

If you're new to NETwise, we highly recommend you go back and listen to the first episode in this series. It goes over the basics of neuroendocrine tumors and how they're treated. And you can find a whole library of episodes on different topics at netrf.org/podcast, where you'll also find infographics and videos that expand on this material.

If you have a story to tell about your own NET journey, please email us and let us know - podcast@netrf.org.

When patients come to see Dr. Robin Lockridge, it's never because they're doing great.

***Lockridge:** Oftentimes, when people come to me, they don't remember a time that they were happy. And they don't see happiness in their future.*

Dr. Lockridge is a neuropsychologist. She works at the pediatric oncology branch of the National Cancer Institute at the National Institutes of Health. Many of her patients have rare cancers, including neuroendocrine cancer.

As a therapist, Dr. Lockridge will often start by asking her patients when they last remember feeling happy.

***Lockridge:** Initially, you know, when, when people are really sort of in a difficult place, they don't know, or they say, 'Any time before I had cancer.'*

A diagnosis like this can turn reality completely on its head. It can shift our understanding of ourselves, and how we fit into the world around us. Amid all the change, stress, and worry that often comes with cancer, *happiness* might start to feel out of reach.

Dr. Lockridge says that for many people, happiness isn't even something they've thought much about until, all of a sudden, it feels unattainable.

***Lockridge:** We sort of just move through life and when it's really disruptive, then we sort of freeze.*

You're listening to NETWise. I'm Jessica Thomas, Director of Patient Education at NETRF.

In each episode of this podcast, we share expert information and patient perspectives to help neuroendocrine cancer patients and caregivers navigate their journeys.

Happiness is something that can be difficult to find in life, no matter what. Having a rare cancer can make it infinitely harder.

In this episode of NETWise, we're going to talk about what happiness means, and how cancer can affect the way we think about it. We'll also talk about the things we all can do to be more resilient.

Welcome.

Am I happy? Are you happy? These are questions we ask all the time. But what do we really mean when we're talking about happiness?

Dr. Lockridge says happiness is relative - it depends a lot on who you are.

***Lockridge:** Happiness is going to have a different definition for. Everyone, and not just everyone, but at*

different points in your life, you're going to define it differently.

It could mean anything from being surrounded by loved ones to financial security. It could mean traveling to a new place, doing well at your job, or going for a long bike ride. Any of these things might be accompanied by emotions like satisfaction, joy, and pleasure.

But no matter where we find happiness in the world, we all experience the same thing inside our bodies when we feel it.

Lockridge: *There are chemicals or movements in our bodies and in our brains that really start to not just generate a sort of emotional response, but a physical response.*

When you are happy and when you're experiencing happiness, I could put your body in a scanner and I could see it. I could see it moving through your body. I could see different pieces of your brain firing off.

Let's talk a bit about what we understand about happiness from a scientific perspective.

James Bibb chairs the department of translational neurosciences at the University of Arizona College of Medicine in Phoenix.

Bibb: *We go through this world and we have senses. We have eyes, ears, we have taste buds and we can feel things on our skin. And these are environmental sensory inputs. And those inputs stimulate brain circuitry in our head that allows us to experience the environment.*

This "brain circuitry" involves something called neurotransmission. Neurotransmission is when specific molecules travel between neurons in the brain to deliver messages. These molecules are called "neurotransmitters."

You've probably heard of some of them - for example, cortisol is the neurotransmitter that causes us to feel stress. Dopamine and serotonin are the neurotransmitters associated with feelings of joy and satisfaction.

On the most basic level, these neurotransmitters deliver messages about whether something in our environment is good or bad.

***Lockridge:** You know, when your body's under a state of stress, there are certain neurotransmitters that activate that allow you to basically respond to that stress. So if you need to run, if you need to, you know, not be using the bathroom that moment, but your body is doing all of that work for you saying, 'Hey, get out of here.'*

On the alternate side, you have other neurotransmitters like dopamine and serotonin that sort of have the opposite effect, they have a sort of immediate pleasure reflect, an immediate calming reflect, and that's sort of, 'Okay. The danger has left and now I'm okay.'

For the most part, positive and negative feelings ebb and flow. But sometimes we find ourselves in a situation where we experience a high proportion of one or the other over a prolonged period of time.

***Lockridge:** The challenge is when you're constantly under that stress, and that constant stress keeps your body in that mode of activation.*

These prolonged negative mood states can lead to anxiety and depression, among other conditions.

On the other hand, if we are having mostly positive experiences, we'll be releasing more of those neurotransmitters associated with joy and pleasure. We might be more alert and engaged - and feel something we'd call *happiness*.

When you're dealing with an uncommon cancer, you'll probably feel the opposite of "happy."

From diagnosis, to symptoms, to treatment, disease disrupts our lives. It's a source of stress and anxiety, and it can change everything from what activities we're able to do, to our expectations of ourselves.

Inside the body, the neurotransmitters having to do with stress and fear can outweigh those associated with satisfaction and joy.

Every patient has a unique emotional experience, but for many people, this is a time of great unhappiness.

Diagnosis is often where this begins. The process of getting a diagnosis can be intensely stressful, with signals in the brain sending messages of fear and worry - not to mention the many other complicated emotions someone might feel.

Kevin Payne is a former social psychologist, and now runs an organization dedicated to helping people thrive with the challenges of chronic illness. He himself lives with multiple sclerosis.

Payne: *Getting a conclusive diagnosis that has weight, like, MS, like cancer, it is world shattering.*

Neuroendocrine cancer comes with an added challenge: it's a rare disease. This can make getting diagnosed take longer, and add a layer of isolation and worry to the experience.

Lockridge: *I mean, everybody I think goes to the Internet first thing when they get a diagnosis of any kind and you just find that... I can't find it. I can't find much on it.*

I don't know of many providers. My provider may not know much about it, and now they're seeking help.

For many patients, the intensity of this time period eases once they have found specialists to work with and have started to form a treatment plan. But they are facing a whole new reality: the reality of living with neuroendocrine cancer.

This looks different for every patient, depending on who they are and the nature of their tumors. But it's safe to say that this new reality comes with increased levels of physical and psychological stress.

When it comes to physical stress, there's the simple fact that a tumor is physically taxing on the body. While most neuroendocrine cancers tend to be slow-growing, these tumors still take up space, absorb nutrients, and can impede the normal functioning of organs.

The effects of a tumor are different from a momentary stress response to an external stimulus - it's happening constantly, inside the body. Stress signals are continually being sent to the brain.

Lockridge: *And so, as a result of that, you're just feeling the effects of it. You're just feeling stressed. You're feeling feverish. You're feeling tired. You're feeling, you know, the fatigue. You may be having trouble sleeping or just sleeping all the time.*

For patients with a functional neuroendocrine tumor, there are additional factors to deal with. Functional tumors secrete excess hormones into the body, causing another layer of physical stress.

Bibb: *They can affect our other systems such as our heart, our blood pressure, our vascular systems, and there's a consequence of that. And that is that you end*

up with some impairment of a system. It may not be that noticeable at first, but then you're left with this series of symptoms that are impairing your ability to function, or to just be healthy.

This can include everything from changes in the way the gut is functioning, to the state of the immune system, to the functions of the nervous system. All of these put even more stress on the body.

At the same time, functional neuroendocrine tumors can cause a wide variety of unique symptoms. These vary depending on the hormone that's produced, and they can include everything from fatigue and severe diarrhea, to pain and high blood pressure. While many of these symptoms can be managed, they can be both physically and psychologically demanding.

By the way - we mentioned earlier that serotonin is one of the chemicals associated with positive feelings. Some functional NETs secrete excessive quantities of serotonin, but the serotonin these tumors produce is confined to the body, and does not enter the brain.

Bibb: *The brain is, is really kind of in a capsule, it's isolated from our bodies by barriers. And one of those is called the blood brain barrier. Serotonin doesn't do such a good job of crossing across the blood brain barrier, so it doesn't interfere with that neurotransmission.*

Instead, the excess serotonin in the body can cause the condition known as carcinoid syndrome. This is marked by several unpleasant symptoms, including flushing and diarrhea. In other words, even though these tumors secrete a so-called "happiness chemical," they don't make people happier - they tend to do the opposite.

On top of the physical challenges of the cancer itself, there are also the impacts of treatment. Surgeries and other procedures can be taxing on the body, and drugs come with side effects. All these things add up.

Bibb: *And so cumulatively, there's signals that are getting into the brain as a result of that.*

These signals say: this body is under attack.

Over a prolonged period of time, this translates as stress, fatigue, and anxiety, contributing to an overall feeling of unhappiness.

While all these physical symptoms contribute to a decrease in overall happiness, there are also psychological challenges to contend with. Like the physical difficulties of living with cancer, these challenges do not go away after the initial diagnosis.

Lockridge: *It's throughout. It's the worry of remission. It's the worry of: 'what does this mean for my family?' It's the financial worry. There are- it's so multifaceted.*

Because many neuroendocrine tumors grow slowly, they can be treated almost like a chronic condition. Lots of people who are diagnosed can go on to live almost normal lives. But the "almost" is important here. It's still a new reality, and one that has been fundamentally changed by disease. It's a reality that includes symptoms, treatments, financial challenges, lifestyle changes, and often limitations. Because this is a disease that does not yet have a definitive cure, these challenges never entirely go away.

Lockridge: *One of the things that my patients often tell me that has really resonated with me over time is that it becomes the constant. And in almost an annoying way. 'I'm tired of talking about it, but it's always here. It's all encompassing.'*

Not only is the disease constant, but it's also constantly changing.

Dr. Lori Wiener is a clinical social worker. She directs the psychosocial support and research program at the National Cancer Institute.

Wiener: *You have a prescribed treatment and that could change. You live from scan to scan. You may have multiple surgeries. Your body is different. It feels different. It's adapting to that. Your day to day existence of what you were able to do may be different from what you're able to do now. Your short term and long term planning may be impacted.*

This persistent uncertainty can be another source of stress, worry, and anxiety.

All these factors taken together - the physical stress of tumors and symptoms, plus the psychological challenges of symptoms, treatment, life changes, and uncertainty - can have profoundly negative impacts on our mental health. Unhappiness is a completely normal response to these circumstances.

But over a prolonged period of time, unhappiness can impact quality of life - especially when it reaches the point of depression, which is a common condition among people with cancer. Fortunately, there are a lot of things people living with cancer can do to find more happiness in their lives.

Burt Rosen: *My name is Burt Rosen. I live in Portland, Oregon, and I was actually diagnosed with two primary cancers. So I have a pancreatic neuroendocrine tumor, which has metastasized to my liver. And for those who understand what this means, it's grade two with a KI 67 of, I think, 8 percent right now. Um, and then I also have renal clear cell carcinoma or a kidney cancer.*

I like to joke that I went to the cancer store on buy one get one free day.

So, I was diagnosed in July of 22. The kidney cancer is in an early enough stage that they don't want to treat the kidney at the risk of messing up treatments for the PNET.

So my primary oncologist is a neuroendocrine tumor specialist. And I started off on seven rounds of, CAPTEM, which is a chemo protocol, capacetabine and temozolomide.

My tumors all shrunk, even the kidney shrunk. But my platelet counts dropped too low. So they wanted to stop me on the CAPTEM. They put me on three shots of octreotide. Then in June of 23, I had a liver resection. I was supposed to have a liver resection, gallbladder removal, distal pancreatectomy and splenectomy. I lost too much blood after the liver resection. So technically I'm in the middle of a stage surgery.

And then, the only Western treatment I've been on since then is lanreotide every 28 days. I am very, very involved in the integrative oncology world, and I do a lot of things, outside of, you know, medical, radiation, chemo, et cetera, so.

My big question was always, what else can I do to help myself?

So I started to focus on: how do I make Bert healthier overall, right? So my oncologist, his sole goal is how do I kill the bad stuff, but killing the bad stuff is only half the battle, right? I heard this quote from an integrative doctor that I loved, which is: cancer is the weed, but we need to tend to the garden.

So the things I do - and this is all science backed, so it's not alternative, which there's a difference for those who don't know. Alternative is, I don't want to do

that, I want to do this. Integrative pretty much says all modalities have a place.

I realized I get one shot of lanreotide once every 28 days for 30 minutes. So when you think about that, that means it's less than one percent of my month is focused on getting treated by medication. So the other 99, and actually it's 99.75 percent or something like that time in the month, I have time to focus on how do I help Bert get better overall.

So I do things that are meant to improve my overall health. So my diet's better, I meditate every day, I go to therapy weekly, I try to exercise as much as I can. I'm not good on that one yet. Uh, I try to be outside when I can. I'm trying to get back into yoga. So I do a lot of things like that to help too.

You know, through meditation I've learned a lot to focus on my breath and how that can calm me down. So if I'm, you know, about to get my lanreotide and I'm anxious, like I just focus on my breathing or, if I go take a walk outside, a lot of times I'll listen to music or podcasts, but sometimes I'll just shut it off and I'll just feel what it feels like to put my feet down, left, right, left right, or to watch the leaves in a tree move, right?

And on the therapy side, like if I'm in a crappy mood, I'll have these internal discussions, like, it's okay to be in a crappy mood sometimes, or, oh, this puts you in a crappy mood? Let's, you know, let's think about that more. And how do we get you out of it? So meditation and like mindfulness and therapy are probably the tools I use the most.

Like make an easiest impact for me on a one to one basis, but certainly everything all helps together. And it's worked. I mean, I feel like my attitude is probably one of my strongest suits right now. Like I'm genuinely

happy. I'm extremely optimistic. This is something I'm dealing with not something that defines me.

There are days that you wake up and you think, oh crap I have cancer. But for the most part, I try to give myself things to look forward to, and I try to keep myself involved.

In my mind, there's two parts to having cancer. There's treating your cancer, and then there's the experience of living with your cancer. I'll never ever call myself a cancer patient. Like I refer to myself as Bert who has cancer, right? Because I'm Bert and I have allergies too. Right? Like cancer is just harder to deal with. Like that's the way I look at it.

There are a few ways we can all increase the happiness in our lives. Some of these are external, involving things we can seek in the world around us. Others are internal, having to do with how we interpret events and experiences.

When it comes to external sources of happiness, we know that there are certain activities that cause us to release those positive neurotransmitters, resulting in some amount of joy or pleasure.

The most important of these involves other people. According to neurologist James Bibb, overall happiness is directly related to the strength and number of the relationships we have.

Bibb: *Humans are social animals. People that are more isolated have more stress and they have more unhappiness and depression by far. We're not meant to be alone.*

The people we can connect with might include family or friends, as well as support groups and mental health professionals. These individuals can provide practical or emotional support, as well as companionship.

In difficult times, we might be tempted to withdraw from the world. But Dr. Lockridge says it's crucial to make these connections early, and maintain them.

Lockridge: *Even if you feel in the moment that's not for you, I just want to focus on my treatment, because what I have found is that oftentimes, people don't reach out until sort of they're already in a hole in an emotional sort of whole of depression or anxiety. And now they're trying to get out of it in the midst of everything else.*

In addition to our relationships with others, we can find external sources of happiness in all kinds of places. This will be unique to each individual, but might include things like spending time in nature, exercise, playing an instrument, or making art.

Payne: *If you don't have those kinds of things in your life, think back and, and recall, well, what's something that I tried before that I really liked that I haven't done in a while, or what's something that I had the opportunity to do, but I said no to, and, and now I've always kind of wondered what if.*

Or go to one of those websites that lists local activities, like Eventbrite or, you know, something like that, and just start looking through and see, and just, and just, you know, pick something that you are able to do and give it a try.

Alongside these external sources of connection, pleasure, and joy, there is a lot we can do internally to find more happiness in our lives.

Kevin Payne says that in his experience, the key thing is to redefine how we think about happiness in the first place.

Payne: *Happiness tends to be rather limiting in the way that we conceive of it. And happiness often is*

unattainable in a moment. So what I prefer to have people think about is living a good life.

He says life contains so much more than happiness and unhappiness. It's full of satisfaction, engagement, and meaning.

Payne: *And we need all of those different kinds of experiences so that we can not only feel like we're having a good life in the moment, but our future selves will look back on it and think, 'Yeah, we lived well.'*

The experts we spoke with for this episode all said that ultimately, the most important thing is to turn the focus on where we find value in our lives.

Lockridge: *And that's probably really the most exciting work, because I think that a lot of times we don't realize the areas of our life or the people in our life that we really find valuable.*

Turning the focus to these kinds of experiences can help us recalibrate our emotional responses, reducing the intensity of stress and anxiety.

That looks different for everyone, and might include some of the things we just talked about - family, friends, community, nature, exercise, art, and so on.

Wiener: *Is it that connection? Is it to be able to be with people that you care about and you love? Is it to be able to get up and to be able to read a new book that you wanted to be able to read? So it's prioritizing what's most important to you, your values.*

And not getting hung up on the "shoulds" or the things that I can't do. The more we fight, saying, 'I can't get upset. I can't cry. I can't, you know, have another bad day.' That is not resilience. In the sense that you are already writing the script for what that day may be.

This doesn't mean ignoring the hard things, like cancer - it means allowing them to be part of life.

Payne: *For many people with chronic illness, there is always, in the background, some really negative noise. And we have to learn to be okay with that.*

This is easier said than done, and a therapist or other supporter can be helpful. They can offer strategies that can assist in recalibrating to the reality of living with disease.

Wiener: *Something that we often recommend is that we get rid of the word "but," and we exchange it with the word "and." I really want to go to the movies with my family, but I may have diarrhea. I really want to go to the movies with my family, and I may have diarrhea.*

Lockridge: *And that's not without its fallbacks. It happens. And I think that's important, too. Even when you have learned those lessons and you have all the skills and tools and you reframe on your own and you don't get caught in those sort of circular thoughts that keep you up all night, there are moments that you, that you take a few steps back. And now you are finding yourself ruminating and you are finding yourself going, 'Oh, no, what if.'*

Dr. Lockridge says that's ok, too. Everyone is going to have bad days. The important thing is to allow those emotions to come and go.

Wiener: *To be able to just be present that day for what that day is to bring. And yes, there may be some sadness and yes, there may be some anxiety but at the same time, you're here, you're alive, you're breathing. You can connect with other people if you want to, and you have permission to find those things that can bring you some joy, or at least comfort for that day.*

Payne: All of us have, have spent time, you know, at one time or another laying on the grass, watching the clouds go by. Imagine that. Take that feeling that you have and attach it to that cloud. And let the wind carry it away.

And the next feeling that comes along is going to be something different. And maybe it might be negative feeling, negative feeling, negative feeling nine or 10 times in a row. That's okay. You let it go. And eventually you got one, you know, all those, you got nine storm clouds coming along and then one happy little puffy cloud that comes along. Okay. But the secret is: don't hang on to that, either.

Nancy Lewis: I'm Nancy Lewis. I am in Kansas city, Missouri, and my diagnosis is GI nets that have metastasized to my liver.

So I was having laparoscopic surgery and the doctor looked over and saw that things did not look right on my liver. She sent me to a liver specialist, who then brought in an oncologist, and they're the ones that let me know that I had neuroendocrine cancer.

So, originally, I had about 36 tumors. I am on octreotide and I take that once a month, and I have had two bland embolizations. And then one surgery that was a whole host of things being taken out of my body from, 28 tumors in my liver, gallbladder, a bowel resection, et cetera, et cetera.

Before I found the specialists who said, "okay, this is chronic," I remember the doctor looking me deeply in the eyes and holding my hand and telling me I had cancer. At that time, he was not a specialist. And from what he knew, this was a fatal cancer. And I remember hearing the words "days or weeks." And believing that this was

something that was going to not allow me to live much longer.

And I remember in that moment thinking, "I've lived a noble life. And a lot of people haven't had what I've had and haven't been able to experience what I've experienced and had the joy and the happiness that I've had." And I remember, in that moment, making that decision to not be sad about it or angry.

I am a big believer that your thoughts shape your reality. And so because of that, I am a happy person, generally, because I choose to be. I think if I'm sad, I'm allowing myself to be sad and that is normally not my choice.

It's not that it is the most happy and joyful thing going through this cancer. I mean, there are times when it's really painful and... not easy. But there are a lot of times when it's not. I mean, there are a lot of times - you know how this cancer goes. There are times when you're struggling and dealing with procedures or surgeries. And then there are times in between.

So in those times in between, I like to make sure that I am not focusing on the bad parts, and focusing on the other positive parts of my life, instead of thinking about cancer when I don't have to. When I do, I do, and I will, but when I don't have to, I try not to spend my life time focusing on it.

Every single morning- every single morning, my husband and I say a prayer and we talk about all the things that we are thankful for. And that's it. And even on the mornings that are really tough I still have that same prayer and still find what I'm thankful for in that moment.

I am thankful for Wordle. I am thankful for, you know, the birds in the backyard. I am thankful for Wheel of

Fortune. I am very thankful - and we always say our thanks - for a job that has insurance that allows me to get wonderful care.

And I know that, you know, there are some people for whom this kind of mindset may be really difficult. And it's not like I'm just fooling myself. I mean, it's not like I'm telling myself, 'Oh, you have to be happy,' when deep down I'm really sad. That's, that's not what it is. I am finding what is within me to bring out the joy that exists.

There are people who say, 'Oh, she's fighting cancer. She's battling cancer. She's doing this. She's doing that.' And that's- it's not how I view it. I, I just view it as cancer is something that is part of me, within me, happening to me, and I am going to live my best life with it. And for me, it just doesn't feel good to be angry and fighting and struggling all the time. It's more that I'm living a happy life with cancer.

Throughout this episode, we've talked about happiness from a variety of perspectives. We've come to understand what happens in our brains and in our bodies when we're happy - and what can make it hard to find. We've also talked about the importance of shifting perspective in order to live life well - not *despite* neuroendocrine cancer, but *with* it.

Dr. Robin Lockridge acknowledges that to some, this might sound absurd, or even impossible.

Lockridge: *I myself, when someone said to me when I was training in psychology, "Ask your patient: what has cancer given them?" I thought it was the most ridiculous question I'd ever heard. I thought, there's no way I can ask that question. They're going to look at me like I've lost it.*

And so for years, she didn't ask her patients that question.

Lockridge: *I just couldn't bring myself to do it when I was training because I thought it was very- I just couldn't. It was insensitive. I had all these thoughts.*

But over time, she found that her patients offered her the answer anyway.

Lockridge: *And they have said, you know, 'I, I wish I never, obviously, I wish I never got cancer. But, since I have, my friends and I have gotten so much closer. I've realized how strong I am. I don't worry about the things that don't matter.'*

Instead, she says, people learn what's most important to them, and that's what they focus on.

Lockridge: *And, oftentimes, those people are the ones that I see, they, they do okay, you know, when, when something gets hard, they know they'll be okay and that they can see that through because they've done it before and they've learned so much about themselves throughout their process.*

The people who have a harder time are those that sort of live in that, 'I wish this never happened to me.' And they sort of live in the "I wish."

And often I say to them, 'I wish that too. I wish that too, but I worry that if you stay there, we won't be able to find happiness for you again.' And that becomes the question and the work.

Wherever you are on your journey with neuroendocrine cancer, know this: happiness is not out of reach. If you know where to look - and how to look - you can find it almost anywhere.

Thanks for listening to NETWise. I'm Jessica Thomas, Director of Patient Education at NETRF.

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Special thanks to everyone we interviewed for this episode. We are grateful for your expertise.

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