured from large numbers of carefully screened human donors who have been tested for the absence of hepatitis B surface antigen, hepatitis C antibody and HIV antibody, and by nucleic acid testing for HIV and HCV. In addition, all products are produced using techniques to remove or inactivate potentially contaminating viral pathogens. Viral inactivation and removal processes have demonstrated reduction of the potential presence of pathogenic prion agents that have been associated with the development of transmissible spongiform encephalopathy such as variant Creutzfeldt-Jakob disease. Each manufacturer's package insert will delineate these processes.

- Thrombotic Events: Thrombotic (vascular occlusive) events have been reported in association with IVIG. The mechanisms for these episodes may include increased blood viscosity after high-dose IgG and/or the presence of procoagulant proteins in the IVIG preparation. These episodes have been noted with increased frequency in patients following rapid infusion protocols or patients with risk factors, such as prior thromboembolic events, thrombocytosis, or immobility. Thrombotic events are serious in nature and include chest pain, myocardial infarction, congestive cardiac failure, transient (cerebral) ischemic attack (TIA), and stroke. Patients with risk factors for thrombotic events should follow a conservative infusion protocol, using a product with a low (5%) concentration, and proceed slowly and cautiously with incremental increases in the rate of infusion to a maximum of 4 ml per kg of body weight per hour. Patients should be given clear instructions regarding what post-infusion symptoms should be reported immediately by their prescriber.
- Renal Adverse Events: Potential adverse effects involving the kidneys include acute renal failure, acute tubular necrosis, proximal tubular nephropathy and osmotic nephrosis. There have been rare reports of increased serum creatinine, oliguria and acute renal failure occurring from one to seven days after IVIG administration. Hyperosmolality and the presence of sucrose have been implicated as factors contributing to renal adverse events. Patients who are not adequately hydrated prior to onset of the infusion, who have diabetes mellitus or any pre-existing renal insufficiency, those receiving nephrotoxic antibiotics, those who have paraproteinemia, and/or those who are over age 65 are at the greatest risk for these problems. Renal function (serum Creatinine and BUN) and urine output should be carefully monitored in patients at risk for developing renal adverse events. Using slow infusion rates during administration of IVIG and assuring adequate hydration are advised for such at risk patients. As with patients at greater risk for thrombotic problems, patients with the potential for renal adverse events should be given clear instructions regarding what post-infusion symptoms should be reported immediately to their prescriber.

- Aseptic Meningitis: Cases of aseptic meningitis with headache and positive meningeal signs have been reported with the use of IVIG in both standard replacement therapy dosing and high dose therapy. The symptoms may occur during the infusion, but more typically they usually develop within 24 hours of the infusion. A previous history of migraine headaches has been noted to be a risk factor. A neurologic exam is indicated for these patients to rule our bacterial or viral meningitis. Patients with aseptic meningitis have pleocytosis but no organisms in their cerebrospinal fluid. Treatment is symptomatic. The development of aseptic meningitis is an indication for a change in the immunoglobulin product used for future infusions. Premedication with corticosteroids is also indicated for those with a previous history of infusion related aseptic meningitis.
- Transfusion-related Acute Lung Injury (TRALI): TRALI is a rare but potentially devastating complication of blood component therapy characterized by severe respiratory distress, hypotension, fever, dyspnea, and tachycardia. Patients exhibit pulmonary edema, hypoxemia, abnormal left ventricular function, and fever with a typical onset within one to six hours after infusion of the product. Pulmonary embolism and lung dysfunction due to "transfusion related acute lung injury" have also been observed during or immediately after IVIG infusions. Patients at risk include those with a history of atherosclerosis, those who have multiple cardiovascular risk factors, those of advanced age, those with impaired cardiac output, and/or those with known or suspected hyperviscosity or hypercoagulable disorders. This last group of patients include women taking oral contraceptives, especially if they also smoke, and anyone who has had prolonged periods of immobilization. Patients with TRALI may be managed using oxygen therapy and appropriate ventilator support, with symptoms usually resolving within 96 hours. If TRALI is suspected, appropriate tests should be performed for the presence of anti-neutrophil antibodies in both the product and patient serum.

Subcutaneous Immunoglobulin Therapy

In 1952, when Dr. Bruton began to treat his antibody deficient patient, he actually used subcutaneous immunoglobulin (SCIG). In the United States, the therapy evolved into intramuscular injections and then intravenous infusions. Since the 1980s, SCIG has been widely used in Europe. In January 2006, the U.S. Food and Drug Administration (FDA) approved a preparation of SCIG for use in the U.S. Currently the only FDA approved indication for SCIG is as antibody replacement therapy. At this time products for subcutaneous infusions are available in concentrations of 10 or 20%.

For the majority of patients, IVIG and SCIG are equally efficacious; however, there are differences between the therapies. While IVIG is usually given as a single large infusion every three to four weeks, SCIG involves giving smaller doses more often, once or twice a week in most cases. Fractionating the total dose into smaller portions decreases the changes in serum IgG levels that are the hallmark of intermittent IV infusions. This fractionation of the dose may eliminate some of the systemic adverse effects associated with IV infusions. Since infusions are given more often, the low "trough" IgG levels that occur just before the next IVIG infusion are also eliminated. With SCIG, the serum IgG concentration becomes remarkably consistent once a steady state is achieved and the patient is compliant with the therapy.

SCIG is self-administered by the patient. For children or those patients with some physical limitation, someone else can assist with the infusion. Dependent on the volume of drug to be infused, multiple small needles may be used simultaneously. The drug can be administered via a small syringe driver pump or a manual push. Many studies have demonstrated that patients can tolerate relatively rapid infusions and those patients who deliver their infusions via a manual push can do so in a matter of minutes.

A great deal of flexibility in the regimen, including the number of sites, duration of the infusion, and frequency of infusions, is possible. Because of these multiple permutations, the patient can design a regimen which "works" for him/her; that is one with which he/she can be compliant. For example a dose of 10 grams/week if given with a 20% solution would have a volume of 50 ml. The typical adult could receive this dose via a once

weekly infusion, using two needles connected to bifurcated tubing and a pump. The infusion could take approximately 30-40 minutes, although it could be made to go faster or slower based on the patient's tolerability and wishes. This dose could be split into a twice weekly infusion, using a single needle for each infusion. Some patients could even choose to give themselves 10 cc on five days every week. This flexibility in "custom designing" a regimen can be very attractive to patients who seek greater control over their illness and treatment. Deciding how, where and when the infusion occurs may help to minimize time lost from work or school, and allow greater freedom for patients who travel frequently.

Nurse's Role

The nursing role in SCIG is primarily that of an educator and facilitator. The goal for care is to help the patient/caregiver to become independent. Patients and/or caregivers will need to be taught the skills necessary to administer their infusions in a safe and aseptic manner. A systematic, step-wise teaching approach is usually effective. This starts with the nurse first demonstrating the procedure, then allowing the patient to practice the skill, and finally observing a return demonstration by the patient/caregiver to demonstrate mastery. After the patient is independent, follow up and support are critical in managing issues and/or problems. There may be multiple small "tweaks" necessary to ensure success. These might include changing the gauge or length of the needle, a recommendation about using a different site, or changing the rate of the infusion. The important thing to remember is that the vast majority of patients can be successful with this therapy.

The most important factors in assuring the success of subcutaneous therapy are teaching and support. The nurse needs to develop a teaching plan which takes into consideration the patient's ability to learn, independence, self-motivation, compliance, ability to read and/or follow instructions, physical limitations, (especially regarding manual dexterity), and presence of someone to assist or actually perform the infusion (if necessary).

Much of the education for SCIG administration includes basic nursing, i.e. hand washing and aseptic technique. A systematic approach to setting up the equipment and drawing up the

product, inserting the needle(s), monitoring local effects, discontinuing the infusion, and safely discarding the used equipment and needles needs to be developed.

Specific teaching topics can include:

- Storage and handling of medication
- Traveling with medication, supplies and pumps
- Using aseptic technique for drawing up the drug
- Priming tubing
- Subcutaneous site selection and preparation
- Insertion, securing and removal of needles
- Checking needle placement to ensure that it has not been inadvertently placed in the intravascular space
- Setting up the pump (if a pump is going to be used)
- Anticipating and troubleshooting infusion problems
- Discontinuing infusion
- Comfort measures and site care
- Appropriate waste disposal

Another important teaching topic is ensuring that the patient understands adverse reactions and/or complications, as well as how to initiate the appropriate action should something untoward occur. Expectations regarding site reactions and management should be discussed. The patient must be taught the signs of anaphylaxis and what to do should they occur. EpiPen training should be provided when an EpiPen has been prescribed.

Documentation of the patient's mastery of skills is important. The number of sessions required for the patient to master all of these steps may vary widely depending on the individual's capacity for learning, coupled with their anxiety level.

Adverse Reactions

Systemic reactions such as headache, nausea, fever, chills, and more serious adverse reactions are less frequent with SCIG than with IVIG, and published studies on SCIG consistently demonstrate a low rate of systemic reactions. The most common reported adverse events with SCIG are localized site reactions including itching, a burning sensation, mild redness and/or swelling. These local reactions are very common when a patient starts SCIG therapy because initially the body does not recognize the drug and perceives it as an irritant or something foreign. The normal inflammatory cascade is

activated, so there is swelling and erythema at the site(s). In almost all cases, these symptoms resolve within 12 to 24 hours. The intensity of these local reactions decreases with every infusion as the body comes to "recognize" the drug. If redness, irritation and swelling persist after the patient has been on therapy for more than a month or six weeks, it may be an indication of a mechanical issue such as a too short needle causing the drug to leak into the dermal layer or an infusion rate higher than the patient can tolerate. It may also be an indication that the patient needs to "work up" to the desired number of sites, volume per site and rate.

As with IVIG in patients with humoral immunodeficiencies, true anaphylaxis with SCIG is extremely rare. Local site reactions can be managed with adjustments to the infusion regimen, gentle massage, warm or cold compresses, and/or mild pain medications such as ibuprofen or acetaminophen.

Table 6: Potential Nursing Interventions for Dealing with Adverse Reactions to SCIG

Reaction	Nursing Interventions
Local Itching	• Apply cold compress (do not apply cold pack directly to skin) **For future infusions, consider:** • Use of a longer needle • Decrease volume per site and working up to desired site volume gradually • Ensure that a dry needle insertion technique has been used • Topical diphenhydramine • Over-the-counter topical steroid
Redness	• Apply cold or warm compress depending on which the patient feels will help • Consider irritation from tape or adhesive and change this product • Assure patient that redness should decrease with each subsequent infusion
Burning	• Clamp off catheter for 5-10 minutes, if desired • Slow the rate of infusion • Cold compress • Distraction techniques for younger children • Consider removing the needle and replacing it in another site • Assess needle placement as the needle may be partially intramuscular instead of subcutaneous. Consider the use of a shorter needle • Assess antiseptic used for skin prep

Table 6: Potential Nursing Interventions for Dealing with Adverse Reactions to SCIG

Reaction	Nursing Interventions
Swelling *(There will always be some degree of swelling as the patient is infusing fluid under the skin.)*	• Warm compresses for 5-10 minutes • If using a heating pad, use low setting • Gentle massage • Move area as tolerated e.g. if using a leg site: take a walk to help mobilize the fluid
Urticaria/Hives	• Stop infusion • Contact prescriber for instructions and to determine if infusion should continue • Antihistamine
Rash	• Stop SCIG • Contact prescriber for instructions and to determine if infusion should continue • Consider the possibility of tape or latex sensitivity
Discomfort	• Slow infusion • If intolerable pain, needle may be intramuscular, remove the needle and change sites • Warm compresses • Gentle massage • Over-the-counter analgesics can be used, but are rarely necessary

Additional Responsibilities

The nurse, the prescriber and the patient form an interdependent triad. Each person in this triad has individual as well as overlapping responsibilities. All must work together to achieve the goals for care.

Prescriber

The prescriber's responsibility is to make a diagnosis and educate the patient about the diagnosis. Decisions for therapy should be made collaboratively. The prescriber should explain available options for therapy. The therapy regimen, both the rationale for the therapy and practicalities involving the therapy, need to be explained clearly. The prescriber should make plans and expectations clear regarding follow up and sick visits, referrals to other providers, and laboratory monitoring.

Patients

Patients need to assume responsibility for themselves while maintaining close connections with the prescriber and the nurse. They should identify the need for education and/or assistance and should communicate problems or issues, especially potential barriers to care appropriately, effectively and in a timely manner. Ultimately, it is the patient who establishes the parameters and/or boundaries for the partnerships in this interdependent triad with nurse and prescriber.

Nurse

The nurse's first responsibility is to safely and effectively provide the prescribed therapy. However, the nurse has multiple other responsibilities:

Compliance Monitoring

The nurse may oversee the establishment of monitoring parameters for infusions and infusion related issues, including patient compliance. Compliance monitoring should include clear instructions for the patient regarding his/her therapy. The patient should know the name and dose of the drug that he/she is receiving. The patient should be taught to record specifics of each infusion in a personal diary or infusion log.

Information that should be recorded includes: expiration dates and lot numbers of drug, the site(s) used, length of time for infusion to be complete, adverse events, and any other pertinent information.

To record infusions and medical information, patients can use the Immune Deficiency Foundation (IDF) eHealthRecord, which is a free-of-charge, online personal health record developed specifically for the primary immunodeficiency disease community: www.idfehealthrecord.org. Some patients keep handwritten infusion logs, which are often available as downloadable PDF files from manufacturer's websites. The eHealthRecord can keep all medical history, current medications, infusions logs and more all in one place. Either way they choose to log infusions, patients need to understand the importance of keeping a log to record lot numbers and dosages as recalls of products and/or specific lot numbers do sometimes occur. Patients have a right to know if there is a potential problem and to seek appropriate help if there is a concern. Patients can enroll in a patient notification system for information on product withdrawals and recalls at: www.patientnotificationsystem.org.

Documentation

Documentation is another key nursing responsibility. As with all blood products, the nurse needs to keep a record of the product, lot number(s) and expiration date(s). This data needs to be readily retrievable in the event of a product recall or if a reportable patient problem occurs. Other infusion related data including dose, duration of the infusion, and assessments of the patient should also be carefully recorded. This data is important when trending information about the patient's replacement therapy and his/her overall health status.

Communication

The nurse has a critical role in establishing parameters for communication between all members of the triad. Variables to be determined regarding communication include the mode (telephone, e-mail, written), what needs to be communicated to whom, to whom specific problems should be communicated and communication in the event of emergency. The patient needs clear, written directions and needs to demonstrate understanding of these directions. A printed instruction list with relevant contact information is useful as a reference guide in the patient's home.

Education and Advocacy

The nurse plays an important role in patient education and advocacy and should assess the patient's knowledge about the disease state and treatment, and provide necessary education.

There is a multitude of resources available to meet educational needs. IDF has patient education materials readily available: www.primaryimmune.org. Through IDF, patients can also connect with other patients. Additionally, IDF has frequent outreach programs for patients and families. Information about such things as new modalities of treatment, legislative initiatives and insurance issues can be valuable resources. For a complete list of resources available through IDF, see Appendix B.

The nurse should provide ongoing support and education and assist patients in locating resources for such diverse issues as insurance problems, pediatric patients' transition to adulthood and assumption of their own care, attending school/college, concerns regarding traveling and vacations, pregnancy and any other life cycle changes. This includes providing patients with information about their product manufacturer's patient assistance program. Again, information regarding these issues can be found on the IDF website: www.primaryimmune.org.

Nurses should advocate for their patients with primary immunodeficiency diseases and help them to bring issues to the prescriber about ways to improve the patients' quality of life, not only during replacement therapy administration but also in other areas in which the patients' primary immunodeficiency has an impact on their life. Patients should not be defined by their disease; the ultimate goal should be to empower them to take control of their lives.

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Appendix A: Quick Nurse's Guide for Troubleshooting SCIG Administration

Leaking at the site

- Assess the catheter: is it fixed securely?
- Assess placement: may be in a location that is subject to movement – advise regarding the selection of site, assess amount of subcutaneous tissue vs. muscle.
- Assess length of catheter: may be too short – can suggest catheter brand change.
- Assess volume that is being infused: may be too much volume per individual site.

Local irritation, i.e. redness, swelling, itching

- Assure that this is a normal reaction – should diminish in 24-48 hours, if not, definitely by 4 days.
- Assess size: mosquito bite, raised wheel, quarter, plum, peach, or grapefruit? –size should be consistent with volume being infused and amount of subcutaneous tissue on patients; thinner patients may have more prominent raised area and may need to decrease amount of volume per site.
- Assess length of catheter: may be too short, can suggest longer catheter length or brand change to avoid.
- Advise use of gentle massage or warm compress post-infusion.
- Assess if tape allergy: change to paper/hypo-allergenic tape.
- Assess if rotating sites appropriately; may decrease frequency of rotation.
- Decrease volume per site and/or increase infusion time.
- When priming the subcutaneous needle sets, do not allow excessive drops of IgG to cover needle or prime dry leaving a small amount of air before needle. It has been suggested that the IgG tracked through the intradermal space can cause site reactions such as redness and itching in some patients.
- Apply topical Benadryl cream to site during and after infusion.

Extreme discomfort with needle

- Assess length: may be too long and irritating abdominal wall.
- Try catheter that allows introducer needle to be removed (Minimed Sof-Set).
- Try Emla cream or topical anesthetic prior to insertion.

Blood return observed

- In single-site tubing, remove and discard. Use new set. Notify supplier of need for replacement sets.
- In multi-site sets, clamp off the tubing that shows the blood return and then remove the catheter from that site. Check with prescribing physician regarding selecting alternative for accommodating fewer sites.
- Infuse the drug with the remaining appropriately located sites, thus increasing volume per site. May need to recalculate to a slower rate of infusion if appropriate. Consider previous history of site reaction and other factors.
- Infuse the original amount of volume per site with the sites that are in place. When completed, repeat the infusion session with new site to accommodate the remaining volume from the site that had blood return.
- Change entire set up and start over.

Long infusion times

- Assess technique for infusion: solution brought to room temperature?
- Check patency of tubing, number of sites, and volume per site. Decrease volume per site.
- Assess infusion rate settings, correct selection of tubing size and length to match infusion rates, check pump function, battery function, etc.
- Arrange observation of patient technique (SPP or office visit).

Needle contaminated by touching, dropping, etc.

- Discard in appropriate waste container and use new one.

Infusion pump stops during the infusion

- Check battery for any line occlusion. Do not override occlusion alarm and increase psi delivered.
- Check sets for down line occlusion. Multi-site sets may cause occlusion alarm due to co-dependence of lines.
- Change catheter brands or use single independent lines that equally connected off a multi extension pigtail.
- Use a 24 gauge catheter needle.
- Change type of infusion pump to simple syringe driver.
- Contact SPP or supplier for further information.
- If necessary, maintaining a closed system (leaving all connections intact), remove syringe, leave tubing attached to site and manually push plunger forward slowly to deliver remaining volume. Depending on volume, this may take some time.

Difficulty with manipulating syringes for filling

- Lubricate the barrel of syringe for easy manipulation by aseptically pulling back on the syringe, and moving it up and down before drawing up solution or filling with air.
- Pull back the amount of air to be infused into the vial and then attach the needle aseptically to the syringe.
- Mark the level of cc to which the syringe should be drawn back by placing tape on the outside barrel at the necessary level.

A patient guide for administration of subcutaneous immunoglobulin replacement therapy- using a pump:

This Appendix was created by Emma Knight/ Queen Elizabeth Hospital Birmingham. IDF does not warrant the accuracy, reliability or timeliness of any information in this Appendix which is the sole responsibility of Emma Knight/ Queen Elizabeth Hospital Birmingham. Any person or entity who relies on this Appendix does at his or her own risk.

Step 1: Preparing your infusion equipment

- Gather all equipment you need;

Equipment list:	
Mat	Cotton wool
Sharps box	Alcohol wipe
Immunoglobulin vial(s)	Micropore tape
Subcutaneous needle(s)	Infusion log
Green needle(s)	Pump
Syringe(s)	

Step 2: Preparing for your infusion

- Clean your working area using a disposable disinfectant wipe. Then thoroughly wash your hands with soap and water and use a clean towel to dry them.


- Open all the equipment packing and out onto your clean working area.


You should inspect each bottle of immunoglobulin carefully;

- Check that you have the correct dose
- Check the expiry date
- Ensure the bottle is not damaged
- Ensure the immunoglobulin is clear

Do not use the bottle of immunoglobulin if:	What to do:
• The bottle is cracked or broken • The protective cap is missing • The expiry date on the label has passed	• Record the batch number of the immunoglobulin in your infusion diary and state the reason why you are not going to use it • Then throw away into the sharps box
• The immunoglobulin looks cloudy or contains particles	• Record the batch number of the immunoglobulin in your infusion diary and state the reason why you are not going to use it • Inform the immunology team • Do not throw away the bottle – keep it to give it to the immunology team

Step 3: Preparing your immunoglobulin

- Take the needle and attach to the syringe. Pull out the syringe plunger to fill it with air. This should be the same amount of air as the volume of immunoglobulin you want to put into the syringe.

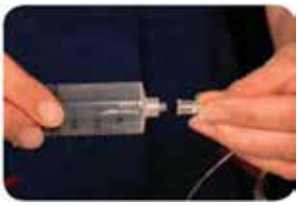
- Place the immunoglobulin bottle onto a flat surface and push the needle through the rubber stopper. Push the plunger on the syringe down. This will inject the air from the syringe into the bottle.

- Leave the needle in the rubber stopper, carefully turn the bottle upside down. The immunoglobulin should automatically fill the syringe but may also need you to pull back on the plunger

- Take the immunoglobulin filled syringe and needle out of the stopper
- Push out air by gently tapping the syringe and pushing the immunoglobulin up to the base of the needle

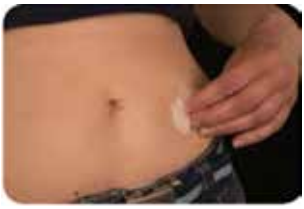
- Take off the needle and discard in the sharps container

- Immediately attach the syringe onto the infusion needle tubing and push on the syringe plunger. This will push the immunoglobulin into the tubing pushing out all the air out of the line. Stop pushing on the plunger when you see immunoglobulin appear at the end of the infusion needle



Step 4: Preparing the Injection site

- Select the area on your abdomen or thigh for your infusion.
- You should use different site from the last time you infused immunoglobulin. Your immunology team will inform you how many infusion sites you need and use how much immunoglobulin to infuse into each site
- Clean the skin at each site with an antiseptic wipe and let the skin dry

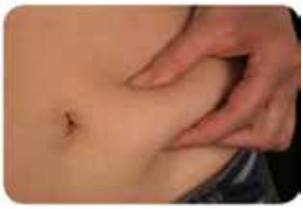


Tips for selecting an area to inject:

- New sites should be at least 5 cm from a previous site
- Never infuse into areas where the skin is tender, bruised, red or hard
- Avoid small veins which are visible on the skin surface
- Avoid injecting into scars or stretch marks

Step 5: Inserting your injection needle

- With two fingers pinch together the skin around the infusion site

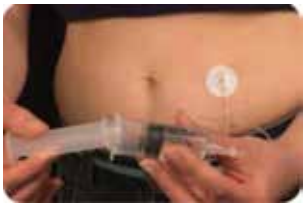


- Insert the needle under the skin at a ninety degree angle and ensure the tape is secure

- To make sure you have not accidently inserted the needle into a vein pull back gently on the syringe plunger. If you see any blood enter the tubing, take the needle out of the infusion site then remove the needle/tubing from the syringe and discard in the sharps box
- Attach another infusion needle and tubing to the filled immunoglobulin syringe and push on the syringe plunger to fill the immunoglobulin into the tubing pushing out the air. Re-insert the needle into a different site. Check again that you are not infusing into a blood vessel

Step6: Infusing the immunoglobulin

- Insert the syringe into the infusion pump
- Turn on the infusion pump. The rate of the infusion will already be programmed into the infusion pump by the immunology team



Step 7: Completing your infusion and cleaning up

- Once you have infused all the immunoglobulin, remove the tape and take the needle out of the infusion site and discard of the needle, tubing and syringe into the sharps box
- Cover the infusion site with gauze, tape or plaster

- Clean your infusion pump and working area. Then wash your hands

Step 8: Recording your injection information

- Record the infusion in your infusion diary. There is a removable sticker on the side of the immunoglobulin bottle that you can peel off and stick in your infusion diary. This contains the batch number of your immunoglobulin. Ensure you complete all sections in your diary and bring this with you to clinic appointments.