Creation of a College-Orientated Program to Raise Awareness for Blood Stem Cell Donation and its Major Implications on Different Types of Blood Cancer, Aplastic Anemia, and Other Blood-Related Diseases

S Agrawal, N Ramesh, S Kumar, P A Clark, M Patel, E Wang, T J Trapp, C E Curtin

Citation

S Agrawal, N Ramesh, S Kumar, P A Clark, M Patel, E Wang, T J Trapp, C E Curtin. *Creation of a College-Orientated Program to Raise Awareness for Blood Stem Cell Donation and its Major Implications on Different Types of Blood Cancer, Aplastic Anemia, and Other Blood-Related Diseases*. The Internet Journal of Public Health. 2024 Volume 10 Number 1.

DOI: 10.5580/IJPH.56944

Abstract

Every 3 minutes, someone is diagnosed with a blood cancer or disease, which often requires a blood stem cell transplant. The majority of these patients do not have a match in their family. Be The Match® is a blood stem cell donor registry that connects patients to matching donors. People ages 18-40 who meet the health guidelines are able to join the registry. It is more likely that a patient will match with a donor of their ethnic background, making a diverse college campus an excellent place to hold a donor registration event.

In this paper, we outline the need for these registration events, specifically on college campuses, as well as the myths and facts associated with joining the registry. A common misconception is that the donation process is painful, deterring possible donors from joining the registry. This is also due to the fact that many people assume bone marrow donation to be the only or predominant form of donation, while peripheral blood stem cell donation is actually more common. The paper also includes a medical analysis of common blood disorders that require blood stem cell transfusion and their possible treatments, as well as an analysis of the transplant process itself. We explain our process for implementing Swab2Save at Saint Joseph's University through the mobilization of students involved in Greek Life, obtaining and training volunteers, and event logistics. We also examine the ethical standpoint of Be The Match® and joining the registry. Finally, we offer recommendations for the expansion of this event to reach more people and potentially save more lives.

INTRODUCTION: BACKGROUND AND THESIS

There are five basic steps to create the chance to save someone's life, yet there is a severe lack of coverage on this straightforward process. This process is blood stem cell donations. Put plainly, blood stem cell donations involve the transfer of healthy stem cells from a donor to a patient in need. People require healthy stem cells for various reasons; therefore, donating blood stem cells aids many of those in need.[1]

Stem cells are cells in our bodies from which all specialized cells are generated. Under the right conditions, stem cells divide to form new stem cells or specialized cells with a specific function such as blood cells, heart muscle cells, brain cells, or bone cells. One reason why stem cells are so important to the human body is that they can be a part of regenerative medicine in which the stem cells generate healthy cells to replace those affected by disease. One important specific type of stem cell is those that go on to create blood cells.[2]

The National Marrow Donor Program® (NMDP) is a nonprofit organization that operates the Be The Match® nationwide registry of volunteer hematopoietic cell donors. This database can be referenced when a person with a blood disease requires a bone marrow transplant. The NMDP created the previously titled National Bone Marrow Donor Registry in 1986 and has since assisted in over 120,000 blood stem cell transplants.[3] It has since changed its name to

the Be The Match® Registry but has kept its same mission of working every day to save lives through transplants.

Stem cell transplants are able to provide life-saving cures. So far in 2023, there have been nearly 60,000 new cases of various types of leukemia according to the American Cancer Society.[4] Stem cell transplants have the possibility of curing or hindering these deadly diseases.

The five steps involved in blood stem cell donations are as follows: registering online, ordering a test kit, swabbing the inner cheek, getting matched, and donating. This process helps to combat over 75 diseases, including acute myeloid leukemia, multiple myeloma, and sickle cell anemia.[5] The first few steps of registering and swabbing are done by the possible donor. A possible donor will register and complete the instructions for the swab kit. The kit will then be sent to Be The Match®. From there, the organization does the rest of the work, running tests, plugging the type of human leukocyte antigens (HLA) into the registry, and referencing the database when finding a donor.[6]

The donor registry targets people aged 18-35 and a diverse range of ethnic backgrounds to combat health disparities.[6] College campuses happen to meet these criteria quite sufficiently through the student body. Our goal is to implement a campus-wide campaign to help increase the number of donors on the Be The Match® national stem cell registry. The more donors we can have enrolled in the registry, the more chances we have to save lives. We will work closely with the NMDP to create an on-campus event and to achieve this goal. To truly make a difference, the registrants need to know what exactly happens when they sign up. Since education is considered an important part of our project, our objective is to inform the students about what they are signing up for, the donation process, and the commitment it takes to help save lives.

Myths and Facts

Blood stem cell donations could save the lives of patients facing life-threatening conditions, but there is still some hesitation in the public about signing up for this process. Many myths and misconceptions circulate, further hindering the outreach and outcome of growing the national donor registry. In addressing these myths, we hope to help provide evidence-based information in an attempt to strengthen the trust between science and the public.

The first big misconception is that donating is very painful. It has been noted that many patients experience little to no pain during the donation process. There have been said to be some side effects ranging from back pain, fatigue, headaches, or bruising for only the next few days. The vast majority report that the donation process was worth the mild, fleeting symptoms if it meant potentially saving a life.[7]

There is hesitation from people with tattoos or body piercings to donate since they believe that these forms of body art can have an effect on a successful transplant. The fact is that tattoos and piercings will not prevent one from joining the registry or from donating. As mentioned before, other health factors will be evaluated when selecting donors, just not this factor.[8]

Another myth that circulates is the idea that someone can not donate if they have traveled internationally recently. The truth is that a person would be able to register regardless of where they have traveled. Once selected as a potential donor, recent travel to areas at risk for infections such as malaria or mad cow disease will be evaluated. This means that a person's travel history will have no effect on the registration process for the database.[8]

The last main fallacy the public hears about is that gay men can not join or donate. Fortunately, the truth is that members of the LGBTQIA+ community can join the registry and donate. Be The Match® does not ask about a member's sexual orientation, so all hopefully feel comfortable and do not fall under the false impression that who they are gives them fewer opportunities to save lives.[7]

A big factor across many affairs is money. Some may believe that donating can be an expensive process due to the possibility of having to travel and miss work. That is false, as donations are completely free to the donor. Be The Match® covers expenses including travel, meals, and hotel for donors and one companion. All medical costs for the donation procedure are covered by the patient's medical insurance or Be The Match®. This includes paying for a babysitter or dog sitter for those who have dependents at home and can not afford a sitter of some type.[7]

In addressing these myths, we hope that more students will be motivated to learn about the registry and donate. By addressing these misconceptions with fact-based information, we can ensure that more students are informed about the entire process and that their worries are allayed, in the hope of causing a ripple effect that will help us achieve

our objective of boosting donors.

MEDICAL ANALYSIS

Acute Myeloid Leukemia

Overview

Acute myeloid leukemia (AML) is a hematopoietic proliferative disorder that involves abnormal proliferation and differentiation of one or more clonal populations of myeloid stem cells. This causes ineffective erythropoiesis and failure of the bone marrow. It is the most common cause of acute leukemia in adults with an incidence of about 20000 cases per year in the United States.[9]

Symptoms & Signs

Patients often experience signs and symptoms related to anemia, thrombocytopenia, and leukopenia. These include pallor, easy fatigability, dyspnea, weakness, bleeding & bruising (Eg. epistaxis, gum bleeding, menorrhagia, GI bleeding, ecchymoses, etc), and early predisposing factors to infections. Some of the other findings include bone pain, CNS symptoms like headache, focal neurological deficits, organomegaly (hepatomegaly, splenomegaly), etc. Laboratory findings also include the presence of circulating myeloblast cells in CBC, peripheral smear and bone marrow samples, elevated lactate dehydrogenase levels, metabolic and electrolyte derangements during complications like tumor lysis syndrome (renal insufficiency, hyperkalemia, hyperuricemia, hyperphosphatemia) among many others.[10]

Causes and Risk Factors

About 50-80% of AMLs are caused due to somatic chromosomal abnormalities such as translocation, deletion of chromosomes, etc. Some of the most common abnormalities include translocations t(8;21) (q22;q22); t(15;17)(q22;q11), deletion of chromosomes 5,7,9 and Y, and trisomy 8, 21.[11] These mutations affect hematopoiesis by causing clonal expansion of undifferentiated myeloid precursor cells.

Some of the common risk factors are addressed in the table below.[11]

Table

Chemical Exposures	Benzene Pesticides Herbicides Embalming fluids Cigarette smoking Drugs like pipobroman
Radiation exposure	Therapeutic radiation Non Therapeutic radiation
Genetic disorders	Down syndrome – 10 to 20-fold increase Bloom syndrome Klinefelter syndrome Patau syndrome Neurofibromatosis Ataxia telangiectasia Li-Fraumeni syndrome Fanconi anemia Kostman syndrome Shwachman syndrome
Chemotherapy agents	Alkylating agents Topoisomerase-II inhibitors Anthracyclines Taxanes
Hematological disorders	Myelodysplastic syndrome Myelofibrosis Aplastic anemia Paroxysmal Nocturnal Hemoglobinuria
Other	Older age Latin American and southern European ethnic groups – especially for acute promyelocytic leukemia Presence of secondary leukemia

Treatments

Treatment of AML generally consists of induction chemotherapy and post-remission therapy. Induction therapy is aimed at achieving remission while post-remission therapy is given to achieve durable disease control.

Induction therapy – Patients for induction therapy are selected based on multiple factors including age, medical fitness, and comorbidities. Induction therapy in medically fit adults generally consists of an intensive chemotherapy regimen with cytarabine and anthracycline (eg. daunorubicin) for 7 days. Other agents include targeted therapies for specific mutations, like Ivosidenib for IDH mutation, midostaurin for FLT3 mutation, etc. The major complications of induction therapy are toxicity causing tumor lysis syndrome, electrolyte imbalances, bleeding, and infections from cytopenia.

Post-Remission Therapy – Post-remission therapy is aimed at achieving long-term durable disease control, and to destroy residual and undetectable cancer cells. It generally comprises a consolidative and maintenance phase. Consolidation therapy is done immediately after complete remission and it consists of chemotherapy (eg. high-dose cytarabine), and hematopoietic stem cell transplantation (HCT). Maintenance therapy again consists of chemotherapy (generally non myelosuppressive agents) with or without

targeted therapies.[12]

Role of HCT in AML – HCT can be autologous and allogenic in nature. Allogenic HCT is preferred, when possible, in the management of AML. Allogenic HCT can be obtained from HLA-matched family members, partially HLA-mismatched donors, or from umbilical cord blood stem cells and they cause a graft-versus-leukemia effect that helps eliminate the cancer cells. Compared to other treatments, HCT is associated with a higher rate of complications including graft-versus-host-disease (GVHD), immunosuppression to prevent GVHD, etc. It is usually preferred for patients with intermediate to poor prognosis and younger adults less than 60 years of age.

Reduced-intensity allogeneic stem cell transplantation – For older patients and those who cannot tolerate higher doses of chemotherapy that are used concurrently with HCT, a reduced-intensity allogeneic HCT is preferred. In this type, a lower-intensity chemotherapy regimen is given. The goal for such treatment is to not intensively treat the AML but to establish donor stem cells in the patient's marrow to produce white blood cells that will act on the cancer cells.[13,14]

MULTIPLE MYELOMA

Multiple myeloma (MM) constitutes about 1.2% of all new cancers diagnosed annually in the US. The mean age of the patients at the time of diagnosis is about 70 years. Males are more commonly affected than females, and Black patients are at an increased risk compared to White patients.[15] MM is characterized by the clonal proliferation of plasma cells resulting in increased production of monoclonal immunoglobulins. Several genetic mutations in oncogenes such as NRAS, KRAS, and BRAF, in addition to other promoter genes, have been implicated in the pathogenesis of the disease.[16] Environmental predisposing factors include alcohol consumption, obesity, and exposure to certain chemical carcinogens in addition to radiation exposure.

MM is known to arise from the premalignant condition called monoclonal gammopathy of undetermined significance (MGUS) which is characterized by monoclonal immunoglobulin overproduction without signs of end-organ damage. Patients with MGUS are at a 1% annual risk of progression to MM, likely from 'second hit' mutations in various oncogenes.

In patients with MM, while the excess production of monoclonal immunoglobulins results in hyperviscosity symptoms, neurological manifestations, renal tubular damage, and dysfunctional platelets, the expanding plasma cell clones occupy the marrow leading to consequent pancytopenia. Osteoclastic resorption of bones with resulting lytic lesions is also seen. Hence patients present with a wide range of manifestations with the most common being fatigue from anemia and bone pain from lytic lesions. Patients are also at risk of pathological fractures from these lytic lesions. Hypercalcemia manifests as abdominal pain, nausea, vomiting, polyuria, and increased thirst. Cast nephropathy leads to manifestations of renal failure including acidosis, edema, uremia, and electrolyte abnormalities. Other rare presentations include peripheral neuropathy and carpal tunnel syndrome. Patients are also predisposed to infections like pneumonia and pyelonephritis given the dysfunctional immunoglobulins and leukopenia.[17]

The criteria for diagnosing MM are the presence of clonal plasma cells constituting more than 10% on bone marrow biopsy in addition to the presence of at least one of the CRAB criteria that includes hypercalcemia, renal insufficiency, anemia, and osteolytic bone lesions. Besides the CRAB criteria, the presence of at least 60% of clonal plasma cells in the marrow, serum free light chain ratio of at least 100, and more than 1 focal bone lesion on MRI are also diagnostic. Immunohistochemical analysis of the marrow is typically positive for CD56, CD38, CD138, CD319, and CD19.[18]

Initial management focuses on addressing the acute complications of MM such as hypercalcemia, and renal failure with adequate hydration, calcitonin, bisphosphonates, and avoidance of nephrotoxins. Other acute complications may include vertebral compression fractures that may warrant neurosurgical intervention and hyperviscosity syndrome requiring plasmapheresis. After initial stabilization, management is based on risk stratification by genetic analysis and transplant eligibility. Transplant-eligible patients are initiated on induction chemotherapy, typically with 4 cycles of daratumumab, bortezomib, lenalidomide, and dexamethasone to reduce tumor burden following which the allogeneic stem cell transplantation is performed. Transplant recipients are then placed on maintenance therapy, typically with proteasome inhibitors. Clinical trials have demonstrated improved long-term survival with an early transplant approach in patients who are deemed to have high-risk diseases. Whereas transplant-ineligible patients are managed with 8-12 cycles of induction

chemotherapy followed by maintenance with bortezomib.[17,19]

Aplastic Anemia

Overview

Aplastic Anemia is a hematological disorder that involves low counts of circulating blood cells also called pancytopenia due to impaired bone marrow function. The epidemiology of aplastic anemia is not well known but based on retrospective data it can range from 0.6 to 6.1 cases per million population. [20,21]

Signs and Symptoms

Signs and symptoms are primarily due to decreased cell counts such as anemia, thrombocytopenia, and leukopenia. Symptoms pertaining to anemia such as pallor, increased fatigue, weakness, and dyspnea are commonly noted. Symptoms pertaining to neutropenia are frequent and persistent minor infections or sudden onset febrile illness. Patients are also prone to ecchymoses, mucosal bleeding, and petechiae given thrombocytopenia.

Causes

1. Autoimmune disorders such as Graft versus host disease, Systemic lupus erythematosus, and Eosinophilic fasciitis
2. Chemicals such as benzene, lindane, arsenicals, toluene
3. Drugs such as carbamazepine, hydantoins, methimazole, propylthiouracil, indomethacin, and phenylbutazone
4. Hereditary causes such as Fanconi syndrome
5. Infections such as Cytomegalovirus, Ebstein Barr Virus, Varicella, HIV
6. Other causes include thymoma, Paroxysmal nocturnal hemoglobinuria, pregnancy

Diagnosis

Aplastic anemia can be diagnosed via a bone marrow aspiration and based on the following criteria:
Bone marrow hypocellularity with 2 or more cytopenias (reticulopodia less than 1% or less than 40,000/microliter, neutropenia less than 500/microliter, or thrombocytopenia less than 20,000/microliter).

Moderate disease has less than 30% bone marrow cellularity with severe disease having less than 25% cellularity or less than 50% cellularity containing fewer than 30% hematopoietic cells, and very severe meets severe criteria plus neutropenia less than 200/μL.
Additional testing depends on the underlying condition responsible for bone marrow failure. Fluorescence in situ hybridization as well as genetic testing with flow cytometry can be pursued to rule out other possible causes for pancytopenia.

Treatment

Management of aplastic anemia is usually dependent on the underlying causative factor and the elimination of the causative agent when possible. When no reversible cause is noted, treatments vary based on age, disease severity, and performance status. Treatment of the disease is primarily done with the help of immunosuppressive agents or allogeneic hematopoietic cell transplants.

Patients with age < 50 years without significant comorbidities who are noted to be in good health should undergo an allogeneic hematopoietic cell transplant (HCT) before initial immunosuppressive therapy.

Patients with age > 50 years without significant co-morbidities and young patients who do not have a hematopoietic cell transplant donor should receive full dose immunosuppressive therapy with Eltrombopag, horst/rabbit anti-thymocyte globulin (ATG), cyclosporine A and prednisone.

For patients who are noted to have significant comorbidities or poor functional status, immunosuppressive therapy with single agent eltrombopag ATG or cyclosporine can be given.

The rationale for Eltrombopag is to increase platelet levels as well as increase in proliferation and differentiation of marrow progenitor cells via activation of intracellular signal transduction. Cyclosporine is noted to inhibit release as well as production of IL – 2 and IL –2 induced activation of T lymphocytes.

ATG induces hematologic response in aplastic anemia via the elimination of antigen-reactive T lymphocytes. Prednisone helps in the induction of cell death of immature lymphocytes.

Supportive care is primarily targeted based on laboratory abnormalities. In patients with Hb less than 7 mg/dl, transfusion with leukoreduced RBCs is recommended. In case of platelet counts with less than 10,000/microliters or less than 50,000/microliters in patients with active bleeding episodes, platelet transfusions are recommended. In patients with hemochromatosis, iron chelators as needed.

Role of HCT in Aplastic Anemia (AA): Hematopoietic cell transplant helps restore progenitor cells and replaces the immune system responsible for depleting progenitor stem cells and is particularly helpful for patients with severe AA. Candidates who qualify for HCT should be further evaluated with a multi-disciplinary team for evaluation of HLA typing. Adverse effects, as well as outcomes of HCT, depend on the age as well as medical fitness of the patients. HLA-matched related donors are optimal donors as they are less likely to be associated with acute or chronic graft versus host disease. 5 Year overall survival in patients < 40 years of age was noted to be 87% and those with age > 40 years was noted around 75% as noted in reports from the British Society for Blood and Marrow Transplantation.[22]

TRANSPLANT THERAPY AND DONOR MATCH: OVERVIEW

Transplant therapy in the context of the Be the Match® program relates to allogeneic transplants of peripheral blood cells or bone marrow transplants. As the transplant is allogeneic, there is a risk of transplant rejection, among other negative outcomes that can affect the recipient. Pre- and post-transplant care is important to decrease the risk of negative outcomes for recipients and increase the chances for proper matches in transplant donations. There are many indications for stem cell transplantation, including and not exclusive to different types of acute and chronic leukemias, lymphomas, anemias, and other hemoglobinopathies.[25]

Hematopoietic stem cell transplant, also commonly referred to as bone marrow transplant, is the implantation of healthy hematopoietic stem cells in a patient with dysfunctional or depleted bone marrow.[23] Hematopoietic stem cell transplant is an example of allogeneic transplantation where the cells are derived from a donor. These donors -- if not familial -- are often recruited through Be the Match®, the largest registry for possible marrow donors and cord blood units in the world.[28] For the best results, the donor and recipient must have a low HLA mismatch. HLA proteins are expressed on the surface of cells and are important in transplant immunity. Split into two types, these proteins are encoded by either Major Histocompatibility Class I or II proteins. HLA-A, HLA-B, and HLA-DR are the three most important HLA proteins that are required to match for increased transplant success.[23] Recent data has also shown that HLA-C may also play a role in improving clinical results.[28] Matching these alleles lowers the risk of graft vs host disease and mortality. There are other HLA proteins, such as some encoded by Major Histocompatibility Class II like HLA-DQ and HLA-DP, but matching them is not crucial to the success of the transplant.[28] Other factors that do affect the success rate of the transplant include donor gender, age, as well as the race of the recipient.[29]

Once transplant therapy is determined to be necessary, preparation for transplantation begins. Pre-transplantation care includes prophylactic medication to reduce the risk of Graft versus host disease (GVHD). Graft vs host disease is a serious complication of stem cell transfusion that commonly occurs in immunosuppressed patients. Graft versus host disease occurs because of the presence of donor-derived leukocytes in the recipients.[26] The T cells from the donor will cause the secretion of cytokines, and macrophage activation and cause rejection of the host's own cells. The presence of donor leukocytes will increase the proliferation of CD4 and CD8 T cells that recognize the host's HLA Class II. This will result in the initiation and expansion of the inflammatory cascade. There will be an increase in tumor necrosis factor (TNF) and Interleukin-1 (IL-1).[26] This is considered a Type IV Hypersensitivity reaction, a delayed-type hypersensitivity. Patients undergoing matched-unrelated donor allogeneic stem-cell transplantation or matched-related donor allogeneic stem-cell transplantation have a high risk of developing GVHD. Thus, prophylaxis for patients often includes rabbit anti-thymocyte globulin or anti-T-lymphocyte globulin, which provide immunosuppressive benefits to prevent acute rejection after transplantation.[24]

Another risk factor for any kind of transplant is the risk of infection. The threat of transplant rejection requires patients to take immunosuppressive medication which increases the risk for infection. Epstein-Barr virus (EBV) is a common infectious agent that can lead to post-transplant lymphoproliferative disorders (PTLD) in organ transplants. PTLD is uncommon for patients going through bone marrow transplant however, a patient going through a "potent combination of T cell marrow depletion, marrow ablative conditioning regimens, and the administration of antibody preparations to promote engraftment experience a significantly greater risk of developing EBV-associated PTLD".[27] The extended time frame of immunodeficiency also increases the proliferation of an EBV infection. The combination of HLA mismatching and T cell depletion increases the risk factor for bone marrow recipients to develop a PTLD as well. Another infectious agent that can

threaten transplant patients is cytomegalovirus (CMV), however, there is no published data to support the specific risk of infection for bone marrow recipients for CMV.

SJU SWAB2SAVE: CAMPUS EVENT

In order to conduct an on-campus event during the school year, thorough preparation must be done to have a successful campaign. Events require coordination with the University, following its standards and guidelines.

Campus Design & Implementation

Proper consent must be granted to host an event on the University's grounds. Once a date and time are decided on by the team, the Office of Student Life is contacted for a space to be reserved regarding that time frame. This assured date should be based on the University calendar, making sure to avoid holidays and other campus functions. The time of the event will be based on the general pattern of foot traffic around campus and aimed at the optimal amount of student interaction. Most students are on campus on weekdays during the afternoons and therefore having the event during the middle of the week, and in the middle of the day ensures that most students will have the opportunity to participate in the event. The location of this event is important to its success. Having it inside the University's Student Center, which is near the main dining hall and popular coffee spot, allows most students to see and access the tables. The goal is to see the greatest amount of student interaction based on the combination of placing and timing. Coordination with the Office of Student Life needs to be done for the purpose of renting tables and chairs for the event. While the tables and chairs are the Office's property, it becomes the team's responsibility to acquire the materials and return them safely after use. Permission must also be obtained from the University to create posters and print copies to put around campus.

Campus Outreach & Volunteering

We will create flyers with information about Be The Match® and its purpose. These flyers will include a link to sign up to become a volunteer and to be trained as a volunteer. These volunteers will be ambassadors for the event and will also work at the table at the event. These flyers will be posted around campus in the Student Center, freshmen and sophomore dorms, and academic buildings. These buildings are part of the everyday lives of students and thus will spread information to a larger amount and wide variety of students. We will directly reach out to the Institute of Clinical Bioethics at Saint Joseph's University and the Saint Joseph's University Biology Club to find volunteers with connections to this project and to the healthcare field. Interested volunteers will have three weeks to fill out the interest form and sign up for a training time. Understanding what is required of a donor is imperative, and will be learned at this required training session.

One to two weeks before the event, the team will present at Chapter Meetings for each sorority to promote the event. Another flyer with information about the event itself, including date, time, and location, will be sent to other organizations on campus including the Jesuit Colleges and Universities Honors Society; National Health Pre Professional Honors Society; Delta Delta Sigma Professional Pre Dental Fraternity; The Institute of Clinical Bioethics; The Biology Club; Pathways to Medical Professions Program; Alpha Gamma Delta Zeta Pi; Alpha Omicron Pi Sigma Beta; Alpha Phi Theta Theta; Phi Sigma Sigma Iota Rho; Sigma Sigma Sigma Delta Psi; Delta Sigma Pi Zeta Pi; Alpha Kappa Psi Chi Delta; Phi Sigma Pi Zeta Iota; and Alpha Phi Omega Alpha Eta Pi. Social sororities and fraternities include approximately 22% of undergraduates at Saint Joseph's University. Those involved in Greek Life often have other involvements on campus. Involving Greek Life in Be The Match® is a way to reach an even greater number of students than those within the sororities and fraternities themselves. Business fraternities, honors fraternities, and honors societies are also ways to reach a diverse population of undergraduate students not in the sciences.

These informational flyers will also be hung around campus in the Student Center, dorm buildings, and academic buildings, which are all areas common to students. Prior knowledge of the event allows students time to educate and acquaint themselves with Be The Match® before donating.

Training

Once a group of volunteers has been gathered, a virtual training session will be held approximately a week before the event. The training sessions are run by members from Be The Match®. If needed, multiple sessions can be appointed for those who can not make the first session. These virtual training sessions are said to be 20-30 minutes long on Zoom, that require no additional work other than listening to the material. The sessions make the most sense to be booked

during the night time of a weekday since students typically have classes and other commitments during the day. Weekdays usually work better for students due to weekends being full of other volunteer work or leisurely activities. Volunteers only need to attend one training session and then they should be equipped with all the knowledge they need to pass along to future donors. If someone is unable to attend any posted times, the information must be passed along to them, and that happens through the work of the team and the members of Be The Match®. On the day of the event, a representative from Be The Match® will be available to provide guidance and aid/help to the volunteers.

Pre-Education

Pre-education merits its own subheading due to its importance within the Be The Match® community. The organization stresses the significance of educating its volunteers and donors before having anyone commit resources. It is very disheartening if a stem cell match is contacted about donating, and they reject the opportunity to save a life due to not knowing what they truly signed up for. The organization does its best to minimize this by assuring all parties are aware of the process and what is needed to fully complete the process of a stem cell transplant. The same responsibility falls on any volunteers since their job is to inform possible stem cell registrants and relay any important information to them, including the commitment to the final donating process.

Day of Event Preparation

On the day of the event, the table from Student Life and Activities will be set up 30 minutes prior to the start of the event in the Student Center. The table will be placed in an area of high foot traffic, whether it be students going to the dining hall, grabbing coffee, or just passing through. The table will have informational flyers, as well as the equipment sent from Be The Match®. The table will be staffed by 4 people (1 representative from Be The Match® and 3 student volunteers) for every hour-long shift.

When the event is over, the area will be cleaned up and the table and chairs will be returned to Student Life and Activities. The kits will be mailed that day to Be The Match® to be processed.

Registration

The main goal of our event is to increase the number of donors on the national stem cell registry, but in order to become a possible donor, the student needs to register with the organization. At our event table, we will have a QR code that the students can scan and load onto the registration page. This self-explanatory task will take only a few minutes, as they plug in their basic demographics and list medical conditions to ensure eligibility. At the end of the registration is a consent form for them to sign.

Once the profile is complete they may move on to the use of the swab kit. We will have swab kits from the organization that we are able to hand out to students once they confirm that they have filled out the registration form. The swab kit can not be uploaded to the national registry without being linked to an account, so students will then scan the code on the kits, or type in the code manually onto their phones on the webpage after the registration. The swab kit has basic instructions inside on how to complete the process, but we will have trained volunteers there the entire time to help with the process.

After the swabbing is complete, the volunteers will collect the enclosed swab kit to be ready for shipping. The postal information is already on each kit, so they are immediately capable of being dispatched. As simple as that, the number of possible donors to the registry increases and gets even closer to saving more lives.

ETHICAL ANALYSIS

"The National Marrow Donor Program® (NMDP) is a non-profit organization dedicated to establishing, maintaining, and improving a system that provides transplants of bone marrow and other hematopoietic cells from volunteer, unrelated donors for individuals with leukemia and other life-threatening blood diseases. Established in 1988, NMDP maintains a registry of almost 3 million volunteer marrow donors; its network consists of a few hundred donor centers, collection centers and transplant centers, and several recruitment centers. There is a special need for volunteer marrow donors from the African American, Asian/Pacific Islander, Hispanic, and American Indian/Alaskan Native communities. To address this need, NMDP is currently conducting four specially targeted national recruitment campaigns to increase registry representation of minority volunteers."[30] The SJU Swab2Save program that was initiated by the Institute of Clinical Bioethics at Saint Joseph's University is focused on increasing the number of bone marrow and other hematopoietic cell donors to help save numerous lives. The Institute of Clinical Bioethics also

runs 5 Health Promoter clinics for the undocumented, underinsured, and uninsured African, Hispanic, and Asian communities in the Philadelphia area. Offering the opportunity for these communities to donate their bone marrow and hematopoietic cells will help to address the special need that NMDP has for minority registration. This is not only a medical necessity but an ethical imperative. It will be argued that—according to the ethical principles of respect for persons, beneficence/nonmaleficence, and justice—action must be taken immediately to address the concerns surrounding the lack of donors who could donate their bone marrow and stem cells and have the possibility of curing or hindering many deadly diseases.

Respect for Persons

This principle incorporates two ethical convictions: first, that persons should be treated as autonomous agents; and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy and the requirement to protect those with diminished autonomy.[31] Respect for human persons refers to the right of a person to exercise self-determination and to be treated with dignity and respect. All people deserve autonomy and to be treated with dignity and respect. Failure to provide any person with adequate knowledge about the Be The Match® program, the process, and registration violates this basic right of respect for persons. Swabbing volunteers to become potential matches for stem cell and bone marrow transplants, will increase our understanding of the biology of the various diseases stated above, will inform future research, and hopefully should result in the development of new, more effective therapies, which have the great potential to save many lives.

Second, as an autonomous agent, an individual has the right to informed consent. The elements of informed consent include professional disclosure, patient comprehension of the information, patient voluntariness, and competence to consent. This means that potential donors have the right to know from the Be The Match® coordinators the registration process, the process of potential donor matching, the pre and post-transplantation care, and the risks, benefits, alternatives, and consequences of agreeing to be a donor. Unless the coordinators, who are trained by the national Be The Match® organization, provide volunteers with full knowledge of the Be The Match® process, and the huge benefits they can provide, the coordinators are not giving these volunteers informed consent. To make themselves aware of the Be The Match® process the coordinators receive training one week in advance of the registration process by a representative of the national offices. These virtual sessions are 20-30 minutes long on Zoom calls. Additional readings are provided to the coordinators and there is oversight by the staff of the Institute of Clinical Bioethics. All coordinators are well prepared to train any donors on the full features of the Be The Match® program. Working collaboratively with other universities and organizations and increasing the national registry of potential donors and recipients has the potential to save more lives not only nationally but worldwide. Informing potential donors about the national Be the Match® Registry and having conversations about the need for stem cell and bone marrow transplants may be difficult for coordinators but unless these conversations are initiated, potential recipients of stem cell and bone marrow therapy will never have the donations needed to fight various diseases like Acute Myeloid Leukemia, Multiple Myeloma, Aplastic Anemia, Sickle Cell anemia, etc. Coordinators may need additional training on when and how to communicate the need for donation but this can be accomplished by following the recommendations that are being proposed in this paper. For informed consent to occur coordinators must have the knowledge needed to explain the full dimensions of stem cell and bone marrow transplants and donors must be reassured about the scientific research, emotional benefits, and practical issues that may follow if they are accepted as a donor. This education is happening thanks to the professionals at the National Be the Match® Registry and the staff at the Institute of Clinical Bioethics at Saint Joseph's University. Education is the key to ensuring that informed consent is given to every potential donor.

The SJU Swab2Save coordinators, who are potential health care professionals, are being proactive in addressing the medical needs of this most vulnerable population in regards to stem cell and bone marrow donation, and as a result, hopefully, needless suffering and possibly even more deaths can be avoided. To deny donors the right to decide to allow for stem cell and bone marrow donation that may help others clearly violates the ethical principle of respect for persons and our responsibility to help others in society.

Beneficence/Nonmaleficence

The principle of beneficence involves the obligation to prevent, remove, or minimize harm and risk to others and to

promote and enhance their good. Beneficence includes nonmaleficence, which prohibits the infliction of harm, injury, or death upon others. In medical ethics, this principle has been closely associated with the maxim primum non nocere ("Above all, do no harm"). All people have a right to know that by becoming a potential donor on the Be the Match® Registry, they can make an invaluable contribution to medical research and even have the possibility of saving thousands of innocent lives.

To increase donors for the Be the Match® Registry it will be necessary, as stated above, to educate the donors on the many misconceptions about being a donor. Explaining to donors the process of registration and the process of donation should relieve any potential donor about any fears of the process being painful, or causing serious risks to the donor. As students who hope to be healthcare professionals in the future, it is their responsibility to educate their peers about the medical needs that are a reality nationally and internationally. As a donor, one has the potential to save an individual's life, with minimal risk for the donor. As healthcare professionals and future healthcare professionals, we all have the responsibility to educate others about the myths and misinformation that surround the donation process. This not only meets the ethical criteria of the principle of beneficence, but failure to do so will cause harm, which then violates the principle of nonmaleficence.

It is clear, after reviewing statistics and studies and identifying the biases and stereotyping that exists regarding hematopoietic stem cell and bone marrow transplants, that failure to increase stem cell and bone marrow donation for this vulnerable population will bring about unnecessary risks, including more suffering and even more deaths. All those in the healthcare field have a moral responsibility to do what is good for their patients and for those who are critically ill. If an individual is impeded in the exercise of his or her reason and free will because of fear or a lack of training on how to communicate the need for stem cell and bone marrow donation, then these individuals have an ethical responsibility to overcome those impediments and do what is demanded by the basic precepts of medicine—seek the patient's good. Hospitals and research universities also have a responsibility to their communities. If hospitals and research universities can increase collaborative approaches to clinical research, optimize research funding programs, can educate physicians and other medical professionals on the need for stem cell and bone marrow donation, then it is the ethical responsibility of hospitals and university administrators and other health care professionals to formulate programs that address this immediate need. Failure to recognize this great need is a failure not only of the test of beneficence; it also is a failure of the test of nonmaleficence.

Justice

This principle recognizes that each person should be treated fairly and equitably, and be given his or her due. The issue of stem cell donation for various medical diseases also focuses on distributive justice: the fair, equitable, and appropriate distribution of medical resources in society. At a time when reforming healthcare in this country has become a high priority, failure to initiate preventative measures and clinical research that would save medical resources and possibly human lives, in the long run, violates the principle of distributive justice. The principle of justice can be applied to the issue of stem cell and bone marrow donation.

Transplant therapy related to the Be the Match® Registry is necessary if we are going to cure different types of acute and chronic leukemias, lymphomas, anemias, and other hemoglobinopathies. There is a critical need for more donors because there have been improvements in medical techniques and technology and as a result, additional stem cell and bone marrow samples are needed to give those impacted by these life-threatening conditions a chance to live. To obtain additional stem cell and bone marrow samples there is a need to create new programs like the SJU Swab2Save program. Justice in the fight against these life-threatening conditions will only be assured if more donors can be added to the Be the Match® National Registry.

Americans espouse the belief that all men and women are created equal. Equality has also been a basic principle of the medical profession. If we truly believe in equality, we should insist that all men, women, and children receive equal medical treatment and resources. Denying medical treatment to individuals because there is a lack of education about the need for stem cell and bone marrow donation or a lack of donors is an unjust allocation of resources and violates a basic tenet of justice. Physicians, clinical researchers, and all in the medical profession have an ethical obligation to use available resources fairly and to distribute them equitably. Failure to do so is ethically irresponsible and morally objectionable. To compromise the basic ethical foundations upon which medicine stands because we fail to educate and

recruit individuals about the need for donation is destructive to society as a whole.

To address these medical and ethical concerns, we propose various recommendations to increase stem cell donation in the United States. Unless we Americans address these needs for additional education and access to stem cell and bone marrow donations we will never attain the goal of eradicating these life-threatening conditions in the United States. Our model will not only save valuable medical resources; but has the potential to save precious human lives. If we do not make this a priority now, everyone will pay a price in the future.

RECOMMENDATIONS/CONCLUSIONS

Through the work done in this paper, the Institute of Clinical Bioethics was able to successfully conduct an on-campus event. At this event, over 100 new possible matches were swabbed and their kits were sent in to be added to the national registry. The knowledge of blood stem cell donation has been extended to the specific demographic that Be The Match® is looking for: groups aged 18-35 with a diverse range of ethnicities. This has shown to be a successful blueprint for creating and facilitating an event. Hosting more on-campus events will lead to spreading awareness of blood stem cell donations, and in turn, give those in need more chances at finding a match.

This event aligns with ethical approaches in healthcare due to the principles it displays. Through education, respect for persons, promoting beneficence, and creating justice, this program exhibits true values of ethics in what Be The Match® stands for, what this college-orientated program delineates, and the hopeful outcome of this donation process. Upholding these ethical principles will help increase donations and save lives.

Our recommendations are as follows:

1. The Institute of Clinical Bioethics has adopted the Mercy Health Promoter Model to aid undocumented and underserved communities who do not have access to healthcare by promoting preventative care. The Health Promoter Program targets chronic and acute conditions such as diabetes, hypertension, and obesity, and has since expanded to include dental screenings, cancer screenings, and physical and occupational therapies. The model promotes wellness, education, and basic primary care. We have 5 clinics among minority communities: African, African-American, Asian, and Hispanic communities. We can offer swabbing at the Health Promoter Programs to encourage donations from minority communities. As described above, many patients match with donors of their ethnic background. Expanding potential donor registration to minority groups can encourage minority donation and increase rates of match.
2. In order to obtain proper consent, the consent forms must be translated into Spanish, French, Vietnamese, Indonesian, Cantonese, and Mandarin. Be The Match® does not turn away undocumented individuals from joining the registry. Information about joining the registry and what the process entails must be provided to the minority communities, as well as education about the impact and importance of joining the registry and potentially donating.
3. Saint Joseph's University recently bought and merged with the former University of the Sciences. Professional health care programs are housed on that campus, including physical and occupational therapy, pharmacy, pharmaceutical chemistry, and physician assistant programs. To expand registration, we recommend hosting multiple registration events in the spring on both campuses. These events would each take place in different buildings to reach more people. For example, registration events can be held in dorm buildings, student centers, and academic buildings on both campuses.
4. Be The Match® encourages education. This includes the education of the signees, the volunteers, and anyone involved in the process. The organization stresses the importance of understanding what the stem cell donation process entails so that there are minimal amounts of matches that turn away the opportunity to save a life due to their lack of knowledge of the process. It is very disheartening for everyone involved when an HLA match turns away their chance to help out because they possibly did not know what they were signing up for. A crucial recommendation is ensuring that all volunteers and people involved are aware and educated about the organization and process as a whole so that they can pass on the information to possible registrants.

References

1. Chen, S.-H., Wang, T.-F., & Yang, K.-L. (2013, February 19). Hematopoietic Stem Cell Donation - International Journal of Hematology. SpringerLink. https://link.springer.com/article/10.1007/s12185-013-1298-8
2. U.S. Department of Health and Human Services. (n.d.). Stem cell basics. National Institutes of Health. https://stemcells.nih.gov/info/basics/stc-basics/#stc-I
3. BeTheMatch.org. (n.d.). Our story. Our Story | Be The Match. https://bethematch.org/about-us/our-story/
4. Key statistics for Acute myeloid leukemia (AML). American Cancer Society. (n.d.). https://www.cancer.org/cancer/types/acute-myeloid-leukemia/about/key-statistics.html#:~:text=The%20American%20Cancer%20Society's%20estimates,deaths%20from%20leukemia%20(all%20kinds)
5. BeTheMatch.org. (n.d.). Donate blood stem cells. Donate Blood Stem Cells | Be The Match. https://bethematch.org/support-the-cause/donate-blood-stem-cells/
6. Francois, R. Training WebEx: Blood Stem Cell/Marrow

Registration Events [PowerPoint slides]. Be The Match.
7. Be The Match (2021). MYTHS VS. FACTS: BLOOD STEM CELL DONATION [Lecture notes]. Be The Match. https://bethematch.org/support-the-cause/donate-bone-marrow/translated-materials-on-marrow-donation/donation-myths-and-facts---english--pdf-/
8. Be The Match (2023). Myth Busters: the truth about blood stem cell donation [Lecture notes]. Be The Match
9. De Kouchkovsky, I., & Abdul-Hay, M. (2016). Acute myeloid leukemia: a comprehensive review and 2016 update. Blood cancer journal, 6(7), e441-e441.
10. Löwenberg B, Downing JR, Burnett A. Acute myeloid leukemia [published correction appears in N Engl J Med 1999 Nov 4;341(19):1484]. N Engl J Med. 1999;341(14):1051-1062. doi:10.1056/NEJM199909303411407
11. Deschler B, Lübbert M. Acute myeloid leukemia: epidemiology and etiology. Cancer. 2006;107(9):2099-2107. doi:10.1002/cncr.22233
12. O'Donnell MR, Abboud CN, Altman J, et al. NCCN Clinical Practice Guidelines Acute myeloid leukemia. J Natl Compr Canc Netw. 2012;10(8):984-1021. doi:10.6004/jnccn.2012.0103
13. Stone RM, O'Donnell MR, Sekeres MA. Acute myeloid leukemia. Hematology Am Soc Hematol Educ Program. 2004;98-117. doi:10.1182/asheducation-2004.1.98
14. Kantarjian H, Kadia T, DiNardo C, et al. Acute myeloid leukemia: current progress and future directions. Blood Cancer J. 2021;11(2):41. Published 2021 Feb 22. doi:10.1038/s41408-021-00425-3
15. Mateos MV, Landgren O. MGUS and Smoldering Multiple Myeloma: Diagnosis and Epidemiology. Cancer Treat Res. 2016;169:3-12. doi: 10.1007/978-3-319-40320-5_1. PMID: 27696254.
16. Pasca S, Tomuleasa C, Teodorescu P, Ghiaur G, Dima D, Moisoiu V, Berce C, Stefan C, Ciechanover A, Einsele H. KRAS/NRAS/BRAF Mutations as Potential Targets in Multiple Myeloma. Front Oncol. 2019 Oct 24;9:1137. doi: 10.3389/fonc.2019.01137. PMID: 31709194; PMCID: PMC6821642.
17. Röllig C, Knop S, Bornhäuser M. Multiple myeloma. Lancet. 2015 May 30;385(9983):2197-208. doi: 10.1016/S0140-6736(14)60493-1. Epub 2014 Dec 23. PMID: 25540889.
18. Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, Kumar S, Hillengass J, Kastritis E, Richardson P, Landgren O, Paiva B, Dispenzieri A, Weiss B, LeLeu X, Zweegman S, Lonial S, Rosinol L, Zamagni E, Jagannath S, Sezer O, Kristinsson SY, Caers J, Usmani SZ, Lahuerta JJ, Johnsen HE, Beksac M, Cavo M, Goldschmidt H, Terpos E, Kyle RA, Anderson KC, Durie BG, Miguel JF. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol. 2014 Nov;15(12):e538-48. doi: 10.1016/S1470-2045(14)70442-5. Epub 2014 Oct 26. PMID: 25439696.
19. Goldman-Mazur S, Kumar SK. Current approaches to management of high-risk multiple myeloma. Am J Hematol. 2021 Jul 1;96(7):854-871. doi: 10.1002/ajh.26161. Epub 2021 Apr 13. PMID: 33725367.
20. Li SS, Hsu YT, Chang C, Lee SC, Yen CC, Cheng CN, Chen JS, Lin SH, Chang KC, Chen TY. Incidence and treatment outcome of aplastic anemia in Taiwan-real-world data from single-institute experience and a nationwide population-based database. Ann Hematol. 2019 Jan;98(1):29-3
21. Vaht K, Göransson M, Carlson K, Isaksson C, Lenhoff S, Sandstedt A, Uggla B, Winiarski J, Ljungman P, Brune M, Andersson PO. Incidence and outcome of acquired aplastic anemia: real-world data from patients diagnosed in Sweden from 2000-2011. Haematologica. 2017 Oct;102(10):1683-1690.
22. Marsh JC, Pearce RM, Koh MB, Lim Z, Pagliuca A, Mufti GJ, Perry J, Snowden JA, Vora AJ, Wynn RT, Russell N, Gibson B, Gilleece M, Milligan D, Veys P, Samarasinghe S, McMullin M, Kirkland K, Cook G; British Society for Blood and Marrow Transplantation, Clinical Trials Committee. Retrospective study of alemtuzumab vs ATG-based conditioning without irradiation for unrelated and matched sibling donor transplants in acquired severe aplastic anemia: a study from the British Society for Blood and Marrow Transplantation. Bone Marrow Transplant. 2014 Jan;49(1):42-8. doi: 10.1038/bmt.2013.115. Epub 2013 Aug 5. PMID: 23912664.
23. P;, K. K. C. (n.d.). Hematopoietic stem cell transplantation. National Center for Biotechnology Information. https://pubmed.ncbi.nlm.nih.gov/30725636/
24. Clinicalkey. ClinicalKey. (n.d.). https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S235230261930256X
25. Kim Schmit-Pokorny, ObjectivesTo provide an overview of the indications for hematopoietic stem cell transplantation (HSCT), Hahn, T., Oliansky, D., Pant, S., Baccarani, M., Jabbour, E., Gratwohl, A., Haller, M., Saccardi, R., Blanc, K. L., Friedman, R., Lazarus, H., Wirthlin, L., Leung, N., Gillmore, J., Ferrera, J., Schmit-Pokorny, K., Niess, D., … Ljungman, P. (2009, May 3). Expanding indications for Stem Cell Transplantation. Seminars in Oncology Nursing. https://www.sciencedirect.com/science/article/pii/S0749208109000217
26. Williamson, L. M. (1998, September 1). Transfusion associated graft versus host disease and its prevention. Heart. https://heart.bmj.com/content/80/3/211
27. Identifying the patient at risk for post ... - Wiley Online Library. (n.d.). https://onlinelibrary.wiley.com/doi/full/10.1034/j.1399-3062.2001.003002070.x
28. Kaster, E. C., Rogers, C. R., Jeon, K. C., & Rosen, B. (2014). Getting to the heart of being the match: A qualitative analysis of bone marrow donor recruitment and retention among college students. Health educator□: Journal of Eta Sigma Gamma. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4306578/
29. Anasetti, C. (2008, December). What are the most important donor and recipient factors affecting the outcome of related and unrelated allogeneic transplantation?. Best practice & research. Clinical hematology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3470825/
30. National Organization for Rare Diseases, “National Marrow Donor Program,” 2023.Https://rarediseases.org/organizations/national-marrow-donor-program.
31. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, U. S. Government Printing Office, Washington, D.C., 1979: B-1.

Author Information

Shubham Agrawal, MD
PGY3 at Mercy Catholic Medical Center
Philadelphia, PA

Nithya Ramesh, MD
PGY3 at Mercy Catholic Medical Center, Internal Medicine
Philadelphia, PA

Shanjeev Kumar, MD
PGY2 at Mercy Catholic Medical Center, Internal Medicine
Philadelphia, PA

Peter A. Clark, PhD
John McShain Chair in Ethics, Saint Joseph's University
Philadelphia, PA

Maanav Patel
2nd-year medical student at Philadelphia College of Osteopathic Medicine
Philadelphia, PA

Emily Wang
3rd-year medical student at Rowan-Virtua School of Osteopathic Medicine

Timothy J. Trapp
Senior Fellow in the Institute of Clinical Bioethics, Saint Joseph's University
Philadelphia, PA

Caroline E. Curtin
Senior Fellow in the Institute of Clinical Bioethics, Saint Joseph's University
Philadelphia, PA