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Explaining Allogeneic Hematopoietic Transplant to Patients through Analogies: For Practicing Oncologists

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Editorial

Comprehending Allogeneic Hematopoietic Stem Cell Transplant (AHCT) can be a daunting task for patients. Many oncologists would defer explaining typical hematopoietic stem cell transplantation process to the Bone Marrow Transplant (BMT) physicians. As practicing oncologist and staff may be emotionally closer to patients and family, it will certainly help patients to learn basics of a typical allogeneic transplant process from their own care providers. This will help facilitate understanding of AHCT and serve as a primer before comprehensive details from a BMT physician. This will also empower the patients to ask pertinent questions and will help alleviate anxiety related to AHCT. Since patients come with heterogeneous educational background, it is important to explain AHCT in a simplified manner using analogies. Described here is our own approach to help leukemia patients understand AHCT. Let's begin with getting a potential confusion out of our way. Sometimes you will hear me stating Stem Cell Transplant (SCT) and other time a BMT. Actually both the process is same; the only difference being the source of stem cells (bone marrow stem cells from iliac bone for BMT and stem cells from blood stream for SCT) are different. From either source one is utilizing stems cells and the outcomes for these two are almost equal (with potentially more chronic graft-versus-host disease in peripheral blood SCT). As you may know, our body constantly undergoes through new cell formation and cell death (cell turnover). It is the job of the immune system to keep this in an orderly fashion. Normally, if production of cells is abnormal (too big, too small, too much DNA or RNA) or too many in numbers, it is the job of the immune system to zap these cells up and put them in the recycling bin so that new cells can be made. This is much like a plastic toy factory where toys undergo quality check (defective, sharp edges, crooked etc.) before releasing for commercial use; those with defects are recycled. The reason patients develop leukemia is due to the fact that their own immune system failed to recognize very initial leukemogenic changes, a process called immune escape. The primary reason why an AHCT works is the fact that patients harbor a new immune system of donor origin. Having a new functioning immune system will help eliminate leukemia from its roots. It is imperative to understand that AHCT works best when leukemia burden is low [1,2]. Now, imagine that there is a room full of dirt (leukemia), if one tries mopping the room without sweeping it with a broom, one will create more clutter. Here, AHCT is more like a mopping or detailing job and conventional chemotherapies are the brooms. The success of AHCT is therefore directly related to successful leukemia reduction prior to transplantation.

Now that we understand how AHCT works, lets discuss what all is involved. First, we identify a potential donor for you. In order to get best outcomes, the donor needs to match with the patient at DNA level; we will call it "finger printing of DNA". This test looks at Human Leukocyte Antigen (HLA) that is present in most nucleated cells; the test therefore can be performed as a blood test or buccal swab. A donor that matches at all 10 points with the patient's DNA is most suitable donor. In absence of finding 10/10 match, lesser matches can be utilized with potentially lesser outcomes. Recently half donors (haploidentical) who match at 5 points (offspring's, parents or siblings) are being successfully performed with added immune manipulation. It is important to point out here that ABO compatibility has no bearing in donor selection as we are able to eliminate most if not all red cells. In a typical family, there is an approximately 25% chance of finding a perfectly matched donor. For the rest, chances of finding a donor from National Marrow Donor Program (NMDP), varies based on total number of donors registered from a particular racial group. For patients from European white decent the chances are highest and lowest for African Americans [3]. Table 1 summarizes chances of finding a suitable donor based on the ethnic background [3]. I must emphasize again that these differences are simply a result of number of potential donors available in the NMDP registry that varies widely between races. I am often asked why someone sitting in some other part of world would be a closure match than my own offspring's, parents or siblings;

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Table 1: Likelihood of finding a HLA matches from NMDP amongst US racial and ethnic groups.

Race/ethnicity	8/8 HLA Match (%)	>7/8 HLA match (%)
White European	75	97
African American	19	76
CKJFV* Asians	37-42	76-88
Southeast Asians	27	76
Hispanics	37-40	80-87
Native Americans	32-52	77-91

CKJFV* = Chinese; Korean; Japanese; Filipino and Vietnamese

the answer is with rare exceptions, the likelihood that they will not match with you at least at 5 points as their half of their DNA comes from each parents. In absence of a suitable donor Umbilical Cord Blood (UCB) can be used in children's for adults however, number of stem cells available in UCB is generally inadequate as stem cell dose is calculated based on body weight of the recipient. Adequate number of stem cell dose is necessary just similar to the fact that one would need more seeds (grass) to grow in an acres land compare to smaller land. Once a potential donor is identified, he or she undergoes physical examination to ensure donors health. He would then undergo blood tests to ensure it safe for the recipient to receive graft from the donor. It is typically choice of the donor whether he or she wishes to collect stem cells using PB or BM. The results for both PB and BM graft are similar with few exceptions that an AHCT physician will explain you. What's involved in part of the patient receiving AHCT is a process rather than an event. To understand this, I want you to imagine that you have a nice front yard with lush green grass. You then start seeing weeds (leukemia) and you would pluck them out weekly or whenever you find time (chemotherapy), just to see that more weeds are coming up or you may leave roots behind. When you get tired of doing this, you burn the entire lawn (conditioning regimen) and germinate new grass with seeds (stem cells). You will be hospitalized for approximately 3 weeks. Let me walk you through these days to explain what is being done and how you are going to feel. First week: Is probably the best week when you will not feel tired or sick. Since the first week, you would be on medications to prevent rejection, infections and mucositis amongst others. Upon hospitalization a central venous catheter is inserted usually under a collar bone and you start receiving a cocktail of chemotherapy (sometimes with total body irradiation) that is administered over approximately 5 days along with supportive medications to prevent nausea, vomiting and other symptoms. During these days you will feel fine. On 6th day we are giving you intravenous fluid and flushing the chemotherapy out of your system (radiation does not need flushing out as it has half-life of 0 minutes). Typically on the 7th day (varies based on the conditioning), stem cells are infused via the central venous catheter just like a blood transfusion that is over in 30 to 60 minutes and is mostly uneventful. Once the stem cells are in the blood stream, based on the receptors present on the cell surface of the stem cells and that in bone marrow stromal cells, these stem cells get in and settle down in the bone marrow. Just like when you through some grass seeds in your yard, you do not see grass next day and it typically takes 10 to 12 days for the new grass to grow. Exactly that is what is going to happen here as well. Second week: The first 3 to 4 days of the first week are pretty much as first week and you feel fine but now you start to feel somewhat tired. Then comes 3 to 4 days at the end of the second week; what has happened here is that your old blood counts along with immune system is wiped out and this is when you feel sick. At this point one feels really sick with neutropenic fever, ulcers in throat and mouth, nausea, vomiting, diarrhea and would receive appropriate medications. Third week: Is the week of recovery in which every single day you would feel better compared to previous day; this relates new blood cell formation from donor stem cells. At the end of the 3rd week, when blood counts have recovered, fever and other symptoms resolved and physical condition improved you will be discharged. At discharge you will have completed 50% of the entire AHCT process. The rest of the 50% will be dealt with in the clinic as out-patient. Remember, it is one thing to grow a plant and equally important is to take care of the plant for sufficient amount of the time so that it has deep enough roots to feed itself. While receiving out-patient care you will be monitored for need for transfusion, prophylactic or therapeutic antibiotics, antiviral, antifungal and supportive care amongst other. Typical monitoring comprises checking for a virus called Cyto-Megalo-Virus (CMV) and that for Graft-versus Host Disease (GvHD). When lymphocytes of donor origin become fully functional (when they wake up, the timing of which is unpredictable), they realize that they are in a completely different environment and recognize host as alien and the host body recognizes new lymphocytes as foreign. This sets in a little fight between donor cells with host organs manifesting as skin rash, rash in the liver causing liver enzyme elevation and rash in the intestine manifesting as diarrhea. This is the most important phenomenon in AHCT. You want to see some reaction (grade I and II GvHD) as it provides with unequivocal evidence that new donor cells are not only physically present but they are functional. A lot of reaction (grade III and IV GvHD) is unwarranted and needs aggressive treatment with IST. GvHD and its treatment make a fertile ground for CMV and Epstein Barr virus reactivation amongst other infections. Unlike cardiac and renal transplant in which Immuno Suppressive Therapy (IST) is administered for life, patients with AHCT over period of time are able to come off IST as their entire immune system has been switched to that of donor type.

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