So, what we do is we take out the stem cells, put them in the freezer to protect them, and then give higher doses of chemotherapy that can kill the cancer more effectively, and then infuse the stem cells back into the patient to allow them to repopulate the bone marrow after the chemotherapy has been used. So that way, you get to use much higher doses of chemotherapy and much more effective killing of malignant cells, but at the same time, sparing the bone marrow with the toxicities of the chemotherapy.

Bone marrow transplants are lifesaving treatments for patients with blood cancers and other diseases. Thanks to advances in blood and marrow transplantation, more patients can now benefit.

Things have really been transformed over the last number of years. The advance in biomarkers for detection of acute graft versus host disease as higher risk is really transforming how we do things and the advances with regard to reducing the risk of relapse with targeted agents. So many of these advances are somewhat incremental, and there are others that are more
transformative like Car-T therapy, but a combination of all these things together is really kind of moving the field forward and allowing us to offer more effective treatments with less toxicity for many patients.

Hello, everyone, and welcome to the Mayo Clinic Q&A podcast. I'm your host Jason Howland sitting in for Dr. Halena Gazelka. Bone marrow transplant is used to treat blood cancers and related disorders by infusing healthy blood forming stem cells into your body to replace unhealthy bone marrow. A bone marrow transplant is also called a stem cell transplant. Recently, Mayo Clinic in Rochester, Minnesota celebrated its 10,000th bone marrow transplant. Researchers are now examining the potential for stem cell transplant to treat other conditions, including multiple sclerosis. Here with us today to discuss advances in bone marrow transplant is Dr. William Hogan, Director of Mayo Clinic Blood and Bone Marrow Transplant Program in Minnesota. Dr. Hogan, welcome to the program.

Thank you very much, Jason. It's pleasure to be here.

So first off Dr. Hogan, what cancers can be treated with bone marrow transplant?

Well, we can treat a lot of both cancerous conditions and benign conditions with bone marrow transplant, but the vast majority of what we treat currently are blood cancers. So cancers such as lymphoma, multiple myeloma and leukemias represent the vast majority of what we use transplant as a treatment for. But there are a variety of other things, including some solid tumors, such as germ cell tumors, and then we use transplant to treat other diseases that are not malignant, such as bone marrow failure syndromes, and aplastic anemia, as well. And, rarely, some other related disorders that are not related to hematology, such as neurologic disorders, occasionally, such as multiple sclerosis, as you mentioned.

How is a bone marrow transplant performed?

So in general, there are two different types of transplants that we do. One is called an autologous transplant. And that means that we take the stem cells that we use for the transplant from the patient themselves. The other form of transplant that we consider is an
allogeneic transplant, and that's where we use a donor in order to provide the stem cells. So for an autologous transplant, this is usually for treating diseases such as multiple myeloma or lymphoma. And that's where we collect the stem cells in advance of the transplant from the patient and we freeze these. And that allows us to get much higher doses of chemotherapy than otherwise would be possible because the doses of chemotherapy would injure the bone marrow permanently. So what we do is we take out the stem cells, put them in the freezer to protect them, and then give higher doses of chemotherapy that can kill the cancer more effectively, and then infuse the stem cells back into the patient to allow them to repopulate the bone marrow after the chemotherapy has been used. So that way, you get to use much higher doses of chemotherapy and much more effective killing of malignant cells. But at the same time, sparing the bone marrow with the toxicities of the chemotherapy. The other type of transplant that we use is allogeneic transplant, and that's where we use a donor. And so that can be helpful if a patient has a bone marrow failure syndrome. For instance, they got exposed to radiation or they took a drug or there's a inherited problem with the bone marrow that causes it to fail. And if that happens, then we can use stem cells from somebody else because our own stem cells are not going to be able to produce because they have the underlying bone marrow failure syndrome. The other possibility is for certain types of bone cancers and blood cancers, such as leukemias, the bone marrow itself is not going to be great if we take it from the original patient because that can have the malignant cells present. And so we use donor bone marrow both to replace the diseased bone marrow and also to provide what we call a graft versus leukemia effect. So that's where the donor bone marrow itself is involved in actually killing the cancer cells in addition to the chemotherapy that we give, and that can actually be a very effective strategy for treating leukemias.

Jason Howland 04:53
Who can donate bone marrow for use in bone marrow transplants and how do they donate?

Dr. William Hogan 04:58
Sure. So there's a variety, maybe about three quarters of the patients that we offer transplant to and donate their own stem cells. And that's through a process called leukapheresis. So generally we give a medication called growth factor or gcsf, or filgrastim. And that releases the stem cells from the bone marrow into the blood, and then we can collect them through a machine called a leukapheresis machine. And that allows us then to take the cells and freeze them. And so that's what we normally do if we're doing an autologous transplant. If we're doing an allogeneic transplant with a donor, options might include a matched brother or sister sibling. Sometimes we use half matched siblings or other family members. We use unrelated donors sometimes if we don't have a family member that's adequately matched. And then occasionally, we use cord blood transplants that have been stored and that's becoming less common, but that's still occasionally an option.

Jason Howland 05:50
So what do patients need to know about recovery from bone marrow transplant? Will they need to take any medications? Will they need to modify their diets or other lifestyle factors?
Dr. William Hogan 06:00
Yes, it's quite variable. It depends on, you know, how healthy the patient is going into transplant and the type of transplant. Autologous transplants tend to be shorter with regard to recovery period, maybe something like four to six weeks in Rochester. But you know, after that, even for many months, there can be some kind of gradual recovery process of regaining stamina and strength and all of that. After allogeneic transplant where we're using a donor, it's a more complicated process. And generally speaking, that person will be in Rochester for three to four months. And that can be even a lifetime a follow up to monitor for complications and treat afterwards. So it's quite variable, depending on the situation.

Jason Howland 06:39
Are there any special considerations for people of diverse backgrounds to consider if they are faced with a cancer diagnosis that requires a bone marrow transplant?

06:49
Sure, well, there are a lot of considerations, but one area that particularly affects us is the ability to find a matched donor. So in general, families don't always have a matched donor within the family. And that's for a variety of reasons. And these are smaller, and many diseases now are being diagnosed at an older age. And then the brothers and sisters are older with other medical problems. So it makes the ability of a healthy donor in the family less common. So in patients of diverse backgrounds, it can be harder to find a fully matched donor in the unrelated donor registry, because there's more diversity of the HLA, which is what we use for matching. So there are some other options that we can consider in that situation. And half-matched transplants have become much more feasible in the last 10 or 15 years using a strategy called post-transplant cyclophosphamide. And so that has allowed us to consider less well-matched transplants for patients that have diverse backgrounds, or even if they don't. And then other possibilities include mismatched, unrelated donor transplants, which is becoming more possible as well. So we have a variety of options that weren't available to us previously, that can now be a good option for patients of diverse backgrounds. And cord blood transplant may also be an option for patients that have no matched donor, but that's becoming less common currently.

Jason Howland 08:09
All right, let's talk about advances in bone marrow transplant and cell therapy. So you touched on it a little bit there the use of mismatched donors, but also treating older, more frail patients. Previously, bone marrow transplant was limited to younger, healthier patients. But that's changing now, isn't it?

Dr. William Hogan 08:25
Yeah, well, at the beginning of this when transplant was really developed in the 1980s and 1970s, very high doses of chemotherapy and radiation were essential in order to prevent the transplant from being rejected. But with the advent of drugs called purine analogues, this has
allowed much less intense regimens to be possible. And so over the last 15, 20, 30 years, we've seen a trend towards using much less intense regimens. And that's allowed us to consider patients that are older and more frail. Also, the antibiotics and the supportive care measures that we have are much better than they were 15, 20 years ago. We've got a lot better antibiotics, antifungal drugs, and other medications to help people through. And so that has made a big difference with regard to being able to consider patients that are a little older, a bit more frail, compared to what was possible even 10, 15 years ago.

Jason Howland 09:18
How about using biomarkers to recognize and treat complications early? Can you explain graft versus host disease.

Dr. William Hogan 09:26
Graft versus host disease generally occurs in patients that have had a allogeneic transplant from a donor. And this is where the donor immune system doesn't just recognize the leukemia that we're trying to treat, which is what we want, but also recognizes the patient's normal tissues. For instance, their gut or liver or their lung. And so this can be anything from a relatively mild to a very devastating problem that can occur after transplant. And one of the challenges was that, by the time that has been fully developed, then it's harder to treat. So one of the goals of research in the last few years, has been to develop markers that will tell us which patients are at risk of having the most severe graft versus host disease, and allowing us to target more effective treatment towards those patients. Whereas sparing patients that are less likely to develop more severe GVHD from the side effects of medications to treat graft versus host disease. And there's been a lot of very useful research that has been developed in the last 10 years that has really advanced the role of biomarkers or acute graft versus host disease. And we've participated and developed many of the trials that have been evaluating this further. And I think it's really making a significant difference with regard to the management of these patients and potentially very devastating complications getting a little bit easier to manage.

Jason Howland 10:44
What about Car-T cell therapy? Is this considered a bone marrow transplant? Or is that something different? And and what are the advantages of this newer form of cell therapy?

Dr. William Hogan 10:54
Yeah, so car-T therapy is a very interesting therapy. It has been developed after many decades of research, and it's really come to fruition in the last five to 10 years. This is similar to bone marrow transplant, but not quite the same. But there are many principles that are similar. It's a cellular-based therapy, so not a drug, but using cells that are modified in order to try and treat leukemias and other cancers. And basically what it does is it takes our native immune system, and then the T cells specifically, and modifies them so that they are much more effective at recognizing targets that are on leukemia cells or other malignant cells. And that really kind of
allows us to use the native immune system in a much more effective way of trying to kill leukemias. Sometimes, when we develop leukemia, our own immune system tends to be suppressed somewhat by the cancer. But this gets around that for many patients. It's a very effective strategy for many diseases. And it's really transformed the management of some of the diseases that we've run into. It's not without some risks, and it's got some limitations, but it has been an extremely valuable advance in the treatment of certain cancers.

Can you tell us a little bit about research into using bone marrow transplant to treat other non-cancerous conditions.

So there are a variety of different projects. So looking at car-T for instance, that is also being developed for many different malignant diseases. But from the standpoint of benign diseases, we routinely use bone marrow transplant for treating conditions such as bone marrow failure syndromes, like aplastic anemia, and inherited bone marrow failure syndromes. There are also a number of diseases that are outside of the realm of blood disorders. So for instance, multiple sclerosis that we mentioned earlier, and it can also be potentially treated by an autologous transplant. Now this is a very well defined or subset of patients with multiple sclerosis. It's not, unfortunately for everybody with multiple sclerosis, but it's those patients that have a particular form that is very inflammatory. And the intense immnosuppression or suppression of the immune system that comes with the transplant can be helpful for some of those patients.

So Dr. Keegan here in neurology, who's a part of our multiple sclerosis unit, and I are working together to try and identify which patients would be good candidates for this and consider doing an autologous transplant as part of a national trial looking at treatment for multiple sclerosis. This is not really a standard treatment at this time. It's an experimental trial. But for selected patients, that could be an option.

So it seems like there's been a lot of advancements in this field in recent years. I would imagine that it's something that you're pretty excited about.

Things have really been transformed over the last number of years. I think, you know, I think in the last five to 10 years with the advent of car-T therapy that has been really kind of groundbreaking. The advance in biomarkers for detection of acute graft versus host disease as higher risk is really transforming how we do things, and the advances with regard to reducing the risk of relapse with targeted agents. So small molecule drugs to try and prevent relapses of acute leukemias is also making a significant impact into the reduction in risk of relapse after transplant. So many of these advances are somewhat incremental. And there are others that
are more transformative like car-T therapy, but the combination of all these things together is really kind of moving the field forward, and allowing us to offer more effective treatments with less toxicity for many patients.

**Jason Howland 14:13**

Well, unfortunately, we are all out of time, but I'd like to thank our guest, Dr. William Hogan, who is director of Mayo Clinic's Blood and Bone Marrow Transplant Program in Minnesota. Thank you Dr. Hogan, for joining us today.

**Dr. William Hogan 14:26**

Thank you very much, Jason. It's been a privilege. Thank you.

**Jason Howland 14:29**

And thank you for watching and listening here on the Mayo Clinic Q&A Podcast. I'm Jason Howland, and thanks for joining.

**Narrator 14:36**

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