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 transfusion oncology with Doctor Edward Snyder.

Doctor Snyder is a professor of laboratory medicine at the Yale School of Medicine where Doctor Chagpar is a professor of surgical oncology. Maybe we can start off by you telling us a little bit about yourself and what it is you do.

I'm a professor of laboratory medicine. I've been in the field for almost four decades, and transfusion medicine is basically what I do, all aspects of it, supplying the blood, seeing people who have any reactions and providing consultation to oncologists whose patients may need a blood transfusion. And they have some difficulties.
Talk a bit more about that whole specialty. Because for many of us we don’t really think about transfusion medicine or transfusion oncology as a specialty in and of itself. Tell us a bit more about what’s the purview of people who specialize in that area? Transfusion medicine is an area that originally started off in pathology and what happened was as the field grew pretty much stimulated by infectious disease concerns, it became much more of a consultive service involving medicine and surgery, so the term blood banking, which was really more of the storing of blood and so forth which we can talk about in a little bit, but the consultative aspect of the service where we talked to other physicians, you had trouble providing blood products for patients because of a variety of concerns and people from a variety of specialties, pathology, my backgrounds in internal medicine and hematology, others are in anesthesiology or surgery. And it is more than just storing blood in a refrigerator. It really has to do with supplying the
appropriate blood component for a patient in the right amount and at the right time. And most physicians, the terminology I use or phrase I use, if you don’t know your jewels, know your jeweler, and most physicians don’t really know much about blood transfusion, so they rely very heavily on the blood bank. Tell us a little bit more about the role of transfusion medicine in oncology. I mean, many of us think about using blood in trauma situations where people have lost a lot of blood. But for cancer patients, things might be a little bit different. What are the needs of cancer patients when it comes to transfusions? Many of the chemotherapeutic regimens that are used to treat cancer cause what’s called a hyperproliferative state in the bone marrow. That is, the bone marrow is affected by the chemotherapy in ways that are similar to the effect it has on the tumor. And the goal of chemotherapy would be to specifically have a negative impact on the tumor and to leave all healthy tissue alone. The chemotherapy also lowers the bone marrow’s ability to make new blood cells,
red cells or platelets, and when that happens, the patient becomes anemic and then they need a blood transfusion or if their platelet count gets very low, they’ll need a platelet transfusion. The concern is that when you start giving blood products to people that they can develop an antibody to the component, the same way when you get a vaccination, you develop an antibody to the material that’s injected and some people develop antibodies to red blood cells. Inside they have hemoglobin, which carries oxygen, which is important. But the surface of the cell is also studded with a variety of chemicals called antigens, which are foreign to some patients. Not everyone has the same blood type. Everyone knows about ABO types, but there are hundreds of other blood types that are on the cell, most of which are not clinically significant, but some are. And when some of those blood types of the transfused blood, even though they’re compatible for the ABO system and also the RH system which many people know of many of the other blood antigens with names that most
people probably haven’t heard of, they can develop antibodies to that, and when that happens, it becomes difficult to find blood for that patient, especially if they’ve had multiple transfusions. And they’ve developed multiple antibodies, so the blood bank director and that point the consults with the oncologist because the patient has gotten chemotherapy, their blood count is dropped and they need to get a transfusion most of the time it’s not a problem if things go smoothly, but on occasion when there are problems they contact the blood bank and we work with the physician to determine how much blood is needed. Also, many surgical patients who have cancer require blood during operative procedures. And we work with the surgeons as well to see how much blood is needed and whether they need platelets. For example, platelets are little fragments of blood cells. Unrelated to red cells, although they all derived from common lineages,
going way back to embryonic cell growth. And platelets are also needed and platelets may be lower because again, the chemotherapy or other illnesses that are part of the illness itself may cause the platelets to drop. So if you were to transfuse a platelet, the platelet count may not go up to the level that’s wanted, and you wind up having a patient who can’t really receive platelet transfusions and get the response that’s needed. The platelet count is not elevated as expected and that definitely requires a consultation from the blood bank with the clinician to determine what other options there are, and there are multiple options for finding compatible platelets.

Then there are other patients who have other illnesses where the plasma levels of some plasma products may be low, and they would need a plasma transfusion, so blood banks get involved in a variety of issues related to oncology, whether it’s surgical or whether it’s chemotherapy, or whether it’s illness based. In some cancers,
the bone marrow is affected by the growth of the tumor and the tumor actually replaces some of the bone marrow causing platelet counts to become too low. For patients who actually have a good lifestyle and we consult for those issues as well, so in addition, if someone gets a transfusion and they have a reaction of some type, whether it’s a allergic reaction or a fever, we consult with that as well. So we're pretty busy. It’s a very clinically oriented specialty. You make a few really good points, and one of which is that some cancer patients will need repetitive transfusions and can build up these antibody responses. So just out of curiosity, how do you get around that? I think this is a question that many patients and their families may have is should we be donating our own blood and banking it, knowing that we may, with chemotherapy, for example, do a transfusion in the future? Are there particular banks that have rare blood types where people who have developed
many antibodies to various antigens can still find blood? How do you work around those issues? Well, one needs to be creative, so let’s get some definitions, orthologous blood autologous who pronounced autologous is your own blood being given back to you, and so some of our listeners may say, why can’t I store my own blood? Well, if your blood count is high enough, you can store your own blood someplace and it used to be very popular to do that during the AIDS epidemic when people were very concerned Part of standard of care the need to provide it their own blood really wasn’t important anymore. And many blood centers stopped that practice. One of the problems with donating your own blood is you have to have a blood count high enough, otherwise you become anemic and you just have to give you the blood right back or they were actually blood banks that were set up where you could freeze blood, which was fine as I used to say, unless you’re on a vacation in Hawaii.
And something happens and you need blood and the blood is frozen in the New York or in Washington or New Haven. And you can’t get to it. It became clear that donating blood for yourself really wasn’t going to be very useful, and practice is not really done much anymore at all. Very some places don’t even accept some blood centers don’t even accept autologous blood. The second would be a directed donation where a family member would donate a unit of blood specifically for. The patient that requires, of course that the blood be compatible, which is often is not. In addition, come, it’s not just a relative, but some people wanted close personal friends, or, as I used to comment, the captain of their bowling team was a close friend, so they wanted the captain of the bowling team to donate blood for them because they believe that they were their friend, they were biologically safer as a donor and they didn’t have to
worry about different diseases. Well, quite frankly, you don’t know what. The captain of your bowling team is, it does after they leave the bowling alley. So directed donations as a means of getting blood from someone you’re comfortable with doesn’t is in practice much anymore either. So that leaves us with the third category, which is what is called allogenic LLOGENEC, which is blood from other people. And that’s what almost all the blood that we provide is blood from people who are concerned about their fellow. Human and they donate blood or they donate platelets or they donate red cells or plasma to blood centers. And that’s the blood that’s given. We have ways of matching the blood so that the antigens I talked about are not a problem. We pick out for someone who was typo. We give old blood. If someone is type A, we can give type A blood or type O blood and so forth and so on for the various antigens. And we have a whole system set up in blood banking of. Of cells that allow us to determine blood that’s compatible and we do
that so that kind of compatibility testing is sort of the bread and butter of what blood banks do and that’s that is taken care of if it comes to problems where someone with a local blood bank can’t find anything that’s compatible. You have systems like the Red Cross that have 35 or 40 blood centers around the country and they have what they call rare donor files where they have peoples blood types on record and they can ask for blood to be sent if they have them frozen or they may have liquid. And there are ways of working with the larger blood providers to work around that issue. There are other blood systems besides the ABO system. One is the HLA system and people may have antibodies to HLA or platelets. There are platelet antigens like there are red cells and again the Red Cross has donor records and we can test and find people who are compatible for the patient. There’s a whole series of things that we have to do.
You can’t just have a small blood bank working on its own. You really need to be part of a large system, certainly a hospital like Yale, with 1600 beds and many, many patients who are fortunately living longer and longer with malignant conditions that are treatable. But when they’re transfused a lot during their therapy when they come back, if they have a relapse then the possibility of having incompatible blood either for red cells or incompatibility with platelets becomes a real issue and you need a large support structure in blood centers to provide blood so that the patient can be treated and go into remission again. So there’s a lot we have to do. We consult on a lot of different issues and it keeps us pretty busy. Great, well, we’re going to take a short break for a medical minute. Please stay tuned to learn more about transfusion oncology with my guest doctor Edward Snyder. Funding for Yale Cancer Answers comes from Smilow Cancer Hospital where 15 care centers offer access to oncologists committed to providing patients with cancer and blood diseases.
individualized, innovative care.

Find a Smilow Care Center near you at yalecancercenter.org.

The American Cancer Society estimates that over 200,000 cases of Melanoma will be diagnosed in the United States this year, with over 1000 patients in Connecticut alone.

While Melanoma accounts for only about 1% of skin cancer cases, it causes the most skin cancer deaths, but when detected early, it is easily treated and highly curable.

Clinical trials are currently underway at federally designated Comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital to test innovative new treatments for Melanoma.

The goal of the specialized programs of research excellence and Skin Cancer Grant is to better understand the biology of skin cancer with a focus on discovering targets that will lead to improved diagnosis and treatment.

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 Ed Snyder.
We’re talking about transfusion oncology and right before the break Ed you were talking about the fact that some cancer patients require multiple transfusions and there’s really a benefit to being part of a large system such as the Red Cross, where if you have developed antibodies to a particular antigen in blood, there still are rare donors who could provide blood for you, but I wonder about other modalities that might actually reduce our need for blood transfusions. So what are your thoughts on things like that? I know that for many of our cancer patients there are drugs, for example, that oncologists use either to increase red blood cells or white blood cells. How effective are they and do you find that that reduces the transfusion needs for patients? Well, yes, the saying that we have in transfusion is the safest unit of blood is the one you don’t get. And even though we do everything we can to ensure the blood safety, there are still the possibility of concerns regarding fever or transmission of illnesses.
As anytime you do any kind of a transplant which really is a transplant is really what a blood transfusion is. Only it’s a transplant of red blood cells.

There are a variety of reagents which are designed to stimulate red cell production from some of those have shown to cause problems and are not used as often as they were.

There are agents that can be used to stimulate platelets as well. But those are predicated on the fact that your bone marrow can actually make more if your bone marrow is damaged and you don’t have the cells that can respond to those chemicals and actually make more of those kinds of cells that they’re not going to be effective.

Although there are those chemical reagents that can be used, they may in some patients have limited usefulness, so a transfusion is needed, they still need to be there. One of the things that’s important about that is a concern about the reactions. And there’s a variety of types of reactions,
and that’s because when you’re giving a foreign protein, which blood cells have proteins on them, you can get a fever. There’s that in and of itself is not dangerous. It’s uncomfortable, and we like to minimize that from happening. But patients do get a fever. They can also get hives, or they can get allergic reactions they can also have some other kinds of complications, all of which the transfusion service is aware of and we try to minimize as much as possible.

One of the areas that’s a really big concern is, as I mentioned earlier, infectious problems and that has led to the production of a whole new field of transfusion medicine, which is pathogen reduction. 10-15 years ago if there was a virus that came out like Zika or West Nile, we knew there was a virus that had entered the blood supply, molecular biology was used to identify the virus, determine where it could be neutralized, and
tests were made to identify it,
treatments were developed.

But then all of that cost money,
and then the hospitals and the blood centers had to spend a lot of money.
For that,
the FDA took a long time to approve the testing and evaluation of donors for that particular illness.
And while all this was going on,
Medicare may or may not have reimbursed for it.
So there was a financial what I call the banking part of blood banking,
and then every time you got through with one virus, another one came along.
So the field decided to move to a new type of tech that is called a reactive approach.
That is, you identify a pathogen of some sort or something that shouldn’t be in blood,
whether it’s a virus or bacteria,
and then you try to mitigate it or get rid of it.
This pathogen reduction technology is not reactive, it’s proactive.
There are reagents that are put into the blood bag that are designed to inactivate pathogens by attacking the DNA and RNA of those pathogens,
the human red cells and platelets do not have DNA or RNA because it’s not part of what that particular cell has, they had them when they were growing, but when they become mature cells, the DNA and RNA isn’t there. So the only thing that has DNA or RNA in a unit of blood is a pathogen. So if you can put chemicals in that affect the DNA or RNA, you’re really sparing the good cells and you’re just trying to get rid of any pathogen. Well, you can say with all the testing why should there be a pathogen there? There shouldn’t be, but sometimes pathogens are in very low levels like bacteria, but then they can grow. Other times, new viruses come in like the COVID-19 virus is not transmitted by blood, fortunately, as bad as it is, and it’s a horrific virus, but it is not transmissible by blood. The HIV virus or AIDS with the pathogen reduction technology puts reagents in the blood bag that will inactivate pathogens
and many pathogens share common DNA or RNA types so that the reagents that are put in will be effective against them. Indeed the pathogen reduction technology that has been studied and proven to be successful doesn’t activate the COVID-19 virus, although it’s not a bloodborne problem, but the next one might be, so pathogen reduction has been approved for platelets and for plasma they are currently doing clinical trials for red cells and we are doing several of those trials at Yale and at 15 other sites around the country. once we have pathogen reduction approved then we will have a much safer blood supply because not only will we be testing for known viruses and pathogens and bacteria, but also for unknown ones, which is critical for the safety of the blood supply. These kinds of technologies, molecular diagnostics and so forth are really the future of transfusion. In addition, there are other types of approaches, immunotherapy to treat patients.
0:22:24.66 –> 0:22:25.749 instead of using chemotherapy that I mentioned earlier,
0:22:25.75 –> 0:22:27.46 which can have cytotoxic,
0:22:27.46 –> 0:22:28.9 which means it’s toxic to cells
0:22:28.9 –> 0:22:31.06 which can lower the amount
0:22:31.125 –> 0:22:33.057 of bone marrow that
0:22:33.057 –> 0:22:34.345 you have. Other types of therapy CAR
0:22:36.55 –> 0:22:38.89 T cell therapy you may have heard
0:22:38.89 –> 0:22:41.002 of or other types of immunotherapy
0:22:41.002 –> 0:22:43.507 where you do not depress the bone
0:22:43.507 –> 0:22:45.59 marrow when those patients may not
0:22:45.59 –> 0:22:47.34 need transfusions because their blood
0:22:47.34 –> 0:22:49.688 counts don’t get that become that low.
0:22:49.69 –> 0:22:52.072 There are other aspects of transfusion
0:22:52.072 –> 0:22:54.066 medicine that those patients
0:22:54.066 –> 0:22:56.754 require and we don’t have time in this
0:22:56.76 –> 0:23:02.07 discussion to go into all of that,
0:23:02.07 –> 0:23:03.637 but you can be sure that the blood
0:23:03.637 –> 0:23:06.091 transfusion service at the Hospital
0:23:06.091 –> 0:23:08.711 is working closely with the oncologists
0:23:08.711 –> 0:23:11.111 and the surgeons to ensure that the
0:23:11.11 –> 0:23:13.09 best and the safest possible blood for
0:23:13.09 –> 0:23:15.629 their patients and our field grows
0:23:15.63 –> 0:23:17.85 as the field of therapeutics grows.
0:23:17.85 –> 0:23:18.96 So we have the patient’s best
0:23:18.96 –> 0:23:22.155 There are many sort of tricks in our bag
0:23:22.155 –> 0:23:25.32 if you will, of how we can provide
0:23:26.86 –> 0:23:29.572 Again, is a critical advance in the field
0:23:29.572 –> 0:23:32.38 and we just have one more cell type.
The red cells that the research is being done on now to have that available in a couple of years. And the goal, of course, is to be able to treat patients and eventually just do away with this field of transfusion, because you won’t need to give blood. But that’s not in the foreseeable future, so the best we can do is provide the safest possible blood, the least amount needed, and the best quality for our patients.

And you mentioned the term pathogen reduction, it’s not pathogen elimination, but it still is really low odds that people get infections with blood these days. Can you remind us about those numbers? What is the risk of getting HIV or hepatitis from a bag of blood these days? The risk of HIV is in the millions, one in a million, one in many millions. That’s for HIV. It’s also true for other types of viruses. Hepatitis is somewhere in the range
of about one in 250,000 to 100.

I’m sorry 1 to 250,000 to 1 to 500,000 for bacteria.

The numbers are higher because bacteria are much different organisms than viruses so the risk of getting a septic transfusion reaction is extremely low,

but the risk of getting some bacteria growing in blood is somewhere in the range of 1 to the 30,000 in that range which are several orders of magnitude less than the HIV.

Part of that problem is you can’t test for all the different kinds of bacteria that there are. Some of them grow slowly.

It depends on where the bacteria came from.

There shouldn’t be any bacteria in blood, and most of the time they’re not.

But that’s where the pathogen reduction comes in,

because pathogen reduction would inactivate any viruses or any bacteria that get through the testing that we have.

So it’s not something to be concerned about.

Because the donor history is extremely inquisitive.

We’re asking a lot of questions,

many of which took years to get accepted because
a lot of the questions relate to sexual practices and many people were offended by those questions when we started asking it when we realized that HIV was sexually transmitted. But it was required to do it for the safety of the patients who are receiving the blood. But now that we know more about how to treat these diseases, many of those individuals come who are negative for these various tests are able to donate blood and it’s a different field. We have to grow with the field as the knowledge grows and that’s what transfusion is, there’s a practical side for the patient care. There’s the collection side and there’s also the research side which is allowing us to advance the field in so many different ways. One last question is, perhaps, we had mentioned the fact that as therapeutics advance we may have less and less need for transfusion, but at the moment it still is a part of clinical care. How do you get around the needs of patients
who cannot take due to religious reasons for example, blood?
Are there other options for them outside of a transfusion?
That’s an excellent question. There are individuals who do not want a blood transfusion. For a variety of religious reasons or other reasons, for those individuals, consultation with the patients physician is required, as well as the family.
We have a family meeting to discuss options and if blood transfusion is not one of them you mentioned the various reagents that are developed to stimulate the production of platelets or red cells in the person. Those chemicals can be given that may be possible to take some blood from the patient prior to treatment and store it so that if the patient’s count does drop, they will have stored their own blood in advance, which in someone who doesn’t want to get transfusion, may be willing to accept their own blood. Some individuals don’t want to accept blood from themselves, that’s been taken out of their body, separated, stored, and then given back.
So it depends on the degree to which the
individual will be willing to accept blood, but those can cause some very difficult treatment situations. That has to be discussed with the patient, the patient’s family, the physician and the blood bank. Doctor Edward Snyder is a professor of laboratory medicine 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. Was provided by Smilow Cancer Hospital and AstraZeneca.