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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 cognitive decline after prostate cancer with doctor Herta Chao. Doctor Chao is the deputy director at the VA Comprehensive Cancer Center and an associate professor of Medicine and medical oncology at the Yale School of Medicine, where doctor Chagpar is a professor of surgical oncology. I hear you work at the VA. I feel very fortunate to work at the West Haven VA Cancer Center because it’s so closely affiliated with Yale Cancer Center, we basically can take advantage of a lot of the knowledge and expertise and
resources that are available at your Cancer Center as well. A particularly important thing for the VA is that we’re a tertiary center, and many resources are available that are not necessarily available in the private sector. For instance, if veterans need transportation, we can actually ask our social worker to help. If a veteran needs additional support and therapy, we can actually ask the physical therapist to meet them in the Cancer Center, so it’s very tailored to veterans. Tell us a little bit about when we think about cancer we kind of think of it ubiquitously but tell us about the prevalence of cancer in the veteran population and whether the incidence of cancers and particular kinds of cancers are different in the veteran population as opposed to the general population? That’s a very very important point. I think we continue to learn. For many decades it was actually debated whether certain cancers are really related to an herbaside like Agent Orange.
We know it was widely used during the Vietnam War and many veterans develop cancers that are unusually aggressive, unusually early in their lifetime, and it took many decades before it was recognized that Agent Orange is a carcinogen. For instance, I think soft tissue sarcoma, which is a connective tissue cancer, occurs early in our lifetime. It was recognized earlier that this is probably related to Agent Orange. Exposure has increased the risks of these veterans to develop these cancers. Prostate cancer, for instance, is so common among men and is the most frequent cancer among veterans. But for the many decades it was actually not acknowledged to be Agent Orange related. Not until 2008 there was a very important study done by Doctor Karen Shami at UCLA that actually proved the rate of prostate cancer and aggressiveness of prostate cancer was much higher in the veterans that were exposed to Agent Orange compared to veterans during the same era but not exposed to Agent Orange, so we know more and more that veterans may be
at risk due to service related exposures to certain type of cancer, including lung cancer, prostate cancer, leukemia and lymphomas. These days for men and women who are in combat al ot of times we don’t think about people using a particular agent like Agent Orange in combat, but more it’s artillery, there’s more roadside bombs and so on. Are those also associated with a higher risk of cancers? I think we will find out very soon. Unfortunately my colleagues and myself have been unpleasantly surprised about how many aggressive cases of cancer we see in very young veterans like in the 40s and 50s, and a whole variety of different type of cancer, not just one specific cancer and the common thread of the story is really they were exposed to the burn pits, where apparently many things were burned, including what I was told was equipment that they wanted to be destroyed, and so there were many
toxic exposures and I fear, and I believe it will be true that we will see many other risk factors for different types of malignancies. I mean I don’t know whether we still see veterans who were exposed to Hiroshima and Nagasaki, but radiation also can expose you to a variety of malignancies too, right? Absolutely, in fact I can talk about this because one of my veterans really wanted to raise more awareness and he and his wife really wanted to publicly speak more about it. He was actually exposed, in regular service to radiation in the nuclear powered submarines, and unfortunately, he was in very close proximity to it and unfortunately now deals with a very aggressive cancer. They were fortunately able to control it with chemotherapy, but it does look like he will be on chemotherapy probably for rest of his life. What about other agents? Do we have any idea about the carcinogenic
potential of things like tear gas, which is commonly used both in combat and in civilian crowd control? I’m not an expert in this regard, so I have to apologize that I can’t answer this question correctly. But I do think that we have to be aware about all the herbicides we are using still commercially and also in the private sector that I believe is under recognized. So certainly there are a whole host of exposures that are unique to veterans and our military families and we have to remember that. And cancer is not uncommon even in the general public. And so when you are seeing patients at the VA, you’re seeing people who may be at increased risk because of their military service. But you’re also seeing people who are just diagnosed with cancers that they would get as part of the general population as well. We serve all veterans, whether they’ve been in combat or not and if they fulfill the criteria.
to receive care at the VA, we will absolutely see all veterans that are eligible for VA health care. We will also see the cancers that are not related to service and we will treat these veterans, as much as we can do, and one of the benefits for me to be an oncologist at the VA, is that we have many other people helping me with their care. One of the things that I do not miss is the billing issues and medication issues. I mean, as you know, there so many very very expensive cancer medications, in fact, we see a stream of new patients into the VA because of the very very expensive drug prices and any veteran that finds out that they can probably get these medications for $9 copay at the VA a month will come to the VA. For those who may or may not know, if you are a veteran, you can get coverage through the VA for your family, your spouse, and your children? That’s a very interesting question. I ask the social worker all the
time and it turns out that spouses of 100% service connected veterans are eligible to get care at the VA until the immediate Medicare age. I believe that the children are not necessarily, but I think there might be mechanisms to take care of the children of veterans, but the spouses of 100% service connected veteran are eligible for care here at the VA. What does 100% service connection mean? It means that these veterans have a condition that disables them and it originated during the time of the military service. And you see patients with all kinds of cancers, and you treat them at the VA. Are there particular things that you’re thinking about in terms of their treatment in terms of side effects and so on that may be of particular concern to veterans? I think there’s several things that we do have to consider, and that is, for instance, service connected post traumatic stress disorder. We unfortunately take care of a fair number of veterans that suffer from post traumatic stress disorder,
and one of the things that we have to be aware of is sometimes when the cancer treatment itself causes stress, some of the PTSD symptoms can flare up and that is the reason why even before we start treatment, we actually frequently have palliative care and the health psychology team, in addition to psychiatry, if necessary, be involved in the management of the patient. For instance, when our veterans have to undergo complicated cancer surgery there is actually a service for elderly veterans called Champions where the geriatrician and the psychologists are involved before even the surgery and really prepare the patients for the surgery and follows them all along through the hospitalization and after discharge. Yeah, because I can imagine that for any patient cancer is a big diagnosis, it’s a scary diagnosis, but for veterans it may be even more so that it kind of adds to the stress that they’ve already gone through.
And that is one of the things where we are incredibly grateful for at the VA in Connecticut, we actually over the years we have developed a cancer care coordination system where the cancer care coordinator actually tracks patients that may develop cancer, but it’s still in the work up and the primary care physician or any provider can council the cancer care coordination team to try to expedite the work up and navigate for the patients going through the treatment.

Yeah, that’s so important. We’re going to talk a lot more about cancer treatment and the side effects in our veterans right after we take a short break for a medical minute.

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This is a medical minute about smoking cessation.
face when quitting smoking.
As smoking involves the potent drug nicotine.
But it’s a very important lifestyle change, especially for patients undergoing cancer treatment.
Quitting smoking has been shown to positively impact response to treatments, decrease the likelihood that patients will develop second malignancies and increase rates of survival.
Tobacco treatment programs are currently being offered at federally designated comprehensive cancer centers and operate on the principles of the US Public Health Service clinical practice guidelines. All treatment components are evidence based and therefore all patients are treated with FDA approved first line medications for smoking cessation as well as smoking cessation counseling that stresses appropriate coping skills. More information is available at Yale Cancer Answers. Welcome back to Yale Cancer Answers. This is doctor Anees Chagpar and I’m joined tonight by my guest doctor Herta Chao. We’re talking about cancer, particularly in veterans and
right before the break you were telling me about the really fabulous services that the VA offers veterans who are diagnosed with cancer. It is really a comprehensive approach, a multidisciplinary approach with social work, with geriatricians, with psychologists and psychiatrists to really provide the best treatment to veterans facing cancer. Because many of these veterans may face an increased risk of cancer due to military based exposure. The other thing that I think a lot of people may not know about the VA is that the VA actually supports a lot of research in the area of cancer, including veterans with cancer. Can you talk a little bit about the DoD, the Department of Defense, and the support that it provides for research into cancer? Yes, they had several mechanisms at the VA to apply for funding for research in veterans, including veterans with cancer. One is the DoD Department of Defense which has several grant mechanisms in many different cancers, including prostate cancer, lung cancer, breast cancer,
there’s another mechanism that’s called VA Merit which is internally within the VA you can apply for funding to conduct research, obviously there are others like the National Institutes of Health sponsored grants that physicians and researchers at the VA can apply so I certainly benefited from these grant mechanisms. One of my research interests, in addition to conducting clinical trials at the VA and making clinical trials accessible for veterans, is to look at the potential cognitive side effects and toxicity of prostate cancer treatment with hormonal therapy. And this actually was not something that I thought about, this was prompted by one of my patients who is a decorated Vietnam War veteran, and he developed aggressive prostate cancer at a fairly young age. He was just in his early 60s when he was diagnosed with metastatic prostate cancer and then found out that it was eligible for the VA benefits. He came to the VA and participated.
in several studies.

Finally, after three years taking care of him and his prostate cancer it was beautiful controlled.

He finally told me, I don’t want to be ungrateful, but I think these hormone shots are frying my brain. And I asked him, what do you mean?

And he said well, you know I’ve been busy all my life I can multitask, I can do so many things. But since I started the hormone shot, I have to write down and remind myself what I want to do. So then I thought, oh, that’s easy. I’ll refer you for neurocognitive testing and it turns out that he scored beautifully. There was no deficit that we could find on regular neurocognitive testing. And then I started looking into
0:19:09.752 -> 0:19:13.32 it and it’s
0:19:13.32 -> 0:19:15.92 still not well understood
0:19:15.92 -> 0:19:18.74 what hormone therapy for prostate cancer can do to the brain.
0:19:22.72 -> 0:19:26.122 I think that the breast cancer experts are way ahead.
0:19:28.39 -> 0:19:31.984 I mean the recognition that chemotherapy or hormonal therapy for breast cancer has been for many years already
0:19:34.38 -> 0:19:37.603 suspected and many studies actually support
0:19:43.74 -> 0:19:47.125 the suspicion that chemotherapy and hormonal therapy for breast cancer can cause chemo fog, or chemo brain.
0:19:54.888 -> 0:19:58.98 It’s not as well understood in prostate cancer so around 2009
0:20:03.18 -> 0:20:07.14 I started looking into that.
0:20:09.085 -> 0:20:11.03 And the interesting part is that it’s not very easy
0:20:11.109 -> 0:20:14.581 to characterize these impact of hormone shots
0:20:17.747 for prostate cancer, effects on the brain.
0:20:19.96 -> 0:20:21.358 If you do regular testing, neurocognitive testing,
0:20:24.154 -> 0:20:26.15 whether it’s a paper and pencil or whether it’s on a computer,
0:20:29.406 -> 0:20:31.89 certain amount of practice effect.
0:20:35.43 -> 0:20:38.559 if you do it every three months,
0:20:38.56 -> 0:20:41.78 you know what to expect to do in the test,
so your test score may actually hold up despite the fact there might be a deficit. And that is probably true for many, many patients. That is what prompted me to think about what other people do to study effects of anything in the brain, whether it’s depression, whether it’s dementia, whether it’s psychiatric illnesses. So that’s the reason why I approached my colleagues at the Yale Medical School in psychiatry that are involved in functional brain imaging to see whether or not hormone therapy can affect functional brain imaging. Just to clarify, what are these hormone shots that you’re giving for prostate cancer? giving for prostate cancer? What exactly is that? Because when we talk about hormonal therapy or endocrine therapy in breast cancer, that’s often a pill. Is it the same kind of thing? It’s not exactly the same because we know that if we just use a pill form like something called by Bicalutamide which is a testosterone receptor blocker, it usually is not sufficient to suppress
the effects on the prostate cancer cells. So usually men with both prostate cancer need to get something called Leuprolide, which is, I’m going to use the technical term LHRH agonist, that can shut down the testosterone production in a patient’s body and we use these shots to cause the testicles and also the remainder of the body to turn off testosterone.

So the key point being that the pills that many breast cancer patients take for five or ten years is different than these shots that men get for prostate cancer, especially advanced prostate cancer. They work through different mechanisms. They have different targets as it were. And so the side effects are pretty different, so many women, while it’s true that with chemotherapy they certainly can get chemo brain or chemo fog, it’s a little less common for women taking endocrine therapy, something like tamoxifen or some of the aromatase inhibitors. So how common is it that people can get this chemo brain or chemo fog or this cognitive decline when taking an LHRH agonist for prostate cancer? I think that’s a very hot topic right now.
now in prostate cancer research. I think for the longest time, and I would say like 10 years ago I was equally guilty. We recognized the potential effect on the brain and we really just focus on like how to control cancer. Because as Oncologists, we want to control cancer. Now I think we have to recognize there so many different treatments, and that’s the exciting part about being a cancer doctor nowadays. There’s so many different treatments and you can treat cancer so many different ways that I think it’s actually very important to know what each treatment could cause in terms of side effects, whether it’s inside the body or whether it’s inside the brain. And what did you find with the functional imaging study that you did? It’s still a very active, ongoing study. We’re trying to right now look at the effect of lowering the testosterone level what we call androgen deprivation, what it does over two years.
My original pilot study only investigated effects in 30 veterans. Leuprolide injection and as a control that underwent surgery or just radiation alone. It actually showed that the newer cognitive testing was the same. People scored the same, but when you look at the functional brain imaging just six months of hormone therapy for prostate cancer completely changed the way the brain shows activation. What does this mean? That’s something I think I need to find out, but it was very striking and to be honest I was a bit surprised because I initially thought if the newer cognitive test scores are the same, why should the brain MRI be different? And so I was educated that it can be different and apparently in other disease processes it can be different too. Thanks to the support of pilot studies through the Yale Cancer Center through Dr. Herbst, who supported this project, we were able to do an additional study of these 30 patients. It actually turns out that certain circuits that are connecting
different brain areas to process things seem to be affected by hormone therapy for prostate cancer, so I suspect that the longer we give somebody hormone therapy for prostate cancer, the more effects we can see.

Now that being said, I don’t want to create any fear among patients to get hormone therapy. I think it’s a very important treatment for prostate cancer, especially for stage four prostate cancer, and I think this is actually part of the cognitive side effects of hormone therapy. That’s something we need to study, and I believe not everybody is vulnerable to it. There are certain individual vulnerability that we have to identify and study. That was going to be one of my questions. Was that in that functional MRI study where you had some patients who had the LHRH agonist and some patients who didn’t, and you found that there was a difference in the functional brain imaging between the two groups.
the hormones were frying their brain or were some of them quite functional?
I would say some of them were quite functional and that is the reason why I was surprised to find on the brain imaging study that they're still changes.
And some were complaining of maybe hot flashes. So I think frequently we say, maybe you feel more fatigued because of hot flashes that you can get with those LHRH agonist, or whether there could be some component of depression affecting your cognitive out, but I think that’s the reason why it’s actually important to have something that’s not just subjective, it’s actually fairly objective for the patients to see actually on brain imaging, there are changes and while this is all still very much a topic of research, for my patient, who was the original one to actually complain to me about it, was very, very comforted actually, to know that it’s not just in his mind. It is actually something that we can see.
Dr. Herta Chao is the deputy director at the VA comprehensive Cancer Center and an associate professor of Medicine and medical oncology 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.