Dr. John Marinelli:

Hey everybody. Welcome back for another episode of ENT in a Nutshell, my name is John Marinelli. And today we're joined by Dr. Raj Dedhia, who has done a fellowship in sleep medicine and is also dual board certified in ENT and sleep medicine. So Dr. Dedhia, thank you so much for being here today.

Dr. Raj Dedhia:

My pleasure, let's do this.

Dr. John Marinelli:

All right. By way of introduction, I just wanted to mention that we will cover sleep stages today. However, we're going to hit that a little bit harder in our polysomnogram interpretation episode, but this episode will be primarily focused on everything from common questions, like how much sleep do you need, effects of sleep deprivation, role of naps. And then we're going to cover some of the high yield aspects surrounding sleep physiology, but to get started, Dr. Dedhia, How much sleep do you need? Why do we think sleep is important?

Dr. Raj Dedhia:

Yeah. So that's two questions and I'll answer those separately. Why is sleep important? Well, the truth is we don't really understand the entire role of sleep for humans or other animals, but I would say there's four things that most of us would agree upon as functions of sleep.

The first is physical growth. This is important for young persons because during stage three sleep, which we'll talk about later, is when growth hormone is released. So you grow during sleep. REM sleep is important for memory consolidation. Overall, sleep for energy conservation, and I can tell you from personal experience, getting a good night's sleep certainly helps preserve your immune function. So that's why we sleep.

How much do we need? Patients love to ask this question, and it depends on how old you are. So there are eight specific guides. This is by the National Sleep Foundation telling us how many hours of sleep we need. So newborns, 14 to 17 hours. And if you're over at 65, it goes to seven to eight hours. And so along that spectrum, your sleep needs decrease. So most of us listening to this podcast I'm going to say are 18 to 64 year olds, seven to nine hours is the recommendation. And I tell patients seven hours at least of uninterrupted sleep.

Dr. John Marinelli:

And I know there's a little bit of genetic variation in that. Is that correct?

Dr. Raj Dedhia:

Yeah. We have these phenotypes, what we describe as long and short sleepers, and there's a lot of interest. I would say people are intrigued by these people that sleep four to five hours and seem to function reasonably well without any impairments. Those are exceedingly rare. Patients who have that kind of short phenotype, most, well some, of the more high achieving people do have lower sleep requirements, but that's certainly not true across all persons. And then you have other people that require nine hours. And again, there's a whole lot here we don't understand. Sleep is a very young field, about 40 years old. So there's a lot of work here to be done to figure out who these people are.

Dr. John Marinelli:

And this idea of a two process model, can you tell us a little bit about that?

Dr. Raj Dedhia:

Yeah. What you're referring to is that there are these two governing forces for our sleep. You have something called the circadian rhythm, circadian process. That's an internal rhythm or clock that every cell in our body has, every being on this planet has, that wants to guide us as to when we're going to be awakened when we're going to sleep. Counter to that, or I should say coupled with that, is something called the homeostatic process. This is a pretty simple concept that the longer you're awake, the more that you want to sleep. And so there's a buildup of sleep. The way that I think about it is as you are awake, you start putting bricks in your backpack and things get heavier. And then once you sleep, you can shell off these bricks to make you less heavy and less likely to sleep.

So this, again, two process model, very important here. You have the circadian process and the homeostatic process. I'll go in a little more detail here. The circadian process is governed by melatonin and we have these things called zeitgebers or time givers. Sunlight is the strongest of these, but that sunlight actually stimulates the retinal hypothalamic track and regulates melatonin release. So if you see the sun, it's going to tell you certain things about how much melatonin to release. And melatonin, of course, is what makes us sleepy. That's the circadian side.

On the homeostatic side, I mentioned those bricks that you have that you stay awake longer. Those bricks are really adenosine. Adenosine is the molecule that's involved with making it sleepy. Again, the more adenosine you have, the more sleepy you're going to feel.

Dr. John Marinelli:

And how exactly does sunlight regulate our circadian process?

Dr. Raj Dedhia:

So sunlight is a photic or a light stimulus, and that light, as the sunlight hits our retina, from the retina back to the hypothalamus to the suprachiasmatic nucleus, where you have that connection to the pineal gland, which releases melatonin. So it's really this elegant track between the retina to the hypothalamus, to the pineal gland that determines release of melatonin. And again, sunlight is the most powerful of these. You can get a light box that you can buy on Amazon that also can help function in the same way, but really sunlight is the most powerful of this.

And I'll go one step further. If you're trying to get sunlight in a way to regulate your sleep, we recommend that you get sunlight in the morning. That morning sunlight tells your brain when it comes evening, time, it's time to sleep. If you get evening sunlight, which is happening now as the days get longer right now, this is end of May, this is a challenge because people are getting sunlight later and that makes their brains want to stay up longer.

Dr. John Marinelli:

The next topic I wanted to touch on was neuroanatomy and neurophysiology as it relates to sleep, I know you can get in the weeds on this, but for an otolaryngologist or a resident, what do you think is high yield to know regarding that topic?

Dr. Raj Dedhia:

Yeah. John, this is something that we don't think about on a clinical basis. Even my sleep medicine colleagues who do just sleep medicine really don't use this information that often. It has to do with

newer drugs that are coming out, understanding some of that basic mechanisms, but there are some high yield points that I can touch on.

In our brains, we have different areas that are going to responsible for things like wake promotion, and then also conversely for making people sleepy. And these are really governed by a set of neuro-transmitters. So the neuro-transmitters that I think about that are wake promoting are going to be things like epinephrine and norepinephrine, other things like serotonin, these things are going to make us stay awake. I should include things like histamine, dopamine, or orexin.

And this gets really a bit of a jumble, but you can think about when a person takes Benadryl and they get sleepy, why do they get sleepy with Benadryl? Benadryl is an antihistamine. And I just mentioned that histamine is one of our wake promoting agents. So we see side effects of medications that make people sleepy. And if you can remember that histamine promotes wakefulness and if you have an anti-histamine, you're going to get sleepy, that can be pretty helpful.

We talk about the other side, what things promote sleep? And these are sort of these sleep agents are things like acetylcholine, glutamate, glycine, GABA, adenosine I mentioned earlier. And so the way I think about this is you have some things that have anticholinergic effects. We know alcohol potentiates GABA, benzodiazepines potentiate GABA. Those things are sedatives by definition. So again, if you just remember, there's a handful of molecules that are going to make you awake. And histamine is an easy one to remember because of the effect of the drug of anti-histamines. And then you have things like GABA, for example, and I think about alcohol and benzodiazepines as being sedative and they really work on GABA.

Dr. John Marinelli:

And we talked a little bit about melatonin earlier as a significant hormonal influence related to sleep physiology. Could we just touch on the several different aspects of endocrine and hormone regulation as it pertains to sleep physiology?

Dr. Raj Dedhia:

Sure. And I think there are a handful here and I get for the purposes of this podcast for our audience, I'll say a couple that should come to mind. One is growth hormone. I mentioned that earlier, but growth hormone is released during stage three sleep. So when we have children in the clinic and we talk about potential sleep apnea and the detrimental effects, one of the effects of sleep apnea in children is growth retardation. And it's because the inability for them to get consistent sleep, to get in that stage three sleep and to release adequate growth hormone. So that's an important one, during sleep growth hormone.

And then the other one that I think about is cortisol. You know, the ACTH cortisol, the adrenergic axis, the hypothalamic pituitary axis is important because cortisol, we typically see this rise right before you wake up. And so that, that peak near the wake up time is important. And other things that counter that are TSH, thyroid hormone, where it actually peaks during sleep and then decreases during the day.

And I think John, the point here is that all of these hormones or neurotransmitters that are released, they themselves have a circadian pattern. And that's why this field of circadian science is blowing up because every medication, every cell in our body has its own internal clock. And if we can understand that better, it really has implications on clinical care for patients that are having issues in a certain area, or in general, how to optimize our health based on the clocks of these cells.

Dr. John Marinelli:

One other kind of set of hormones that I've heard a little bit about that I just wanted to get your take on is leptin and ghrelin. I feel like I see those when I'm being asked questions on pieces of paper, sometimes.

Dr. Raj Dedhia:

Pieces of paper. That's a great point, John and I have to be sensitive to that because that is a lot of the learning here is some of the basics. Leptin is a hormone that's released from our fat cells and in general it causes a decrease in hunger. So you can think of a body's way to auto-regulate. If you put on weight, get more fat cells. Leptins can make you less hungry. However, in a lot of our sleep apnea patients we have discovered something called leptin resistance. That's where patients continue to be hungry despite having increased leptin from the increased adipocytes.

Ghrelin, on the other hand, is supposed to counter leptin. So ghrelin, I think you can think about mnemonic leptin leans and ghrelin gains. So ghrelin makes you gain weight. This typically peaks at night. So you have this push and pull between leptin and ghrelin in theory, but understanding things like leptin resistance can cause an imbalance in that push pull.

Dr. John Marinelli:

And transitioning here to a hot topic for ENT residents, but also just as it relates to things like obstructive sleep apnea, I wanted to just touch on sleep deprivation. And if we could maybe first touch on acute sleep deprivation and how that affects patients. Would you mind going into that?

Dr. Raj Dedhia:

Sure. So we're going to talk about acute and chronic sleep deprivation, and these are important for different populations. Acute sleep deprivation, we think about whether it's a resident on call, police officers or persons that are doing things that are requiring one or two days of not sleeping at all or not sleeping much, recovery can take a few days. And the first day, what you'll see is a rebound of what we call slow wave sleep, or Delta sleep.

So imagine you're up all night for tests the next day you crash. And when you crash, it doesn't take you long to sleep. So we call that a decreased sleep latency, and then you're going to have this beautiful consolidated period of this stage three sleep. That's when you're totally out. Somebody wakes you up, you're so groggy. I think about being woken up post call and I don't know where I am. It's sort of that feeling where you're in this slumber and that's the rebound that you see after that first day of being acutely sleep deprived.

Second day, you'll get an increase in REM sleep. And by the third day, you often see a return to normal, depending on your age with sleep deprivation. It has a lot of physiologic and hormonal implications. You increase things like sympathetic tone, it can decrease your growth hormone. There's of course, it's quite an inflammatory state. As I mentioned, sleep is an important function in immune function restoration. So if you're not getting that sleep, you're more prone to get sick. So these are some of the things that you're seeing. Again, it's sort of a widespread effect of not getting sleep in the short term.

Dr. John Marinelli:

And what about chronic sleep deprivation?

Dr. Raj Dedhia:

Yeah. Most of the listeners here have experienced that at some point, it's called residency. And when you have that sleep deprivation, there's a lot of study now and there's some NIH funded trials, understanding what is the impact, particularly on surgical residents, on their function, on their mental state. And we're learning some of that now.

And it seems like one thing that's clear is that there is not this sleep debt that you withdraw from the bank five hours of sleep during the week because you got a lot to do and then, hey you know what? I'm going to pay it back on the weekend. Yeah. It's not really clear. It doesn't seem to be the case that you can do that effectively. If you have several nights of, let's say more than three nights of not sleeping well, or in most cases it's many years in residency, but if you have a string of nights where you're not sleeping much and you go back to sleep, you actually rebound here in something called a REM rebound. So you get more of this REM sleep. I mentioned that in acute sleep deprivation, you get a slow wave rebound. Here, think about a REM rebound.

So that's important point one. The other point is that as far as your performance, the subjective reporting of that individual's performance is very different from objective reporting. In other words, if you put somebody in from a simulator after a week of poor sleep, or let's say longer, their ability to tell you how they're doing will not reflect objective scores. This is true for both acute and chronic sleep deprivation. But I say this again because of our residents who are experiencing this. And it's important for us to understand and to protect them from not having prolonged episodes of acute or chronic sleep deprivation.

Dr. John Marinelli:

And another topic I wanted to touch on related to this was the role of napping. What is the role of napping in sleep deprivation?

Dr. Raj Dedhia:

So when I ask a patient their history, one question I always ask is do you nap, because they may sleep five hours a day, but they take a two hour nap in the middle. Well, that's important to know. So first of all, you want to ask about napping in your clinical history. Then you want to tell them about napping. Napping is one of the two proven ways to fight sleepiness, caffeine being the other one. So naps typically less than 15 minutes, what we recommend so they don't get into that stage three sleep slumber and have sleep inertia. But if you can nap for less than 15 minutes, what you can do is actually drive down your adenosine levels. I mentioned the adenosine gets built up in the backpack, the bricks that you're putting in as you're awake, but once you take a nap, you actually unload those bricks and the adenosine goes down.

So we recommend if you needed to, let's say you had to drive so many hours to get somewhere. Well pull over and take a nap. Don't roll the windows down, don't go outside and do pushups, pull over, take a short nap. That's been proven to help fight sleepiness.

Dr. John Marinelli:

And you mentioned caffeine. How does caffeine fight sleepiness?

Dr. Raj Dedhia:

Yeah, this is a great question. Caffeine is a non-selective adenosine antagonist. So it's going to antagonize those adenosine receptors, which is directly how that fights sleepiness. That's 100, 150

milligrams of caffeine is the dose we recommend. So that's about a cup, I think. Eight or 12 ounces of a Starbucks coffee, for example, that is going to help antagonize the adenosine and make you less sleepy.

Dr. John Marinelli:

And we touched in the beginning a little bit on the role of light therapy, but could you just touch on that a little bit more in depth surrounding not only both regulation in the morning, but also avoiding certain types of light and whatnot at night?

Dr. Raj Dedhia:

Yeah, John, this is something that we're seeing more in our devices that are built in, these night modes. And it has to do again with the retinal hypothalamic track and how that affects sleep. So I'll try to explain it in a bit of a nutshell, just like our podcast, ENT in a Nutshell.

Dr. John Marinelli:

That's right.

Dr. Raj Dedhia:

So if you have light that's in the morning, now this really applies when I have patients who are coming to me that have something called delayed sleep phase syndrome, and I'm sure John we'll get into this in other podcasts. That's a very common disorder, particularly in our youngsters where their tendency is to go to bed at 1:00, 2:00 in the morning and wake up at 9:00 or 10:00. Most occupations don't condone that, or they don't promote that because you got to be up by 6:00 to get to work at 8:00, for example.

So how do you shift somebody to have a more desirable bedtime? Let's say 10:00 PM, wake up at 6:00 AM. Well, light is so important in this. So if you get morning light, you're telling your body and it's something called a phase shift, that I'm getting light in the morning. I take my dog out for a walk at 6:00 in the morning. That's so helpful because then your body will interpret that as when it comes 8:00, 9:00, 10:00 that, hey I'm tired. It's time to go to sleep. So you want to maximize morning light. Conversely, you minimize evening lights. On the way home, put those sunglasses on, draw your shades and curtains when you get home. I do this with my own family to help promote that sleep so that it's not light seeping in at 8:00 pm, 9:00 pm. It's really hard to go to sleep.

And then John, the idea of light colors is important. So blue light is the most stimulating light that there is. If you guys, those who are listening, remember back in, I think it was the eighties. I mean, I was young, but I remember this. A lot of the computers would have these DOS screens that were blue. And the idea was for the programmers that it kept them going. So the blue light in the back was done intentionally to help keep the programmers alert and maybe even the users alert. So again, that blue light is going to be alerting. So you don't want that. And so in fact, they now have their sunglasses off and are going to be yellow tinted. Yellow, orange, that's a softer light. So you want to make things in that yellow tint. Even at home, I've replaced my bright whites to the soft yellow bulbs. I think that all that helps keep people's circadian rhythms in check.

And the last piece I'll talk about, John, is along with light comes melatonin. And we've talked about melatonin already, but melatonin has an important role when you trying to shift somebody earlier in their sleep. Melatonin can be used in two ways. It can be a help like a sleep aid. So you take it 30 minutes before bed. Something like five milligrams, that'll help you fall asleep. But if you want to shift your rhythms, you can take a micro dose of this about 0.5 milligrams, five hours before bed, and that'll shift your rhythms, not just for that night, hopefully, but for the long-term. That has to do with the way

our bodies process melatonin and something called this phase response curve, which I won't get into. But the timing of all these things is super relevant. So the same dose of melatonin can have bi-directional effects of different magnitudes just based on the timing. So, really important.

And then the third tenant of phase shifting, we talked about light, melatonin, but the third tenant is a strict sleep schedule. This is the hardest for compliance. You can imagine telling a 20 year old, hey Friday, Saturday night, you're in bed at 10:00. They look at you like, okay you're trying to kill my social life. Well, we might be trying to do that. It's not our goal, but this is really important to try to keep this consistent across seven days a week. So light, melatonin, sleep schedule for patients that are trying to shift their rhythms.

Dr. John Marinelli:

All right. Well, I think that was really awesome. Was there anything else you would like to add before we transition to the summary?

Dr. Raj Dedhia:

No, I think we covered all the high points, John. Thank you.

Dr. John Marinelli:

All right. Now I'll transition to the summary portion of the podcast. So today in this episode, we've talked a little bit about how much sleep humans need, with the vast majority of adults needing seven to nine hours and a very few select genetically lucky folks requiring less than that. We can then cover this idea of a two process model where you have this ongoing homeostatic process that kind of builds throughout the day through the neuro-transmitter adenosine. It slowly builds and promotes sleep. And then this idea of a circadian process where your body's kind of balanced the other way towards wakefulness that's primarily driven by the hormone melatonin.

There are numerous effects on your endocrine system through sleep. Some of the most notable ones, just being insignificant, influence of growth hormone on sleep, which is released in the first half of sleep. And then we also touched on the idea of sleep deprivation and how it really takes in acute sleep deprivation about three days for the EEG to normalize. And in chronic sleep deprivation, as well as acute sleep deprivation, there's this interesting phenomenon where study subjects will report performing as well as they think they would if they had gotten normal sleep, but objective testing reveals that that's not the case.

And lastly, we touched on different ideas surrounding combating sleepiness and regulating your sleep schedule, the importance of morning light and avoiding a light, especially blue light in the evening, the how to use melatonin and then the importance of maintaining a strict sleep schedule.

Dr. Dedhia, anything else you want to mention?

Dr. Raj Dedhia:

You nailed it, John.

Dr. John Marinelli:

Well, thank you so much for being here today.

Dr. Raj Dedhia:

It's my pleasure.

Dr. John Marinelli:

All right. And now we'll transition to the last portion of our podcast. We'll ask a couple of questions and give you a chance to think about it and respond. Today we only have two questions. The first of which is, what is the two process model as it relates to physiology?

So the two process model is this ongoing balance between your homeostatic drive that constantly builds throughout the day and is driven by the neuro-transmitter adenosine. And that is kind of counteracted or constantly imbalanced with this idea of a circadian process that is strongly influenced by the hormone melatonin.

And second and last question, how are the hormones ghrelin and leptin affected by sleep deprivation? Recall ghrelin grows and leptin leans. In sleep deprivation, we actually find subjects have an increased level of circulating ghrelin and there's this phenomena of leptin resistance that we sometimes see in our obstructive sleep apnea patients, which can cause even in the setting of increased adipocyte content, some resistance to leptin.

That will wrap things up for today's episode. Thanks so much for joining us and we'll catch you next time.