



Guide to
**Hematopoietic
Stem Cell
Transplantation**

Immune Deficiency Foundation Guide to Hematopoietic Stem Cell Transplantation

This publication contains general medical information that cannot be applied safely to any individual case. Medical knowledge and practice can change rapidly. Therefore, this publication should not be used as a substitute for professional medical advice. In all cases, patients and caregivers should consult their healthcare providers. Each patient's condition and treatment are unique.

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Table of Contents

Introduction.....	2
Chapter 1 - Primary Immunodeficiency Diseases That May Be Treated by Transplantation.....	3
Chapter 2 - The Evaluation Process for Hematopoietic Stem Cell Transplantation	5
Chapter 3 - The Transplantation Process	7
Chapter 4 - Life after Transplant	10
Questions to Ask.....	11
Resources	12

Introduction

Primary immunodeficiency diseases (PI) are a group of more than 350 rare conditions in which part of the body's immune system is missing or functions improperly. Some affect a single part of the immune system; others may affect one or more components of the system. Cells of the immune system normally arise from blood-forming "hematopoietic" stem cells (HSCs) in the bone marrow that is in the middle of every bone in the body; when this process is impaired, transplanting new HSCs from a healthy donor can be a potential cure. In some cases, replacing the immune system with one that functions normally is the best option in order to have a prolonged life with better quality. The procedure is commonly known in the medical world as hematopoietic stem cell transplant (HSCT), hematopoietic cell transplant (HCT) or bone marrow transplant (BMT). Unlike transplantation of a solid organ (such as a kidney or liver), HSCT does not involve surgery. It is similar to a blood transfusion. But instead of just blood, the transfusion contains hematopoietic cells, including the stem cells that both self-renew and mature, as needed, to give rise to white blood cells that fight infections, red blood cells that carry oxygen to the tissues, and platelets that help control bleeding. Traditionally, HSCs are obtained from the bone marrow. This process is called "bone marrow transplantation." HSCs may also be obtained from peripheral blood, or blood taken from the placenta at birth ("cord blood"), so that a more general term is HSCT.

This guide includes HSCT approaches that could potentially benefit patients with several types of PI. Subsequent chapters provide more details as to how a patient is prepared for a transplant, what the transplant experience is like, and what life can be like after a transplant.

1

CHAPTER

Primary Immunodeficiency Diseases That May Be Treated by Transplantation

Although many primary immunodeficiency diseases (PI) result in complications that have mild to moderate effects on the person's daily life, others are severe and require more definitive treatment, such as a hematopoietic stem cell transplantation (HSCT). This chapter describes the types of PI that may require HSCT as treatment, or for which HSCT is a consideration, depending on the assessment of an individual patient's risks and benefits.

Severe Combined Immune Deficiency (SCID)

Severe Combined Immune Deficiency (SCID), sometimes referred to as the "bubble boy disease," refers to the most severe group of primary immunodeficiency diseases, which place the affected child at a high risk for life-threatening infections. The term "combined" refers to the fact that both T lymphocytes (with many functions, including the direct killing of virus-infected cells) and B lymphocytes (antibody producing cells) are affected. Infants born with SCID can be identified shortly after birth through state newborn screening (NBS) programs. In some instances, there is a family history of SCID and, because of that history, the immune evaluation can be performed on an infant shortly after birth, or even prenatally.

Infants not picked up by NBS or family history can still be identified through a traditional immune evaluation. Patients should undergo evaluation if they experience recurrent, persistent or severe infections, or if they get infections with organisms that do not cause illness in healthy people.

Infants with SCID who completely lack T lymphocytes are not able to reject transplanted cells from a healthy donor; therefore, most SCID transplants can be performed without prior treatment (chemotherapy or conditioning) depending on the type of SCID and the tissue matching between the donor and recipient. SCID has many different genetic causes. In some cases, the exact genetic cause cannot be identified. Despite different genetic causes, however, the children are unable to fight infections. When SCID is diagnosed, the only curative option is to provide them with a functional immune system, most often through HSCT. In some forms of SCID, gene therapy and enzyme replacement therapy may represent valid alternatives. Studies have shown that when HSCT is performed in an infant with SCID soon after birth and before infectious complications occur, the outcomes are very good with survival rates approaching 95%. Babies with SCID must be isolated from exposure to infections and may be treated with immunoglobulin (Ig) replacement therapy and preventive antibiotics while awaiting transplant. Based on the circumstances and practices of the transplant center, some infants may be cared for at home pre-transplant with

strict isolation guidelines in place; other infants, however, are admitted to the hospital until the transplant has occurred and immune function is restored.

Combined Immunodeficiencies (CID)

These disorders, like SCID, are characterized by problems with both T cell and B cell immunity and can be caused by defects in any of a number of genes. They include: "Leaky SCID" in which the gene mutation is incomplete and some poorly functioning T cells are present; Omenn syndrome, a special form of Leaky SCID in which lymphocytes may reproduce in an unregulated manner and attack the infant's tissues; ZAP70 deficiency; bare lymphocyte syndrome; and others. Depending on the defect, CID may or may not be detected by newborn screening. While minimal lymphocyte function is preserved, it is not sufficient for effective responses to infections. HSCT can be curative for these disorders, but the residual host immunity is a barrier to successful transplantation. Therefore, chemotherapy to eliminate host lymphocytes prior to transplant is generally required.

Hyper IgM Syndrome (HIGM)

Hyper IgM Syndrome (HIGM) can vary in severity because there are different genetic causes, and different environmental exposures for each patient. One form of HIGM is carried on the X chromosome (X-linked), and the mutation can be passed from unaffected mothers to their sons. (The chance of a carrier mother passing the mutation to male offspring is 50%.) People with HIGM cannot make protective IgG antibodies, despite levels of IgM antibodies that are often high (giving the disorder its name). HIGM requires Ig replacement therapy and preventive antibiotics. Some affected individuals develop low white blood cell counts and may need medication to stimulate production of their white blood cells. Some patients may develop chronic intestinal infections leading to liver and intestinal damage. HSCT from a well-matched donor can cure HIGM, but like all non-SCID primary immunodeficiency diseases, host lymphocytes must be eliminated with chemotherapy to allow engraftment of the new stem cells. Pre-transplant infections and other complications increase risks of HSCT. Therefore, risks and benefits of HSCT must be carefully weighed for each case.

Chronic Granulomatous Disease (CGD)

Individuals with Chronic Granulomatous Disease (CGD) have white blood cells that can engulf bacteria and fungi, but the white blood cells then fail to kill them, leading to chronic and severe infections. Some patients have been managed with lifelong preventive antibiotics and, in some cases, injections of an immune system hormone or cytokine, gamma-interferon. This approach, however, does not cure the disease. Individuals with CGD may experience progressive infections that do not respond to treatment. HSCT is increasingly being used to treat CGD and can be curative, but it is not necessarily indicated for all patients, as some do well on medical management, depending on the severity of their condition. The risks and benefits of the all treatments and procedures must always be carefully weighed. There are ongoing trials of gene therapy for CGD.

Wiskott Aldrich Syndrome (WAS)

Wiskott Aldrich Syndrome (WAS) affects several types of immune cells as well as platelets (the clotting particles in the blood). Individuals with WAS may experience bleeding or bruising as well as frequent infections, usually affecting the sinuses, ears, lungs and/or skin. Patients frequently have significant eczema as well. In many cases, they require Ig replacement therapy. They often require placement of ear tubes, sinus procedures and frequent antibiotics to manage their infections. They are at high risk for bleeding due to low platelet counts if they experience physical trauma. There is also an increased risk of malignancy. Many patients with WAS are candidates for HSCT, which can be curative. The decision to perform HSCT depends on many factors, including what type of donor is available. There are ongoing clinical trials of gene therapy for WAS.

Immune Dysregulation-Polyendocrinopathy-Enteropathy-X linked Syndrome (IPEX)

Immune Dysregulation-Polyendocrinopathy-Enteropathy-X-Linked Syndrome (IPEX) is a PI in which immune cells are not regulated properly, resulting in an attack on the body's own tissue. Therefore, IPEX has symptoms of severe failure to thrive, severe eczema and endocrine disorders such as hypothyroidism, diabetes, growth hormone deficiency, and/or adrenal insufficiency. Individuals with IPEX often present with chronic diarrhea and eczema, and they may have been diagnosed with food allergies or inflammatory bowel disease and/or celiac disease in some cases. They may have infections and, unfortunately, they are typically not diagnosed until the disease process has done severe damage to the body, as their

symptoms can mimic other diseases. HSCT is recommended for treatment to resolve their multiple problems and help with proper growth and nutrition.

Common Variable Immune Deficiency (CVID)

Common Variable Immune Deficiency (CVID) is characterized by the inability to make sufficient immune proteins (antibodies) to fight infection. Most individuals with CVID do well on Ig replacement therapy alone. Some people with CVID, however, experience autoimmune complications involving the lung, central nervous system, blood components, intestines, and muscles, or develop lymphoma, a cancer of the lymphocytes. These complications can severely impair the patient's daily function or even be life threatening. In certain select cases, HSCT has been performed in patients with CVID. Due to the multiple systems affected and the general older age of the patient, however, HSCT is much riskier in this population. Up until the present, HSCT has only rarely been recommended for CVID.

Other Primary Immunodeficiency Diseases

The aforementioned disorders are only some of the types of PI that may be treated by HSCT. There are many more rare diseases of the immune system that could benefit from HSCT. An immunologist is the best source of information as to the disease state and whether HSCT would be a good option. HSCT is not without risk or complications and should be undertaken only for severe disorders.

Most PIs can be successfully managed without HSCT. Typically, diseases such as CVID, X-linked Agammaglobulinemia (XLA or Bruton's disease) and most 22q11 deletion syndrome (incomplete DiGeorge Syndrome) are not candidates for transplant as affected individuals can achieve a good quality of life and normal life expectancy with treatments, such as Ig replacement therapy alone or no immune therapy. Rarely, there are patients with the complete DiGeorge syndrome who require a thymus transplant, not HSCT. Other PIs have significant health impairments besides the immune disorder that would not be helped by HSCT, and still others are due to immune system factors such as complement proteins that are not part of the hematopoietic system.

As will be explained in the next few chapters, HSCT is a very involved process with potential for serious complications. It should only be considered in a patient where alternative treatments are not effective or if the patient is at high risk for complications if not transplanted.

2

CHAPTER

The Evaluation Process for Hematopoietic Stem Cell Transplantation

This chapter includes how patients are evaluated for hematopoietic stem cell Transplantation (HSCT), how donors are selected and the different types of HSCT.

HCST Evaluation

Once it has been determined that an individual with primary immunodeficiency disease (PI) may need HSCT, that individual is usually referred to a transplant team for evaluation and care. The team will do a thorough evaluation to determine any underlying health issues that would affect the timing and type of transplant or cause the patient to have additional risks. The evaluation typically involves human leukocyte antigen (HLA) typing of the patient and his/her family members to find out if there is a possible family member who could serve as a donor. The patient/family will meet extensively with the transplant physician and other team members to discuss in detail important items such as donor selection, conditioning regimen (chemotherapy) if needed [patients with Severe Combined Immune Deficiency (SCID) might not need it, but all other PIs do need conditioning], and post-transplant monitoring. Risks and benefits of transplant are discussed at this time. The evaluation may include scans, X-rays, lung function test, echocardiogram (heart testing), hearing evaluation and blood tests. The patient and family will usually meet with a social worker to discuss the impact of the transplant on patient/family functioning, support systems and financial issues.

If the patient is going to receive pre-transplant conditioning, he/she will have a long-term catheter (tube) placed in a large vein typically in the neck. This is needed for the multiple medications (including chemotherapy), IV fluids, blood tests and the stem cells that the patient will receive while in the hospital.

Finding a Donor Match

There are several types of donors who can be used for any patient undergoing HSCT. Finding the best matched donor is key to getting the patient's body to accept the transplant and to avoid having the transplant react against the patient. It can be a lengthy process to find and prepare a suitable donor, sometimes taking months. Poorly matched donor transplants can result in the patient's body rejecting the new cells. Poorly matched donors also greatly increase the risk of Graft versus Host Disease (GVHD) after transplant. In GVHD, the "new" immune system sees the patient's body organs and tissue as "foreign" and will attack it, causing damage. There are national and international donor registries that are searched for possible

donors if there are no suitable donors within the family. In some cases, a partially matched family member can safely be a donor providing the donor T cells in the HSC collection can be eliminated either before or after the transplant. HLA typing: The most important evaluation in finding a donor is to HLA type all potential donors and the patient (recipient). There are 10 critical HLA genes that are evaluated for most HSCT. These genes are inherited by the patient, 5 from the mother and 5 from the father. Each sibling has a 25% chance of inheriting the same 10 genes from the parents and this is called a "genotypic" match, the best possible match for HSCT.

Donor Types:

- **Identical Twin:** This is an identical twin of the patient and is the best possible match. Since all the tissues of identical twins match, there is no risk of GVHD occurring. An identical twin, however, is usually affected with the same PI as the patient, so would not be considered if also diagnosed with PI.
- **Sibling HLA matched donor:** This is a full brother or sister who matches the patient at the 10 major HLA genes. This is considered an optimal donor. Even though there is a perfect match for the major HLA genes, however, there could still be minor mismatches at other genes that differ, so GVHD is still possible.
- **Haploidentical family match:** This is a half-matched donor and is usually a parent but can be a sibling or even an aunt, uncle or cousin. Transplants from half-matched donors must have the donor T cells removed before or destroyed after the transplant to minimize the risk of severe GVHD. These donors are used when matched sibling donors or a very good matched unrelated donor are not available. Many patients with SCID have accepted T cell-depleted parental donor marrow or peripheral blood stem cells without any preconditioning and with excellent outcomes. The transplant physician will determine which patients are candidates for this type of transplant. For recipients of a haplocompatible HSCT, the risks for complications such as rejection of the cells or GVHD are higher. There may also be a delay in recovery of T cells so that infection risks may also be higher.

- **Unrelated HLA matched donor (also referred to as matched unrelated donor or “MUD”):** This is an unrelated adult donor (identified through the donor registries) whose HLA type closely matches the patient. This is considered a good donor choice, although the risk of rejection and the chance of GVHD is higher than with a related matched donor due to possible mismatches at non-HLA factors and the fact that these are not genotypic matches as in a matched sibling.
- **Umbilical cord blood donor (also referred to as cord blood transplant):** Cord blood donations to banks, or “repositories,” have expanded the options for many patients who need a transplant and lack an HLA matched donor. Use of cord blood can be limited due to the lower number of cells that are available, which can limit the size of the recipient for whom it can be used. GVHD is still a problem because of the fact that most unrelated cord bloods are HLA mismatched. However, despite some degree of HLA mismatch, cord blood may induce somewhat less GVHD than other types of donor cells. Also, the risk of rejection is much higher with cord blood transplants, and there is a delay in recovery of the red and white cells and platelets compared to other donor types. Finally, there is no opportunity to repeat the transplant from the same donor if the graft fails. Conditioning using high dose chemotherapy is most often used with cord blood transplants.
- **Autologous (or “self”) transplant with gene-corrected cells, also known as gene therapy:** Correcting a patient’s own hematopoietic stem cells (HSCs) would avoid problems with rejection and GVHD, and these advantages have spurred promising research in gene therapy. Almost all gene therapy is restricted to experimental clinical trials, and it is available for only a limited number of PIs. Immunologists are a good source on the most current information about gene therapy, which is beyond the scope of this discussion.

Donor Sources:

- **Bone marrow:** This is liquid tissue found inside all bones that contains the HSCs which generate the cells in the blood including red cells, white cells and platelets. This marrow can be harvested and prepared to infuse into the selected recipient. Typically, the marrow is harvested through multiple needle sticks into the pelvic bones until an adequate volume of cells is harvested. The donor is anesthetized for the procedure.
- **Peripheral blood stem cells:** HSCs are normally found in the bone marrow, but they can be mobilized into the peripheral blood circulation for collection. For this, the donor is given injections of a medication for several days prior to the harvest that causes some of the HSCs in the bone marrow to temporarily go into the blood circulation. A special IV is placed in the donor’s veins (usually veins in the arms or sometimes in the neck), and the blood is passed through a machine that removes those white cells containing the HSCs and returns the rest of the white cells plus the red cells, platelets and plasma back into the donor. This procedure is called leukapheresis and it is similar to donating platelets. This process usually takes 4 or more hours until enough stem cells are collected.
- **Umbilical cord blood:** Cord blood is a rich source of HSC and can be used for HSCT. The cord donor is usually non-related, although sibling’s cord blood can be used if available. A search for an unrelated cord blood that has been stored for HSCT is usually done through a bone marrow registry. In the US this is the National Marrow Donor Program (NMDP). Your transplant physician can tell you more about this process.

3

CHAPTER

The Transplant Process

Pre-admission

Once a patient has been determined to be a suitable candidate for hematopoietic stem cell transplantation (HSCT) and an acceptable donor has been found, the transplant is scheduled. There are several elements to the pre-admission process for transplant:

- **Transplant consent:** The physician and other team members meet with the patient and family to discuss in detail all aspects of the transplant procedure. Depending on the type of primary immunodeficiency disease (PI), the patient may or may not require a conditioning regimen. The team discusses the risks, benefits and complications associated with transplant. The family should ask all the questions they feel are necessary to be sure they fully understand the proposed treatment including the short-term and long-term risks as well as the benefits. Other family members, the family physician and outside experts can be involved if desired. If the patient and family agree to the procedure, formal consent is obtained.
- **Conditioning regimen:** This refers to administration of chemotherapy and other medicines for several days before the transplant. The conditioning regimen helps to make “space” in the recipient’s marrow for the new donor cells and to prevent rejection of these cells by the recipient’s immune system. The chemotherapy agents used for conditioning may have short-term and long-term side effects. Many patients with Severe Combined Immune Deficiency (SCID) can accept donor cells without any preconditioning because they do not have any T cells to reject the transplant. In some SCID cases (depending on the type of SCID, donor, and donor match with the recipient), there may be a choice of conditioning or no conditioning. For patients who do not have SCID, conditioning treatments vary widely. The transplant physician will determine which patients are candidates for conditioning and will explain the possible outcomes depending on whether or not conditioning is used.
- **Transplant date:** The transplant team has many components to coordinate in order to accomplish the transplant. If a related donor is to be used, a time must be arranged for the hematopoietic stem cells (HSCs) to be harvested (also for the T cell depletion if this is a half-matched parental donor) prior to giving the cells to a recipient with SCID. If pre-transplant conditioning is given, the timing of the harvest has to coincide with the patient’s completion of his/her conditioning. If an unrelated donor is to be used, arrangements must be made with the National Marrow Donor Program (NMDP) for collection and shipping of HSCs to the transplant center to arrive when the patient is prepared to receive the donor cells. Cord blood has to be analyzed to determine if it contains enough cells for the size of the patient. Finally, the patient must be kept as healthy as possible to undergo the transplant.
- **Insurance approval:** Since HSCT is expensive, the transplant center will need to work with the patient’s insurance to obtain approval before the transplant can be scheduled. This is usually started during the referral process.

Transplant Hospitalization

- **Admission:** If the patient requires pre-transplant chemotherapy, the patient will be admitted several days to a couple of weeks before the actual transplant to receive the conditioning regimen and to prepare for the transplant. The transplant itself is not a surgical procedure and occurs in the patient’s room. It is similar to a blood transfusion. On the day of the transplant, the donor’s cells arrive at the patient’s room suspended in a liquid solution and are infused into the patient intravenously. The length of the infusion depends on the volume and source of cells and can take anywhere from less than 30 minutes in a baby to several hours in a young adult.
- **Inpatient stay:** After a conditioned transplant, the amount of time the patient will be in the hospital varies significantly from a few weeks to several months. Patients who are more subject to a prolonged hospital stay are those who experience transplant-related complications or infections. The type of donor and transplant also influence the length of hospitalization, e.g., recipients of unrelated donor cells including cord blood tend to have longer hospital stays.
- **Discharge:** Most patients who receive pre-transplant conditioning may require some type of home healthcare assistance once discharged. They will likely go home with an IV in place and may be receiving IV fluids and IV medications at home. They will need to take several oral medicines as well.

Complications

Failure to engraft:

- After a sufficient period of time has passed following the transplant, the patient's blood is tested for the presence of donor cells (also called "chimerism"). If there are no "donor cells" found after multiple tests, the donor cells have not "taken." This means the transplant has failed, and the patient will likely need to receive another transplant. This may be accomplished using more cells from the original donor. Sometimes the original donor cannot be used again, and a new donor must be found. The patient might require conditioning before a second transplant.

Graft rejection:

- This means that the donor cells initially engrafted, but at some point, the patient's body "rejected" the cells. This typically occurs in patients with non-SCID PIs who received mild (called "reduced intensity") conditioning or in patients with SCID who received no conditioning. The recipient's original immune system may still be present enough to eliminate the new donor cells. In this case, the patient will likely require another transplant with a different conditioning regimen to prevent this from occurring again, but in rare cases the effect can be reversed with a "boost" of more cells from the original donor.

Graft versus Host Disease (GVHD):

- Graft versus Host Disease (GVHD) occurs when the new immune system attacks the patients' organs and tissues as they appear "foreign" to the donor T cells. Prevention and treatment of GVHD involve additional medications to quiet down or suppress elements of the new immune system that may recognize and injure the tissues of the patient. GVHD can be mild or severe. It usually attacks the skin, the gastrointestinal tract, the mucous membranes and certain organs such as the liver and lungs.

Acute and Chronic GVHD:

- Acute GVHD typically appears in the first 100 days after transplant. Chronic GVHD can appear any time after day 100 and may last for weeks, months or years. Common symptoms of both acute and chronic GVHD are inflamed skin (rashes), nausea, vomiting and diarrhea, and impairment of organ function, especially the lung and the liver. Treatment usually consists of topical steroid creams to the skin (for mild skin GVHD), and systemic medications such as steroids and other types of immunosuppressive agents for more severe symptoms. Acute and chronic GVHD can be mild or severe, and life threatening.

Mucositis (ulcers):

- Conditioning chemotherapy drugs can affect all tissues, including the mouth, throat and intestines. The patient may experience ulcers (sores) in these areas leading to pain, drooling, nausea, vomiting, diarrhea and sometimes bleeding. This is temporary and improves within 2-4 weeks. The ulcers are managed with good oral hygiene and pain medications, as well as bowel rest, which can be further discussed with the provider. Depending on the severity of the pain, narcotics may be used. The severity of mucositis correlates with the intensity of the chemotherapy conditioning.

Infections:

- Patients with PI are already at risk to develop infections and may have an ongoing infection at the time of transplant. A conditioning regimen for the transplant will remove their neutrophils (another type of white blood cell). This means the patient cannot fight infections. All patients are given preventive antibiotics during the transplant, but at times breakthrough infections can occur. It can take sometimes several weeks for the new donor cells to start producing enough neutrophils to help fight infection. Injections to stimulate neutrophil production are given, and neutrophil infusions are occasionally needed. Immunoglobulin (Ig) replacement therapy is given regularly during the transplant process to help control infection, and strict precautions are used to prevent infections. Monitoring for infections is of utmost importance.

Bleeding:

- As mentioned above, the patient's own blood forming cells are destroyed during conditioning. Platelets work to help the blood clot. A low number of platelets can result in spontaneous bleeding. The patient's blood counts are closely monitored during transplant and platelet and red blood cell transfusions may be administered.

Nausea, vomiting and diarrhea:

- Both the conditioning regimen and subsequent GVHD can cause these symptoms. Nutrition is important for patients to handle the stress of transplant and to heal their mucositis. Patients may be given medications to combat nausea and vomiting. They may receive tube feedings during the post-transplant period, or they may be given liquid nutrition through their veins. The latter is known as total parenteral nutrition (TPN).

Organ toxicity:

- The conditioning regimen can adversely affect the body's functioning, particularly the lungs, kidneys and liver. Tissue damage from the conditioning is variable depending on the intensity of the chemotherapy and most often, but not always, reversible with medication. Usually the damage to the organs is mild and temporary, but there can be long-term damage such as a liver condition called sinusoidal obstruction syndrome (SOS) or veno-occlusive disease (VOD).

Psychological/Social Issues:

- The hospital stay for a transplant can be long. The patient is kept in isolation due to the risk of infection, and patients may also be irritable and in pain. This can be difficult for the family to experience, and they may feel stressed with all the medical procedures. Also, it may be difficult for a parent/caregiver to get adequate sleep in the hospital room with the patient being evaluated frequently during the night by the nursing staff. The family may feel isolated from others as well and not always receive the social support they need. They may have competing demands on their time from others who are left at home. Families also have associated financial issues to handle. The longer the hospital stay, the more the pressures can build up. Social workers are available to help families with these issues. In addition, having supportive extended family and/or friends can help make this process easier to handle.
- Families can become very close with other patients and families during the hospital stay. While this can be helpful, awareness of events in the hospital, including other patients' adverse events or even death, can be traumatic and can make the transplant stay more difficult. Many hospitals have trained personnel to assist with stress, grief and depression. These emotions are common among families of children with severe illness, and medical personnel will be able to provide support. Support from other families with PI can be found through the Immune Deficiency Foundation (IDF): 800-296-4433.

Discharge from the Hospital

Discharge readiness: Discharge readiness of patients who have received a transplant generally requires resolution of any serious complications or side effects, absence of fevers and active infections. Patients are usually showing some signs of the new immune system producing blood cells prior to discharge. They are able to tolerate some type of feeding. They may still require an occasional blood transfusion.

- The patient and family are prepared for discharge by the hospital staff. The patient/family are trained in daily care including hygiene, administering medications and monitoring for complications.
- If the patient is going home with a central line in place, the family and/or patient is trained in care of the central line (most patients will be discharged with the central line in place).
- A discharge planner will help coordinate delivery of supplies and ensure that medications are ready at the pharmacy before discharge.
- If the family does not live locally, they may initially be discharged to a nearby housing facility managed by a medical facility or nonprofit organization.

4

CHAPTER

Life After Transplant

First Years after Transplant

Home Healthcare Company

While primary caregivers are generally expected to oversee patient care post-transplant, in some cases, a home healthcare company may be involved to help the family care for patients upon discharge from the hospital. A nurse or other home healthcare provider will meet the patient/family at home to provide a smooth transition, supervising and training family members on use of the equipment, IV fluids and IV medications. Other care such as tube feedings or dressing changes will also be addressed. Rarely is the home healthcare provider in the home to provide direct care to the patient. The home healthcare provider may check the patient's blood pressure and temperature as well as check on his/her general well-being and recovery. The intention is for the family to take over as much of the care as possible.

Outpatient Clinic Visits

Patients will require frequent visits to the transplant clinic. This can be as often as daily or once per week but becomes less frequent as the patient becomes more stable. Clinic visits can be lengthy at times as the patient will have blood tests performed, exams by healthcare providers, and, in some cases, transfusions of blood products or immunoglobulin (Ig) replacement therapy. If a patient lives a distance away, the family may need to stay in the area at a hotel or a nearby approved housing facility.

Illnesses after Discharge

The new immune system is not fully functional for many months; therefore, the patient remains at risk from infections for quite some time after transplant, although the risk typically decreases over time. Illnesses need to be assessed by the healthcare team when they occur. Often, the patient will need to make an unanticipated clinic visit or be hospitalized.

Healthcare Team

The bone marrow transplant specialist is the primary healthcare provider for patients following transplant and makes the majority of the decisions about the patient's plan of care. In some centers, immunologists participate in post-transplant management, helping to assess the function of the new immune system after transplant and sharing long-term follow-up.

Dealing with Complications after Transplant

Patients can experience complications after being sent home from the hospital. Often these are similar to what inpatients

experience. Some of these complications can become chronic issues that require care and attention for months, even years after transplant.

Most patients will receive Ig replacement therapy during the transplant and for up to a year or longer afterwards. Unfortunately, some patients, in particular with SCID, may not achieve good antibody production after the transplant and still require Ig replacement therapy indefinitely. Families may be disappointed that the hematopoietic stem cell transplantation (HSCT) did not totally resolve the immune deficiency. Nevertheless, if the T cells are engrafted and functional, the patient is protected from the most serious infections.

Long-Term Outlook

Most people with primary immunodeficiency diseases (PI) do well after transplant. Because their disease is not a cancerous condition, some people with PI can undergo a transplant with less intense chemotherapy, which decreases the risk of complications. Some patients will end up with "mixed chimerism," meaning that they have some donor and some of their own cells coexisting. In many cases, the new donor cells provide just enough immune function to keep the patient healthy.

People with PI who have had a HSCT and are stable can generally expect to live full and healthy lives. Once they get past the first year or two, many require only an annual or every-other-year visit to their transplant doctors and immunologist. It has recently been emphasized by PI specialists, however, that long-term follow-up is needed to monitor patients for the side effects of conditioning, such as sterility or effects on growth and organ function. Also, the immune function of the patient may wane or unanticipated problems may arise.

Coping with Stress after Transplant

Patients and families will have different experiences as they move through the transplant process. Each patient will vary in his/her response to illness and treatment based on his/her age, development, environment, physical and mental health, family support, and social and financial resources. A key aspect is that family members should feel free to discuss their stressors with each other and outsiders as needed, and everyone involved should have an outlet for stress. Parents/caregivers should feel comfortable to ask their healthcare team for help at any time.

Questions to Ask

The following are suggested questions for a parent/caregiver (or adult patient) to ask their healthcare care team when considering a hematopoietic stem cell transplantation (HSCT).

- What should go into picking a transplant center/doctor?
- A transplant center is near us, but they do not specialize in my child's/my particular type of PI. The doctors at the center say they can perform the procedure. Should I stay local, which would be easier/less expensive, or travel to a place that specializes in transplants for this type of PI?
- How important is it to choose a transplant center with experience in my/my child's type of PI?
- Centers differ in the amount of conditioning recommended (sometimes none at all for SCID, all the way to full ablation). How does the use of conditioning depend on the disease, the specific gene, or the preferred practice of a given center?
- What if any options other than HSCT or allogeneic transplant are there? Medical management, gene therapy or enzyme replacement therapy? If so, how do these treatments compare with allogeneic transplant for my/my child's condition?
- We cannot find an unrelated donor match. I understand our other options include haploidentical and umbilical cord blood transplants. What are the risks and benefits of each?
- What special considerations regarding transplant apply to my/my child's specific condition?
- What kind of insurance coverage should I have if a transplant is recommended?
- What precautions should be taken prior to admission for transplant?
- How long will my child/myself be in isolation*?
- What isolation precautions are required before, during, and after transplant?
- What are my responsibilities, as caregiver, to keep isolation precautions in place?
- What are the isolation guidelines and expectations of members of the medical team, and visitors when entering my child's hospital room?
- If things go well during transplant, what is the average amount of time in the hospital and recovery time?
- Which doctor or group of doctors will be in charge of my child's care during transplant?
- What is expected of a primary caregiver while the patient is in the hospital and after he/she goes home?
- Which doctor or group of doctors will be in charge of my child's care after discharge?
- I understand that transplants for PI can be curative. If a patient with PI undergoes a transplant and it is considered a success, will he or she be considered "fully cured?" Will there be any reoccurrence like within other diseases?
- Can my child receive live vaccines?
- In which PI category has there been the most progress in terms of gene therapy?

**To learn more about isolation, watch this video about one family's journey through isolation: <http://bit.ly/SCIDisolation>.*

Resources - Immune Deficiency Foundation

The Immune Deficiency Foundation (IDF), founded in 1980, is the national non-profit patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases (PI) through advocacy, education and research. IDF has a wealth of resources and groundbreaking information developed by a legion of dedicated professionals – healthcare, insurance, education and lifestyle advocates. Because of the generosity of donors and sponsors, most IDF services and resources are provided at no cost. For complete information on all IDF has to offer, please visit www.primaryimmune.org, or call 800-296-4433.

IDF Website – Information Gateway for the PI Community

Features the latest information about diagnosis, treatment, programs, services and much more. Create an account to receive the latest updates: www.primaryimmune.org/my-account.

Education Meetings – Local & National Educational Meetings for all Ages

Education meetings, retreats and conferences held across the country. For regularly updated information on all events, visit www.primaryimmune.org/events-calendar.

Educational Publications – Heralded as Best Patient Resources for PI in the World

IDF publications developed by world renowned immunologists and healthcare professionals. To download or order copies, visit www.primaryimmune.org/idf-publications.

Ask IDF – Individualized Assistance for all Living with PI

IDF offers help with the unique aspects of living with PI. Individuals and caregivers can use Ask IDF to answer their questions, receive peer support, help them locate a specialist in their area and assist them with insurance issues. Go to: www.primaryimmune.org/ask-idf.

Join the PI Community – Learn and Share with Others

- **IDF Friends**, www.idffriends.org, is an exclusive community page for people living with PI.
- **IDF Get Connected Groups** – Individuals and families can meet others living with PI in their local area. To find an upcoming group in your area, visit www.primaryimmune.org/events-calendar. No groups in your area? Contact IDF to learn about starting your own group: volunteer@primaryimmune.org.
- **IDF Advocacy Center** - Monitor public policy issues that are critical to patients at national and state levels. Learn more at www.primaryimmune.org/idf-advocacy-center.

United States Immunodeficiency Network (USIDNET)* – Patient Registry and Research Consortium

USIDNET, a program of the Immune Deficiency Foundation (IDF) funded in part by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institutes of Health (NIH), is a research consortium established to advance scientific research in the field of PI. The current focus of this initiative is on the patient-consented registry, and education and mentoring for young investigators. Learn more at: www.usidnet.org.

Valuable Tools – Improving Health, Powering Research

IDF ePHR, www.idfephr.org, is the electronic personal health record for people with PI to track their health and the opportunity to consent into PI CONNECT, the IDF Patient-Powered Research Network, www.idfpconnect.org, which transforms research by bringing together patient data with clinical data in USIDNET.

* *The United States Immunodeficiency Network (USIDNET) is funded by a cooperative agreement, U24AI086037, from the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institutes of Health (NIH), awarded to the Immune Deficiency Foundation (IDF). NIAID supports basic and applied research to better understand, treat and ultimately prevent infectious, immunologic, and allergic diseases*

Resources - Other Organizations and Programs

FILL – Following Infants with Low Lymphocytes

www.usidnet.org/fill

FILL (Following Infants with Low Lymphocytes) is a program of the Clinical Immunology Society (CIS) and the United States Immunodeficiency Network* (USIDNET) sponsored by the Jeffrey Modell Foundation. Infants with low lymphocytes are being identified, often by newborn screening for Severe Combined Immune Deficiency (SCID). This research study will track their diagnoses and outcomes. For more information about how to include your child's information in the FILL program, contact USIDNET:

contact@USIDNET.org.

International Patient Organization for Primary Immunodeficiencies

www.ipopi.org

International Patient Organization for Primary Immunodeficiencies (IPOPI) is an international organization whose members are national patient organizations for primary immunodeficiencies. The website provides general information on primary immunodeficiency disease and resource contacts for patients and professionals worldwide.

National Institutes of Health: National Heart, Lung and Blood Institute

www.nhlbi.nih.gov

The National Heart, Lung and Blood Institute (NHLBI) provides leadership for a national program in diseases of the heart, blood vessels, lung, and blood; blood resources; and sleep disorders.

National Institutes of Health: Laboratory of Immunology and Microbiology

www.niaid.nih.gov/research/lab-clinical-immunology-and-microbiology

The research program of includes both clinical trials and basic bench research. The gene therapy program has a particular focus at the bench and in the clinic on development of gene transfer treatments for X-linked chronic granulomatous disease (CGD) and X-linked severe combined immune deficiency (X-SCID).

National Organization for Rare Disorders

www.rarediseases.org 800-999-NORD

The National Organization for Rare Disorders (NORD) is a non-profit organization which provides information, programs and services for thousands of rare medical conditions, including primary immunodeficiencies.

Primary Immune Deficiency Treatment Consortium

www.rarediseasesnetwork.org/cms/pidtc/

The Primary Immune Deficiency Treatment Consortium (PIDTC) consists of 45 centers in North America whose shared goal is to improve the outcome of patients with rare, life threatening, inherited disorders of the immune system. Basic scientists, immunologists, and transplant physicians from the participating centers have contributed much of the current knowledge of the cause and treatments of PID. The immediate focus of the consortium is to concentrate on severe immune disorders which can be cured by hematopoietic stem

cell transplantation, enzyme replacement, and/or gene therapy by bringing together physician/scientists who evaluate and care for the majority of children with PID in North America. Helpful resources from PIDTC:

- What is a Blood and Marrow Transplantation (also known as a stem cell transplant)? www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Therapies/BMT
- What are the complications of a Blood and Marrow Transplantation? www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Therapies/BMT
- What is gene therapy? www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Therapies/Gene-Therapy
- What is PEG-ADA enzyme replacement? www.rarediseasesnetwork.org/cms/pidtc/Learn-More/Therapies/PEG-ADA

SCID, Angels for Life Foundation

www.SCIDAngelsforlife.com

The SCID, Angels for Life Foundation offers emotional support to affected families while also providing limited financial assistance to families currently going through treatment for Severe Combined Immune Deficiency (SCID).

The SCID Group

www.scid.net

The SCID Group is designed to help families dealing with Severe Combined Immune Deficiency (SCID) find a support network of similar families. Go to www.scid.net, and select the "SCID Email Listserv Support Group" to sign up.

The Jeffrey Modell Foundation

www.jmfworld.org

The Jeffrey Modell Foundation is dedicated to early and precise diagnosis, meaningful treatments, and ultimately cures of primary immunodeficiencies.

Wiskott-Aldrich Foundation

www.wiskott.org

This site provides information about Wiskott-Aldrich Syndrome (WAS). The links on this site include information for patients and families, the latest research related to WAS and financial support.

Articles / Websites

American Psychological Association: "When your child is diagnosed with chronic illness: how to cope"

www.apa.org/helpcenter/chronic-illness-child.aspx

American Academy of Child and Adolescent Psychiatry: "Helping children cope with chronic illness"

www.aacap.org/aacap/medical_students_and_residents/mentorship_matters/developmentor/Helping_Children_Cope_with_Chronic_Illness.aspx

Centers for Disease Control and Prevention: "Child Development Section" www.cdc.gov/ncbddd/childdevelopment/index.html

The Immune Deficiency Foundation, founded in 1980, is the national patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research.



SCID, Angels for Life Foundation

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