

Dr. Sukru Emre, Organ Transplants for Cancer Treatment January 16, 2011 Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. I am Bruce Barber. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Wilson is a Professor of Therapeutic Radiology and an expert in the use of radiation to treat lung cancers and cutaneous lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1-888-234-4YCC. This evening, Francine and Lynn are pleased to welcome Dr. Sukru Emre to the program for a conversation about transplantation. Dr. Emre is Section Chief of Transplantation Surgery and Director of the Yale-New Haven Transplant Center. Here is Francine Foss. Foss Could you start us off by telling us what the transplant program is, and what it does? Emre For anyone who develops end-stage organ disease, we will be able to change the organ, getting the organs from cadaveric donors, some of the transplants are with living donors and we can change the organs and handle the problem accordingly. Wilson How did you become interested in transplantation and what are your specific clinical interests? Emre My subspecialty is hepatobiliary surgery and I was trained before the 1980s. At that time transplantation was just coming to the surface, especially with the liver in those days, and we did not have anything to do but hold the patient's hands while they are dying, because when we diagnosed cirrhosis, we had very minimal options to offer them. For someone who has bleeding we used to do shunt surgeries or sometimes with the small tumors we had to do resections in those days. So for me transplantation was a natural extension of the hepatobiliary surgery. Foss Can you tell us what the most common organ is that is transplanted in the United States? Emre In the United States, the most transplanted organ, of course, is the kidney, because we have two kidneys as opposed to one liver, one heart, and one pancreas. Therefore, the kidney is the most common transplantation in the United States and around the world. There are now more patients waiting for kidney transplantation. To be exact, in the United States, a little lower 100,000 patients are waiting for transplantation and among them 70,000, are waiting for a kidney, and 17,000 are waiting for a liver. These are the two big groups. Wilson So with these organs, when is a transplant typically done, say, for a kidney patient and for a patient with a liver problem? Emre For kidneys, we have two categories. For children, we prefer to do the transplant before they start dialysis. On the other hand, for adults, many times we do the transplant once they start dialysis. That is the indication for transplantation. For liver transplantation, we have a set system for allocating the organs, which became the gold standard at this point, what we call, MELD, the Model for End-Stage Liver Disease scoring system. We usually prefer not to transplant anyone with a MELD score less than 15, because those individuals one-year survival, without transplant, is 4:00 into mp3 file <http://yalecancercenter.org/podcast/jan1611new-cancer-answers-emre.mp3> almost 100%. So the transplant is not justified. There are other signs we use to decide whether a patient is eligible for transplantation or not, what we call degree of the illness, or cirrhosis. We categorize the cirrhosis into two types,

one is compensated cirrhosis. Although a patient has cirrhosis, their function is almost 100%, they are 100% functional, they go work and do the work and so on and so forth. As opposed to de-compensated cirrhosis, those individuals develop serious side effects of the cirrhosis, including what we call encephalopathy or cloudy mind, esophageal variceal bleeding, muscle wasting, bone disease, as well as spontaneous bacterial peritonitis and other infections. Those are the signs that will tell us that patient is doing poorly, and we have to hasten the transplant operation.

Foss Can you tell us a little bit about the team approach in transplantation, what other physicians are involved and how does a patient go through the process of getting a transplant?

Emre At Yale we have a real team approach from head to toe. When patients come or are referred to us for transplantation, we have our coordinators, we have our hepatologists and nephrologists, for kidney, they see patients and they evaluate the patients. During this evaluation process, there are many other disciplines that help us out, including cardiac evaluation, pulmonary evaluation, dental evaluation, colonoscopies, other endoscopies if it is necessary, psychologic evaluation, social work evaluation, so on and so forth, and there are specific cases where we ask for more evaluation, for example, patients with bone problems, and there we can talk with orthopedics or endocrine people, especially metabolic bone diseases, and patients with liver tumors, and we always discuss with a medical oncologist about what to do with that, and plus we ask anesthesia intensive care units and other disciplines. For example, for pediatrics, we work with the child psychiatric services for their psychologic evaluation or whether they have any post-traumatic stress. We do some studies to decrease the post-traumatic stress of these patients. We have a special program with the psychiatrists, especially for adult patients with substance abuse, called the liver SMART study that we do group therapies for these patients in order to increase their sobriety and insight about drinking and other problems so they will become better candidates for transplantation. After transplant, definitely, they do better. Therefore, it is a perfect setup before moving to this team approach, and in inpatient, after transplantation or in a patient before a transplant, they get sick, requiring admission to the hospital, so we have social workers, we have pharmacists, we have nutritionists, and they work with them and if there is a problem, we address those issues, and our job is just to make sure that we take care of every aspects of the care of our patients.

Wilson I know that you have a very robust and busy surgical service, where do your patients come from? Are they from Connecticut, the region, other states, other countries?

Emre We have a mix of everything. The first thing is to help our local patients, especially citizens of Connecticut, but we have other patients and they are from Chicago, from Oklahoma, from Puerto Rico, from Turkey and Italy and Gulf countries and many different patients, and they come to us because of our reputation and because of our good results.

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Foss Can you talk to us a little bit about the complications that can happen with a transplant?

Emre Transplantation is a very difficult operation. First of all, we are crossing the line and we are doing certain things against a modern nature, so there are many hurdles to overcome, and in pre-

transplant for livers a major problem is development of esophageal variceal bleeding or what we call spontaneous bacterial peritonitis, because of the severe portal hypertension, patients develop fluid in the abdomen, what we call ascites that ascites may get infected, and therefore, we have to deal with this infectious problem, and the other thing is muscle wasting related issues. Fractures are more common with patients with cholestatic liver diseases, such as PSC, PBC and we need to take care of that and we communicate with the bone metabolism experts to make their bones sturdier. For kidney transplant patients with dialysis, although we are very grateful that at least we have some remedy while they are waiting for a transplant to alleviate the degree of toxins in the body, dialysis is not an easy process for the patients. In every dialysis episode, the patient's blood sugar comes down to 35-40, and blood pressure is always down, and they really feel bad after every dialysis session; it is not ideal. As a result, especially in patients more than age 50 with kidney diseases and cardiovascular problems, complications are more common leading to their demise. So that is the major problem for the kidney. The second problem is bone problems, and because of the dialysis they lose their bone minerals and their bones are very weak as well. Post-transplant, early after transplantation, there are many problems, for example, clotting in the vessels, what we call hepatic arteriothrombosis, portal vein thrombosis or hepatic vein thrombosis. When we look at the nationwide data, the incidence of these complications is around 5% to 7%, in our case, it is 0%. We have bile duct complications, or what we call bile duct stricture or bile leaks after surgery. Nationwide it is somewhere around 20%, ours is 15% here, and also we have infectious complications. I am really grateful to the hospital because we have a very robust infection control system, hand washing, wearing gowns and gloves before touching the patients. Therefore, our infection rates overall are really, really low, somewhere around 2% to 3% after transplant operations. As opposed to nationwide, this number goes to 30% to 35%. For me, the most important problem in early post-operative period is the infection, because in order to treat the infection, we have to decrease the immunosuppression. On the other hand, in order to make the liver function or kidney function, we have to give immunosuppression. In a way that pushes us into a corner and it makes the case very difficult for us. Late complications, especially in pediatric patients, are opportunistic infections, what we call major culprits such as CMV and EBV infections. The reason I say pediatric patients are more of a problem is because most of them are aged less than 5, their CMV and EBV titers are negative. Since we are doing split and living donor liver transplants most of the organs come from the adult patient population. They are CMV and EBV positive, and that creates a high-risk group for the patients and children can develop CMV and EBV infections. Especially EBV is really important because EBV can lead to what we call post-transplant lymphoproliferative disease, which is tumor development. Therefore, we check out patients routinely and we control monthly CMV and EBV titers and make sure that everything is under control.

13:03 into mp3 file <http://yalecancercenter.org/podcast/jan1611new-cancer-answers-emre.mp3> Wilson What sort of cancer patients do you see? Emre For adults

the main cancers for liver are hepatocellular carcinoma and cholangiocarcinoma. Most of our patients have hepatocellular carcinoma, the reason for that is underlying cirrhosis. We rarely see a patient with normal liver functions. Normal liver structure without cirrhosis with hepatocellular carcinoma may be 3% to 5% of our patient population. For the cancer development it may include hepatitis C, as we know, hepatitis C is the major reason at this point for development of liver cirrhosis and our estimates tell us that up until year 2020 we are going to see increase in hepatitis C cases. Our calculations tell us that in someone who is diagnosed with hepatitis C cirrhosis, approximately 20% will develop hepatocellular carcinoma within 5 years. So this is a major problem for us, and of course in pediatric patients we have another tumor, what we call hepatoblastoma, which is a totally different etiology without underlying liver injury.

Wilson Welcome back to Yale Cancer Center Answers. This is Dr. Lynn Wilson and I am joined by my co-host Dr. Francine Foss. Today, we are joined by Dr. Sukru Emre and we are discussing the Yale transplant program. Dr. Emre, could you talk to us a little bit about the hepatobiliary cancer program?

Emre When I came to Yale and was developing and improving the kidney program and developing the liver program, I thought that it was wise to develop a hepatobiliary cancer program and that is the program we have now. It is a multidisciplinary program and involves a transplant surgeon and medical oncologists, hepatologists, interventional radiologists, diagnostic radiologists and the oncologic surgeons. The advantage is providing comprehensive care to our patients. To give an example, someone with liver cancer and underlying liver cirrhosis, this individual does not need to go one place to another place and one consult to another consult. The patient will be prepared and presented in our meeting and there will be only one decision made for this patient. They will of course reach a decision quickly without wasting any time and also that will be the best decision for the patient because it is coming from an expert panel and is based on the patient's disease.

17:34 into mp3 file <http://yalecancercenter.org/podcast/jan1611new-cancer-answers-emre.mp3> category, underlying cirrhosis and degree of cirrhosis. The treatments included are removing the tumor together with part of the healthy liver, what we call a liver resection. In order to do that the patient should have very good liver functions. If the patient has cirrhosis which is not treatable for resection, those individuals will undergo what we call ablation techniques, either radiofrequency ablation or what we call transarterial chemoembolization. Those techniques allow us to keep the tumor in the liver and control the tumor; therefore, the patients never lose the chance of transplantation later on. And of course, a patient with a liver tumor is still a candidate for transplantation if they have living donor options. We prefer to go directly to a living donor or liver transplant patient. Transplant will take care of two problems, one it takes care of the tumor, and two, it takes care of the underlying liver disease, but the aim of this program is to provide our patients the best possible care.

Foss You mentioned that in some cases you might resect only part of the liver. How often can patients with liver cancer expect to be able to save their liver?

Emre If there is underlying cirrhosis, eventually these individuals are going to need transplanta-

tion, there is no doubt about that, but on the other hand, we have a shortage of organ donors. If we think that the patient has what we called Child's A cirrhosis, early cirrhosis, compensated cirrhosis, with normal liver enzymes including INR, bilirubin and a normal platelet count, those are the patients suitable for liver resection. Unfortunately, many of our patients have advanced cirrhosis and as a result performing liver surgery for them is really difficult. We also do resection for patients with different liver diseases such as liver adenoma, liver hemangioma, and other liver tumors such as liver hemangioendothelioma and liver angioma, or angiosarcoma, and in some patients, we prefer liver surgery. Wilson Obviously, these procedures are very complicated and complex and require a tremendous amount of expertise and just for the benefit of our listeners, this is obviously not the type of procedure that is done in every hospital. How many places in Connecticut, for example, provide a service as comprehensive as yours, Dr. Emre? Emre Our program is really the number 1 in the country, not just in Connecticut, but in Connecticut we have two liver transplant programs and two kidney programs and one is in Hartford, one is here at Yale. If we look at the SRTR data which I will explain a little bit, the Federal Government mandates all transplant programs in the United States and they have to submit the results to the Federal Government to what we call the Scientific Register of Transplant Recipients. Therefore, we have center-specific data as well as nationwide data and statistics. Based on those statistics, when you look at our one year survival in pediatric liver transplantation, it is 100%, adult liver transplantation is 98%, and therefore our program is not comparable with any program. We have expertise, we have resources, we have know how and plus that we have a multidisciplinary team approach to serve our patient's in the best possible way.22:00 into mp3 file <http://yalecancercenter.org/podcast/jan1611new-cancer-answers-emre.mp3>Foss You also mentioned that there is a lot of care that goes into the patient after the transplant, that the patient is on immunosuppressive medications. Can you tell us little bit about that? Emre The organs are coming from another individual, therefore, the recipient immune system is going to recognize the organ as a foreign body and will try to get rid of, what we call rejection. In order to prevent rejection, we have to use anti-rejection medications, in other words, the immunosuppressive medications, and of course, those medications are heavy-duty medications with a lot of complications that require all of the expertise to run the immunosuppression. I always give the example to my patients that running the immunosuppression is similar to tightrope walking, one side is rejection and one side are all the side effects of all these medications, thus this medical act to run the immunosuppressive medications. If anyone reads all the complications of these immunosuppressive medications they definitely can freak out because there are many complications. On the other hand, we rarely see all these complications because we follow our patients very carefully, and for example, after we discharge the patients from the hospital, for the first month we see them two times a week, and during these visits we check their immunosuppressive blood levels, we examine them, we check their kidney functions, liver function, electrolytes, everything, and we make the adjustments accordingly. That will give us the best possible results for our patients. Those

immunosuppressive medications make the immune system very weak and that sets a stage for development of opportunistic infections. Therefore, we have to follow our patients carefully. We have to cover our patients for certain bacterial infections, viral infections, or fungal infections after surgery. Another note I would like to make is early on we use high doses of immunosuppressive medications but as we go we decrease the immunosuppressive medications, dose-wise as well as the number of immunosuppressive medications we use, and usually six months after transplant, our patients are on only one immunosuppressive medication with minimal dosage. Foss Will they ever stop these medications or are they pretty much on them for life? Emre Based on our current knowledge, we tell our patients that they are going to use those medications indefinitely. In my experience with liver transplantation, which is 3000 transplants, I have maybe 50 patients where we were able to stop all the immunosuppressants and they are doing very well, those are mainly pediatrics patients actually. Wilson What sort of changes have you seen in the field of transplantation in the last decade, and as a second question, what changes have happened here at Yale in the last 10 years? Emre When I got involved in the transplant field in the beginning of the 1980s, it was difficult in every aspects of transplantation, in terms of availability of different immunosuppressive medications, where now-a-days we have great immunosuppressive medications. As a result, I do not remember any patient I lost secondary to rejection or chronic rejection, except non-compliance issues. The second issue is development of ICU, anesthesia care and development of the field of hepatology and also technical expertise, performing the liver transplantation, those are the general guidelines. 26:07 into mp3 file <http://yalecancercenter.org/podcast/jan1611new-cancer-answers-emre.mp3> But specifically we also developed something that is very unique, a multidisciplinary team approach, that is the major change and we added it to all transplant fields. When we do rounds, rounds are done everyday, there is one transplant hepatologist, one transplant surgeon, a hepatology fellow, a surgical fellow, a transplant surgical fellow, residents, PAs, MPs, pharmacists, social workers, nutritionists and nurses altogether. Therefore, we give our patients better care. I developed this methodology in our multidisciplinary team approach. It was in 1997, I was assigned to be at the pediatric liver transplant program at Mount Sinai and at that time I built the program in a multidisciplinary fashion. Last year, CMS mandated that all programs should be multidisciplinary. I had that vision, and because I knew what my patients at that time needed, I followed my gut feelings and instincts. What changed at Yale in the last 10 years? I cannot say in the last 10 years, but I can tell you in the last 3-1/2 years I have been here, I believe that many things have changed. The medical school and hospital have come together to build excellent clinical programs and there is a focus on developing translation of research that the researching should be 100% meaningful that can be of use for patient care and improving outcomes. Dr. Sukru Emre is the section chief of transplantation surgery and Director of the Yale-New Haven Transplant Center. If you have questions or would like to share your comments, visit yalecancercenter.org where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening

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