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, Ariel Jaffe is an assistant professor of medicine and the section of digestive diseases at the Yale School of Medicine where Doctor Chagpar is a professor of surgical oncology. Ariel, maybe we can start off by you telling us a little bit about yourself and what exactly you do. Sure, so basically I specialize in the care of patients that have advanced liver disease and I work both in the transplant program, so patients who need to go on to have a liver transplant, and also patients that develop liver cancer, which is an extremely common complication in patients that have chronic liver disease.
So let’s talk a little bit about that. So when you’re talking about patients who require transplant, what kinds of conditions require liver transplants? I mean, are these patients who have hepatitis, cirrhosis, tell us a little bit more about what kinds of conditions will lead you down the path of transplant? Most commonly, patients that develop end stage liver disease, which is what we commonly know as cirrhosis are the ones that we do evaluate for liver transplant, and that could be from a variety of different causes. Some which you alluded to. You know patients that have chronic viral disease. Certain toxins, like alcohol use, certain genetic disorders, patients with obesity and diabetes which can lead to fatty liver and end stage liver disease. Once you start to have complications from that, we generally start to consider you for transplant. There are a subset of patients who may
actually have really well preserved liver function and look and feel well, but in patients that develop liver cancer, which sort of as I mentioned, is an extremely common complication. 8 to 10% of patients with cirrhosis will develop cancer each year. That’s another indication in which we go on to consider them for transplant. Because transplant will not only cure the cancer, but it will actually cure their underlying liver disease, which is the major risk factor for their cancer development. So tell us a little bit more about that in terms of cancer. Are all patients with liver cancer candidates for transplant or is it only those who have that underlying chronic liver disease that would make them potentially a candidate anyways? So not all patients are candidates for transplant. The majority of patients who develop liver cancer will have some form of chronic liver disease, but interestingly, we’re actually seeing a unique population who don’t have underlying advanced liver disease.
0:03:16.97 –> 0:03:19.69 go on to develop liver cancer and it’s
0:03:19.69 –> 0:03:21.335 a little bit of a controversial field
0:03:21.34 –> 0:03:24.56 if those patients should be
0:03:24.56 –> 0:03:26.54 considered for transplant or not.
0:03:26.54 –> 0:03:28.54 But in terms of those that
0:03:28.54 –> 0:03:30.249 may have chronic liver disease
0:03:30.249 –> 0:03:31.777 and develop liver cancer,
0:03:31.78 –> 0:03:33.418 there are certain criteria that need
0:03:33.418 –> 0:03:35.812 to be met for patients to be considered
0:03:35.812 –> 0:03:38.23 for transplant and some of that includes
0:03:38.23 –> 0:03:41.366 how extensive their liver cancer is.
0:03:41.37 –> 0:03:42.357 So for example,
0:03:42.357 –> 0:03:44.66 if it’s spread outside of the liver,
0:03:44.66 –> 0:03:46.245 they would not be good
0:03:46.245 –> 0:03:47.196 candidates for transplant,
0:03:47.2 –> 0:03:49.741 or if they have a large amount
0:03:49.741 –> 0:03:51.68 of tumors within the liver,
0:03:51.68 –> 0:03:54.08 they would not be considered
0:03:54.08 –> 0:03:54.88 good candidates.
0:03:54.88 –> 0:03:57.267 We also sometimes like to look at
0:03:57.267 –> 0:03:59.859 patients if they have recurrent cancer.
0:04:00.586 –> 0:04:02.764 We’re more likely to consider them
0:04:02.764 –> 0:04:04.855 for transplant or if their underlying
0:04:04.855 –> 0:04:07.223 liver is really very very sick so
0:04:07.223 –> 0:04:09.323 that they have other complications of
0:04:09.323 –> 0:04:11.55 liver disease in addition to cancer,
0:04:11.55 –> 0:04:12.72 then you know,
0:04:13.028 –> 0:04:15.184 we’re more likely to want to pursue
0:04:15.184 –> 0:04:16.689 transplant in those patients.
0:04:17.79 –> 0:04:20.009 One of the things that
0:04:20.009 –> 0:04:22.268 people might be thinking about when
we think about transplant is that oftentimes people may be under the impression that patients who have cancers, for example, may not be a potential recipient of organs, but it sounds like for liver cancer, that’s not the case, that if you have liver cancer, even if it’s recurrent liver cancer, you can still be on the organ recipient list. Is that right?

Yes, actually it’s a really unique cancer and it’s a really unique perspective to have. In that transplant is considered one of the curative therapies, and really can’t have spread outside the liver or you can’t have such an extensive tumor burden. But because you’re really replacing the liver, you’re not only treating the cancer, but you’re sort of getting rid of the damaged organ because we like to think of liver cancer in particular as sort of a complication of a failing organ. I think it’s an important perspective to have. Yeah, it does not mean that
0:05:33.555 –> 0:05:34.343 you’re not a candidate.
0:05:34.35 –> 0:05:36.246 It’s actually one of the most curative therapies and really currently in the United States,
0:05:37.568 –> 0:05:39.228 honestly,
0:05:39.23 –> 0:05:39.539 a quarter of transplants
0:05:41.084 –> 0:05:42.744 are done for the indication
0:05:42.744 –> 0:05:44.216 of having liver cancer.
0:05:44.61 –> 0:05:48.018 Wow, so the other thing that we often think about when we think about transplant
0:05:48.018 –> 0:05:51.53 is the universal shortage of organs.
0:05:51.53 –> 0:05:54.8 Liver is one of those nice organs that there
0:05:54.8 –> 0:06:02.402 is a potential for a living related donor.
0:06:02.41 –> 0:06:04.558 How often is that used in patients who have liver cancer?
0:06:04.558 –> 0:06:08.164 Can you talk a little bit more about that?
0:06:09 –> 0:06:11.894 Definitely so the liver is just one of the most remarkable organs, and its ability to regenerate.
0:06:13.24 –> 0:06:15.27 So in certain patients who are candidates for a living donor organ,
0:06:15.27 –> 0:06:17.48 meaning that a part of the liver is taken
0:06:20.126 –> 0:06:22.681 from a donor and put into the recipient and it will actually grow to a normal size,
0:06:33.166 usually in about 12 weeks time.
0:06:34.21 –> 0:06:35.734 To determine if someone is a candidate for a living donor,
0:06:37.48 –> 0:06:39.154 there’s a few factors that we have to take into account.
0:06:43.344 One is the size of the patient
0:06:46.566 because there’s a certain sort of
massive liver that you would need to sufficiently do its job in a person. So if you’re a really really big guy or big girl, your candidates might be limited. You would really need someone who is equally as tall or as large as you. The second thing is, if you’re really incredibly sick and have a lot of complications from your liver disease, there’s concern that you may not be able to tolerate just a piece of an organ. So it’s actually something that we use quite often, and it varies based on programs and how large the programs are, but we definitely do a lot of living donors in our center here, and it’s a really a great option for a certain subset of patients. And tell us a little bit more about how that works, because I think that for many people just the thought of having a relative or a loved one being diagnosed with a potentially treatable cancer, but that you can help with, you can help give them a new life, is really awesome in terms of the actual benefit that you can provide,
but people may have some questions about that.

Yes, so it’s definitely a pretty grueling process and the way that it works is once we determine that someone is ineligible as a transplant candidate, they’re then open to have either relatives or even just altruistic donors that can call in and be screened to see if they’re compatible and usually it starts with just looking at blood typing to see if there is a compatibility. The rejection is a little bit different in the liver compared to other organs, so it’s nice in that there’s not so many factors that have to be directly matched to be considered a compatible donor. But once we think that there’s not going to be overt rejection, and that really comes down a lot of times to compatibility and blood typing. We have a very strict process to make sure that the donor itself is someone who would do very well going to surgery, that they have no underlying liver disease, and that ultimately we feel would essentially come out
unscathed should they decide to go forth with donating their liver. It’s extremely rare in general to have any type of rejection from incompatibility. Just because our ability to screen and make sure that blood types and things match is so great now, so that’s not generally a major major concern, but there’s a lot of strict processes in terms of making sure the size is appropriate that the recipient, whatever portion was donated, that would be enough for the patient not to have what we call post operative liver failure or liver insufficiency. So I would say technology and our screening strategies are just so remarkable now that those factors are really very well detailed generally within a year after transplant, you can get patients down to an extremely
low level of immunosuppression which again is slightly different than other organs where rejection rates are much higher and it’s interesting because there are certain reports of patients being able to completely come off of immunosuppression. And we’ve actually had a few patients within our center that we’ve done that on. It’s a little bit higher risk, and it requires some more close monitoring, but I would say the vast majority of patients are usually on at least one medication for the duration of their life, but it’s again incredibly low dose compared to the majority of other organ transplant recipients. And they quote cured? Yeah, so that’s exactly the hope is that from liver transplant, you’re essentially replacing the entire organ, and so whatever the etiology of that patients, liver diseases is essentially cured. Of course, there’s a risk if patients redevelop viral infections, or if some of the risk factors that led initially to their liver disease are still present. And I think a lot in our population.
the common things are patients who develop fatty liver disease in the post transplant setting, if they continue to have diabetes or obesity, you can develop recurrent disease in the organ. But if patients mitigate their risk factors and go on to live a healthy life, then yes, liver transplant is curative not only for the cancer, but again for the initial cause of their cirrhosis. And so for patients who have liver cancer is transplant one of the things that you think of first or do people have to kind of go through chemotherapy? At least in assessment of surgical resection and so on? Kind of the more commonplace cancer therapies before you think about transplant or is transplant something that is now first line? So it definitely is extremely independent on each patient’s case. If we see a patient who has a single tumor, that’s very small in size, and we think that we can cure them with a local resection, meaning, just cutting out a portion of that liver, that’s generally the first line
therapy that we would actually go to. In patients that have more advanced liver disease and other complications from their liver, if they develop a cancer on top of that, we know that a transplant would cure both of those aspects, so I would not say it’s often firstline, but it’s a curative approach that we definitely have in the back of our heads for a subset of patients that would be good candidates. Terrific, we’re going to learn a lot more about liver cancer and transplant hepatology right after we take a short break for a medical minute. Please stay tuned to learn more with my guest doctor Ariel Jaffe. Funding for Yale Cancer Answers comes from AstraZeneca, dedicated to advancing options and providing hope for people living with cancer. More information at AstraZeneca Dash us.com. 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 family history that includes cancer at unusually early ages, multiple relatives on the same side of the family with the same cancer, more than one diagnosis of cancer in the same individual, rare cancers or a 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 at 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 Ariel Jaffe. We’re talking about patients with liver cancer, and before the break we talked about the whole aspect of transplant as a potential curative modality for patients with liver cancer. But Ariel, just as we were heading to the break,
you mentioned that there are a lot of other things that go into thinking about liver cancer as well, so I wanted to take a step back and talk a little bit about how common is liver cancer?

Primary liver cancer is actually a quite significant global burden. There's over 800,000 new cases diagnosed each year, and actually in the US in particular, it's the fastest increasing cause of cancer and the fastest increasing cause of cancer related death.

When we talk about primary liver cancer we mean cancer that has originated and developed in the liver from the beginning. There are two main types that we think about, so hepatocellular carcinoma, probably accounts for 80 to 90% of primary liver cancer, but another common type that we see that often develops in patients with chronic liver disease is something called cholangiocarcinoma and that arises in the biliary cells, these are the cells that line the little lakes and channels within the liver that sort of drain and modify the
物质是肝脏制造的，称为胆汁。

当你想到肝脏的二次癌症时，很多时候我们讨论的是转移性疾病，即可能已经扩散到肝脏的癌症，但这些癌症的治疗和管理方式与原发性肝脏癌症有很大的不同。

真的很有趣。

我没有意识到在美国，肝脏癌症的发病率和死亡率是增长最快的。为什么是这样？

风险因素是什么？或风险因素？

是的，全球范围内风险因素确实有所转变。以前主要导致肝脏疾病的罪魁祸首是慢性病毒病。

现在我们主要谈论的是慢性乙型肝炎和丙型肝炎，但随着治疗丙型肝炎和控制乙型肝炎的能力，以及在西方世界通过疫苗预防这些疾病，我们现在看到的主要病因是慢性病毒病。
Fatty liver disease or non-alcoholic fatty liver disease, and as we see a rise in the obesity epidemic, we’re seeing more and more patients that develop complications such as diabetes, high cholesterol, central adiposity, meaning a lot of belly fat, which is inflammatory bad fat that the body does not like, and high blood pressure. As we’re seeing more patients develop those complications, we’re seeing a rise in the incidence of fatty liver disease. It is certainly true that there’s just this exponential rise in obesity in America and in the world quite frankly. So let me ask you this, is it possible to reverse that, if you lose weight do you reduce your risk of fatty liver and therefore reduce your risk of hepatocellular carcinoma? Absolutely, generally when patients have developed cirrhosis which is really advanced scarring within the liver, we do say that you can’t reverse completely to having a normal healthy liver, but for a lot of patients who...
are not quite yet cirrhotic, or who may be cirrhotic but have active, ongoing inflammation, which is a big risk factor for the development of cancer, you can absolutely reduce the risk of developing complications from liver disease, and the development of liver cancer.

So in particular for fatty liver disease, really the only kind of approved therapy at this time is the recommendation to lose weight. And generally we say 5 to 10% of weight loss has been associated with reduction in inflammation, reduction in scarring of the liver, and even reduction in the potential to develop liver cancer.

And it’s why we like to really tell patients that a lot of the risk factors to develop liver disease and liver cancer are really preventable. And you see and treat patients with liver disease who may be at risk of developing liver cancer, and you also see patients who have developed liver cancer.

You know if you tell them to lose weight, that’s often easier said than done. Are there any specific recommendations that you give patients?
I’m just thinking that our listeners might be thinking, yeah, I’d love to lose 5 to 10% of my body weight. How exactly do I do that? Yeah, so it is definitely easier said than done, and I think especially in the COVID era where a lot of people were really confined to their home, it’s been an even bigger challenge, so oftentimes what I say to patients is, we kind of go through what they’re eating and their physical activity. And sometimes their food choices. They may think that they’re eating healthy, but when we actually breakdown the calories or the amount of sugar they’re eating, it’s a lot more than they’re aware of so off the bat, I always offer patients to speak with nutrition because I think to have someone hold you accountable and really go through the target of each food group and macro and micro nutrients you should be hitting is very helpful. We also have specific fatty liver clinics and weight loss clinics here, so there are definitely patients even if they’re dieting or exercising, they’re just really stuck in this challenging place and they can’t
0:21:10.25 –> 0:21:12.434 And in that situation there are
0:21:12.434 –> 0:21:14.235 medications that are available to
0:21:15.9 –> 0:21:17.671 So we have a lot of programs
0:21:17.671 –> 0:21:19.24 and a lot of
0:22:22.49 –> 0:22:24.23 Alright, so the news flash
0:22:24.23 –> 0:22:26.55 there is talk to your doctor,
0:22:26.55 –> 0:22:28.79 because there likely is
0:22:28.79 –> 0:22:31.134 help available and we can
0:22:31.134 –> 0:22:33.126 all get through this
0:22:33.126 –> 0:22:34.95 and hopefully reduce our risk.
0:22:34.95 –> 0:22:36.903 But Ariel, I want to just kind
0:22:38.59 –> 0:22:40.858 Let’s suppose it’s a little too late.
0:22:40.86 –> 0:22:44.71 And we develop liver cancer.
0:22:44.71 –> 0:22:47.132 How do you know that you
0:22:47.132 –> 0:22:48.77 have developed liver cancer?
0:22:48.77 –> 0:22:50.75 So how is that diagnosis made?
0:22:50.75 –> 0:22:53.534 Are you going to have signs and symptoms?
0:22:53.54 –> 0:22:56.177 Are you going to go yellow or is this
0:22:56.177 –> 0:22:58.228 something that is picked up
0:22:58.23 –> 0:22:59.92 incidentally?
0:22:59.93 –> 0:22:01.31 That’s a great question.
0:22:01.31 –> 0:22:03.746 You know, the majority of patients
0:22:03.746 –> 0:22:06.426 that develop liver cancer are really
0:22:06.426 –> 0:22:08.638 asymptomatic until it becomes very advanced.
0:22:08.638 –> 0:22:11.059 So at the time that someone may have
0:22:11.06 –> 0:22:14.032 pain or start to have
some vague symptoms like weight loss or significant fatigue or even jaundice or yellowing of the eyes, which suggests that there’s either a blockage in the liver or that the tumor has spread so much in the liver that it’s just kind of taken over any remaining normal tissue, that’s often too late. So really, what’s incredibly important is to identify patients that have chronic liver disease or risk factors for liver cancer. Some which include poorly controlled diabetes, heavy alcohol use, obesity, and make sure that we’re screening those patients. So really all major societies recommend in patients with chronic liver disease that every six months you’re actually screened for liver cancer with the hopes that if you develop a cancer, you can actually pick it up early. And it’s interesting because liver cancer is the only solid organ tumor that could actually be diagnosed based on imaging alone, so it has very unique features when we do a CAT scan or an MRI that basically allow us to definitively tell if this is a hepatocellular carcinoma and oftentimes we don’t even have to do
a biopsy to confirm the diagnosis.

So people who have those risk factors should have a CT or MRI every six months. So we always recommend an ultrasound. That’s the first step for screening, and that’s really just based on sort of cost effectiveness, and you know the fact that it is fairly sensitive, but in some patients, if their liver is very scarred down, so you can’t get a good look at that tissue, or if there’s a lot of obesity, because a lot of fat in the belly can limit how good of a look you can get. In those cases, you may then need to do more advanced imaging, but generally once we see something abnormal on an ultrasound, the next step is to do a cross sectional scan with either a CT or an MRI. And so it’s interesting that liver cancers are one of the few where you don’t need a biopsy to make that diagnosis. So let’s suppose you see that, tell us about some of the medical management, some of the things that are coming down the Pike short of transplant that might be helpful in these patients.
Whenever someone has a new diagnosis of liver cancer, we always want to make sure that it hasn’t spread outside the liver. So that’s a big step, because once it has spread, your treatment is a little bit different, and it’s very important to look at a patient’s underlying liver function, because that plays a major role in understanding if they’re eligible or would tolerate certain treatments.

And outside of transplant, we really do think of liver cancer treatment in either a curative approach or what’s called a palliative approach, and transplant is one of the curative therapies. But other curative therapies include local resection and ablation which destroy the tumor and of course, someone has to be a good candidate to undergo surgery and so if they have really advanced liver disease that would not be an ideal treatment choice, but other curative therapies include something called ablation which is really where you destroy the tumor and...
that can be either through thermal techniques, radiation techniques, electrical injury, and then we think of some of our palliative treatments which include what we call local regional therapies or transarterial therapies, and that’s basically where you can either induce radiation damage or locally give chemotherapy to the tumor to kind of cut off the blood supply and kill that tumor, and then for patients that either are just not responding to those or where the cancer has spread outside of the liver, we start to think about systemic therapy or chemotherapy. And so you know, I can imagine that no patient wants to go through chemotherapy and everybody has heard horror stories about what chemotherapy is like. But very often on this show we’ve been talking about some of the newer advances, especially in systemic therapy, where we really are looking towards personalized medicine, sometimes immunotherapies. Is there anything like that
going on in primary liver cancer?

Absolutely, so I think probably the management for patients with liver cancer that's more advanced has been one of the most innovative fields within liver cancer.

And that's because there have been so many new advancements in systemic therapies. Just a few years ago, we just had one or two medications, and now we have 10 FDA approved therapies. And as of May 2020, so just a little over a year ago, a new combination therapy. One of the components was an immune checkpoint inhibitor, which is one of our immunotherapy medications that actually proved to be the best first line therapy, so it had improvement in overall survival and disease free progression compared to what our prior first line was and is actually now what we try to use for our patients. And I think it's also important to know that oftentimes, when our patients hear that they're going to go on systemic therapy or chemotherapy, they kind of think of the movies or loved ones that they've seen have gotten really very sick.
Or their hair has fallen out or their immune system is completely wiped out, and the medications that we use to treat liver cancer are definitely much more tolerable with significantly reduced side effects compared to what a lot of patients think about for sort of standard chemotherapy for other tumors.

Doctor Ariel Jaffe is an assistant professor of medicine in the section of digestive diseases at the Yale School of Medicine. If you have questions, the address is cancer answers at 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 and AstraZeneca.