Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers with your host, doctor Anees Chagpar. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it’s a conversation about bone marrow transplant with Doctor Niketa Shah. Doctor Shah is director of the pediatric bone Marrow Transplant program at the Yale School of Medicine, where Doctor Chagpar is a professor of surgical oncology. So Niketa, maybe we can start off by you telling us a little bit more about yourself and what it is you do. So I’m a pediatric bone marrow transplant physician and I’ve been here at Yale since 2016 and we do many transplant here. We are the only transplant program in the state of Connecticut and since 2019, we also do CAR T-bone marrow transplant which is something that people may have heard a little bit about but may not be really familiar with what it is. So can you tell us a little bit more about what exactly that
Bone marrow transplant is a process where we remove a patient's own bone marrow and replace it with the new bone marrow from either the patient's own previously collected bone marrow or from a different donor. We will focus today on mainly allogeneic stem cell transplant or allogenic bone marrow transplant where we replace a patient's own bone marrow with a healthy donor.

Bone marrow transplant is required for those patients whose bone marrow is not working properly either from their birth or they acquired some disease like leukemia down the road which is not curable or not treatable with the regular chemotherapy and in those conditions we replace the diseased marrow with the healthy bone marrow with the goal that once this healthy bone marrow is established in the patient's bone marrow and starts working, they produce normal healthy blood cells and thus cure the patients from their underlying disease.

So let's dive a little deeper into that.
whose bone marrow isn’t working properly, either because of a condition from birth or because of an acquired condition, kind of like leukemia. Can you talk a little bit about what some of the conditions from birth might be that people might have bone marrows that aren’t working properly and might require a bone marrow transplant?

Yes, definitely. So there are many patients whose bone marrow is not working from birth which develops down the road either completely aplastic or their bone marrow is not at all working. So there’s some of the elements of the bone marrow is not working.

Now I think most of us know there are three types of blood cells, one is white blood cells, other is red blood cells and the third one is platelets. So if the patients bone marrow is not working from birth they might have complete non functioning bone marrow. So they don’t have any of these three types of different types of blood cells. Or they may just have their red blood cell is not working or white blood cells is not working or platelet is not working so they either have anemia or
their white blood cells is not there so they have more risk of infection or their platelet is not working. So they may have a bleeding disorder. So one of the most common among this is the hemoglobinopathies where within their red blood cells their hemoglobin is not properly developed. And so those patients are called having the hemoglobinopathies where their hemoglobin is not properly developed. So they have less red blood cells and in turn they have also or their red blood cells are destroyed very quickly and in turn they have more anemia and also other related disorders. Maybe give us an example of what some of these conditions might be when we talk about people not having red blood cells or white blood cells or platelets? For many people who may be listening, that may seem really rather odd because many of us are used to having these blood cells. We often take our blood cells really rather for granted, knowing that they’re there and working. So what conditions might lead to these hemoglobinopathies or other conditions that the bone marrow is not working and how common are they?
So one of the most common I will mention here in the hemoglobinopathy where the fact is in their red blood cells hemoglobin and that one is sickle cell anemia which is most common hemoglobinopathy. The other hemoglobinopathy is thalassemia also then if we go through the other red blood cells like white blood cells or the platelets. These are less common where there are congenital neutropenia or congenital thrombocytopenia, or if all cells are not working well. There are few common bone marrow failure conditions which are present since birth. These are called Fanconi anemia or dyskeratosis congenita. But all these disorders are far less common than the most common hemoglobinopathy we see, which is sickle cell anemia. It is almost every year there are 300,000 kids with sickle cell anemia bone in the world, and in the United States, one in every 360 African American or one in every 16,000 Hispanic patients have this hemoglobinopathy, which is called sickle cell anemia. And in this hemoglobinopathy that
hemoglobin that is only one of the building block of their hemoglobin gene is replaced by the different block and that caused their sickle cell. All of the things that cause them to have the sickle cell hemoglobinopathy, which is different than what we all have as a normal hemoglobin in our red blood cells.

So if we have a normal hemoglobin our red blood cell is like a doughnut or soft, spongy, while if they have a sickle cell in their blood cells, their red blood cell looks like sickle. Which is as the name suggests sickle and it is not soft, it’s hard, rigid.

So the red blood cells break down easily and that is the main cause of sickle cell disease which develops in sickle cell anemia patients. And so for all of these kids who have sickle cell anemia where they have these red blood cells that form these Crescent like sickles that are hard instead of being spongy doughnuts like the rest of us who have normal red blood cells, how does that really affect them in terms of their every day health? I mean, can you explain to our listeners
how the shape and consistency, for lack of a better word, of these red blood cells impacts a patient’s day-to-day life? I mean, who really cares about the size and shape and consistency of a red cell? I totally agree that the general population might not know how the sickle cell anemia affects each and every person who has the sickle cell anemia. So as I mentioned earlier that the sickle cell anemia patients have red blood cells which are sickle which are rigid and easily breaking down. Their blood can’t reach each and every organ like the tiny fingers or the where the blood has to reach through the small blood vessels. So particularly when they are experiencing some cold weather or they have infection, their sickle cell can’t reach where it needs to go and they break down. And when your red blood cells are not reaching those areas, like even the bone or the kidneys or the lungs, then you develop all the complications.
and the most common effect initially in their lifespan we see is the pain crisis because their blood is not reaching those required areas where it needs to go and they experience severe pain crisis. They also have an increased rate of infection because their immunity also goes down and then down the road if this continues they may have many lung complication called the acute Chest syndrome where they develop pneumonia like symptoms and they may need hospitalization and we need to bring down their sickle cell number by giving the transfer regular blood transfusion. And if this issue continues most of the other organs also gets affected like kidneys, lungs, eyes, even risk of stroke because the blood flow to the brain also is affected and because of this chronic changes in the lung they may have pulmonary hypertension. They have the eye changes. They also have the spleen also down the road stops working well. So they have also increased risk of infection so that acute complication,
If it continues to develop down the road, they develop into the chronic morbidity and it affects their lifestyle and their quality of life. And down the road their lifespan also is reduced compared to the normal population. And so the size and shape of these blood cells really does make a difference in terms of where they can go and that in turn has an impact on the function of various organs. Now you mentioned that one of the ways to get around this is with blood transfusions. So if these patients get blood transfusions and are transfused with blood cells that are donut shaped and squishy, and potentially those blood cells can get to places, how about that option. I mean does every patient with sickle cell anemia need a bone marrow transplant or are transfusions good enough for some patients? Transfusion is definitely good enough for the acute condition if they develop sickle cell disease. However some of the patients who are very high risk of developing into the chronic conditions like those patients who have experienced early stroke or their brain blood vessels already have started developing the changes because of
the sickle cell anemia in those patients, if you give the chronic blood transfusion like every month, you can give them the normal healthy hemoglobin every month which will dilute their underlying sickle cell hemoglobin numbers and you can reduce the complication. However, blood transfusion in a chronic stage also has many complications, so that you can’t continue for lifelong because you will be exposed to many, many blood transfusion products and each blood transfusion also carries with it the increased iron which comes from our red blood cells. So those patients have to go through those complications down the road. So it is better for them if they have an available donor for blood bone marrow transplant, which is the only curative option right now for sickle cell anemia patients. Well, we’re going to take a short break for a medical minute, but on the other side of the break, we’ll learn more about bone marrow transplantation and how exactly we can help in the care of pediatric patients with my guest, doctor Niketa Shah.
Funding for Yale Cancer Answers comes from Smilow Cancer Hospital, where you can view videos from their survivorship team by searching for the smilow survivorship playlist on YouTube.

Genetic testing can be useful for people with certain types of cancer that seem to run in their families.

Genetic counseling is a process that includes collecting a detailed personal and family history or risk assessment, and a discussion of genetic testing options.

Only about 5 to 10% of all cancers are inherited and genetic testing is not recommended for everyone.

Individuals who have a personal and or family history that includes cancer at unusually early ages, multiple relatives on the same side of the family, more than one diagnosis of cancer, rare cancers or family history of a known altered cancer predisposing gene could be candidates for genetic testing.

Resources for genetic counseling and testing are available at federally designated comprehensive cancer centers, such as Yale Cancer Center and Smilow Cancer Hospital.
More information is available at yalecancercenter.org. You’re listening to Connecticut Public Radio.

Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar and I’m joined tonight by my guest, doctor Niketa Shah.

We’re talking about the care of pediatric patients in bone marrow transplant and right before the break, we were talking about patients with sickle cell anemia. And how many of these patients will need recurrent blood transfusions to try to get over some of these acute crises that they have due to blood vessels that are sickled in shape. And you mentioned that while blood transfusions are great and necessary in the acute setting, doing blood transfusions in a chronic way has a number of potential complications, everything from infections to iron overload to a number of other issues. And one of the things you mentioned was that bone marrow transplant is
at the moment the only curative option. Tell us a little bit more about how that works. Not all patients with sickle cell disease should be taken for bone marrow transplant right away if we know there are many other supportive care therapies available for sickle cell anemia or sickle cell disease patients apart from the blood transfusion.

50 years back prophylaxis penicillin also helped them reduce the infection which was initially started by one of our own mentors here at Yale, Doctor Howard Pearson who suggested that preventing the pneumococcal infection by giving the penicillin prophylaxis you can reduce the infection related death in first decade of life for sickle cell disease later on. A vaccine was also added and there are also some medicines. This approach helped them reduce the complications related to the sickle cell disease. However, it’s not curative, so those patients need to take some of these disease modifying agents lifelong to reduce those complications like hydroxyurea or a newer newly approved medicine.
However, to cure the disease we need to completely change their bone marrow so their bone marrow doesn’t develop sickle cell disease. Which benefits those patients who are experiencing more complication, requires hospitalization, who develops acute chest syndrome like pneumonia every year or they have developed some stroke like symptoms or have developed stroke. So these type of patients can benefit if you do the transplant and we reduce their chronic morbidity. So to do the bone marrow transplant we need somebody else’s bone marrow which is exactly like them. When we give blood transfusion we check the patient and donors blood group so in bone marrow transplant we do this by doing the HLA typing. This is a human leukocyte antigen typing which is all the blood cells in our body. They have some surface markers which helps them to identify that the given new cells are their own or are mimicking like their own and they are not different. So those cells are accepted by the
body very easily and that’s what we do. We type the patient and the initially available siblings who are biological siblings and if they have a match a sibling who doesn’t have sickle cell that we need to make sure we can use that donors or the siblings bone marrow to do the bone marrow transplant and in the last two decades we have done many, many sickle cell transplants and we have identified that if we do the matched sibling, from a siblings bone marrow, the success rate is more than 90% and in less than five, six years of age, it’s up to 99% success rate and we can cure sickle cell disease and all the related complications down the road. So a good reason to be kind to your siblings because you tend to go to the siblings first, rather than to the parents, grandparents, aunts, and uncles who I’m sure are all clamoring to try to help their child. Is that right? Yes. However, the issue with sickle cell disease patients there
are only 20% chance that we find the matched sibling who doesn’t have sickle cell disease as well. So in our transplant world we have already done the other forms of transplant where we can either use the half matched mother or father or half match sibling or as you mentioned another family member. We can also use Be the Match which is our unknown donor registry where many many people have registered themselves and they are ready to donate their bone marrow if their HLA details which are already in the registry are matching to the potential patient. And we can also do those types of transplant using unknown donor either 100% match or even 90% match transplant using those unknown donors bone marrow. And so you know, one of the questions that comes up then is if bone marrow transplant has such a high success rate in terms of curing sickle cell disease, especially if done at a young age, why wouldn’t you do this in everybody? I mean, why wait until people are having frequent hospitalizations and so on and so forth?
What’s the downside to doing bone marrow transplant?

I’m certain that many parents when their child is just diagnosed with sickle cell anemia if you said, well, we have a potentially curative treatment, but we’re going to hold back on that until your child requires multiple hospitalizations, they might look at you kind of funny. That’s a very interesting question and very good debate going on between us as a transplanter and the hematologist who take care of their sickle cell disease patient. Because in sickle cell anemia, not every patient with sickle cell anemia has a severe disease. Some may have just the milder disease in the initial lifespan, and they may develop more complex disease down the road. And particularly by using this penicillin prophylaxis and regular follow up with a multidisciplinary team we pick them up early and support them. So they are not having this severe disease. However, as I mentioned, as a
transplanter we do have a good success rate with them if we do the HLA match sibling transplant. We recommend that they have their HLA typing and if they have a biological sibling we do their actual typing and find out if they have a matched sibling in the family and we keep that in mind. And if they start experiencing this complication related to the sickle cell disease it is better we consider them for a matched sibling donor transplant early in life. So that is one of the recommendations we try to follow.

However, I need to also as a transplanter mention that transplant itself, bone marrow transplant is not a simple process. You remove a patient’s own bone marrow and give them the new bone marrow and it’s not a one day surgery. It is a complex process that takes time. So first we need to remove a patient’s own bone marrow by giving little chemotherapy to remove their underlying bone marrow which is diseased then we give new bone marrow from the donor.
which takes time, maybe two weeks to settle down in the patients and then they start working. So that requires a complex process and hospitalization and afterwards also we need to closely monitor for the initial few months with some medicines and regular follow up so bone marrow transplant is not a simple one day surgery type process. However, over the last 10 years we have learned how to do it better with less side effects and less toxicity. I mentioned earlier that to remove patients own bone marrow we may have to use some little chemotherapy. However because initially we were doing this type of transplant similarly what we do for leukemia.

But in last 10 years we learned that for sickle cell transplant we don’t need to use that high dose of chemotherapy which we use for leukemia patients. So nowadays we do sickle cell transplant with or even some of the protocol in the study we identified that we may do transplant without using any chemotherapy,
just one dose of radiation.
So over the last 10 years there has been a great success in doing sickle cell transplant better with less side effects. So that needs to be considered in overall care or while we manage sickle cell patients to find out if they have a HLA matched sibling.
Bone marrow transplant should be offered to them. And when we think about transplants, I mean, I think many people know a lot more about organ transplants, for example, than maybe they know about bone marrow transplants. But certainly when we think about people who have had transplants, one of the things that we often worry about is something like graft versus host disease, where you can actually reject due to a mismatch or at least a partial mismatch. That either the graft or the new organ, the new bone marrow might start reacting to your native cells, or vice versa, your immune system starts attacking the new bone marrow,
0:26:44.59 –> 0:26:47.628 does that happen in bone marrow transplant?
0:26:47.63 –> 0:26:50.5 And do patients who have a bone
0:26:50.5 –> 0:26:52.933 marrow transplant need to be
0:26:52.933 –> 0:26:54.619 on lifelong immunosuppressants?
0:26:54.62 –> 0:26:55.232 I mean,
0:26:55.232 –> 0:26:56.762 is that something that people
0:26:56.762 –> 0:26:58.827 consider in the decision of whether
0:26:58.827 –> 0:27:00.987 to undergo a bone marrow transplant?
0:27:02.5 –> 0:27:05.9 A very good point and I would like to explain
0:27:05.985 –> 0:27:08.939 that yes similar to organ transplant,
0:27:08.94 –> 0:27:10.836 bone marrow transplant patients
0:27:10.836 –> 0:27:13.68 also experience some
0:27:13.76 –> 0:27:16.22 either graft
0:27:16.22 –> 0:27:18.58 failure where a patients own immunity,
0:27:18.58 –> 0:27:19.864 particularly those patients
0:27:19.864 –> 0:27:21.576 who have received many,
0:27:21.58 –> 0:27:23.628 many blood transfusion before
0:27:23.628 –> 0:27:25.676 they go for transplant,
0:27:25.68 –> 0:27:28.48 they experience complications and they
0:27:28.48 –> 0:27:32.768 reject the donor cells or the donor cells
0:27:32.77 –> 0:27:35.522 fight with the patients own cells and
0:27:35.522 –> 0:27:38.468 that is called graft vs host disease.
0:27:38.47 –> 0:27:41.851 So the main point here if you
0:27:41.851 –> 0:27:44.59 do transplant early in the life,
0:27:44.59 –> 0:27:47.026 particularly less than 10 years of age,
0:27:47.03 –> 0:27:49.754 this type of complication with matched
0:27:49.754 –> 0:27:52.349 sibling donor transplant is less.
0:27:52.35 –> 0:27:54.426 So that’s why we recommend early
0:27:54.426 –> 0:27:55.464 bone marrow transplant.
0:27:55.47 –> 0:27:57.556 And then just the last query
0:27:57.556 –> 0:28:00.255 which you asked is do they need
the lifelong immunosuppression? Not in bone marrow. We are completely changing their immunity so once the new bone marrow has settled down they don’t need this lifelong immunosuppression. That is the main difference between the solid organ transplant and our bone marrow transplant. Bone marrow transplant patients are mainly on immunosuppression for maybe six months or a year or little longer, but afterwards no medicine.

Doctor Niketa Shah is associate professor of Pediatrics and hematology oncology and director of the pediatric bone Marrow Transplant program at the Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu, and past editions of the program are available in audio and written form at yalecancercenter.org. We hope you’ll join us next week to learn more about the fight against cancer here on Connecticut Public Radio. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.