Alright. Time for some differential diagnosis. So basically, what that means is, looking at each disease for what it is, and then determining what exactly is the difference between one and the other. The way I like to do differential diagnosis is not necessarily memorize everything there is to know about one condition, but kind of look and see, how does this condition compare to this other condition, and what is the one key clinical finding that you’ll see that will give you a little bit of hint that it might be one thing or the other?

Now, before we get going, I really want to tell you this: Those intake forms and those... the fillable forms that patients are going to have, the brain region index forms, are going to be really important for this kind of thing. You saw earlier, on the case study that I presented, how there was clear hippocampal problems, and there was clear frontal lobe problems, but the patient couldn’t drive, so there was some visuospatial problems. So there’ll be a little bit that will curl back into some of the parietal temporal regions as well. So these things don’t progress perfectly from front to back. Sometimes they’ll progress to the front, a little bit along the temporal region, back into the parietal-occipital region. So, the way they all progress is very interesting, because they follow pathway circuitry. So you may have Lewy body dementia, versus Alzheimer’s disease, versus vascular dementia, versus Parkinsonian supranuclear palsy, versus a cerebellar degenerative disease, that you hear Dr. Kharrazian talk about those things.

My goal during this section is to make it to where you can sort of say this: “That looks very Alzheimerish.” Or, “This looks like frontotemporal dementia.” Or, “This looks like multiple systems atrophy. So now we’re taking it from the “Here’s just some of the early signs of neurodegeneration,” which you saw things like the peanut butter test, and you saw some of the early signs like, “Hey, pay attention.” So we have that neurodegenerative sort of, you know, everybody’s kind of in a state of neurodegeneration. Once you probably reach about the age thirty-two to thirty-five you lose about one to two percent of your oxidative phosphorylative capacity, meaning the ability to make ATP, per year, supposedly, depending on how healthy you are. So it’s kind of a downhill slide. So, it’s okay. I mean, people are losing function. You want to optimize that. But now we’re going to go to the true neurodegenerative disease model, like, do you have a genetically switched-on condition? And what are we going to do to fight that fight? Identify that fight? And the reason
why we made this Module Three over neurodegenerative disease is because it kind of does this: It really typifies everything that we’ve talked to you about thus far about lobes of the brain, and everything that we’ve gone through. So this the clinical sort of culmination of everything that we’ve looked at.

This is one of my favorite areas. I’ve got to be honest with you. I have some things that I really love in neurology, some things that I don’t love as much. And I like treating some things more than I do others. The reason why I like treating people who are losing cognitive capacity is because, think about it. I mean, you can lose fingers, you can lose a hand, you can have renal disease. You can even have a heart bypass. But you can still recognize your relatives, have a conversation, enjoy a movie, appreciate art, whatever it is that you’d like, you can still love and like. But when you start losing your brain, the very essence of who you are disappears. So this is one of the reasons why I think this is kind of a passionate topic for me, is because I don’t want to see myself, or my family members, or anybody around me... I don’t want to see them lose that cognitive edge to where they can enjoy the things that they really enjoy. You can lose your fitness, you can – like I said – lose a lot of things. Just don’t take the brain. And of course, if you’re a nephrologist, you’d say, “How dare you say that? The kidneys are the most important.” You know, cardiologist: “That’s the most important thing.” They’re all important. But this is really a big deal, okay? I think. Of course I’m just as biased as anybody else. And you guys know all the disclaimers here.

Now, we found that this was also kind of a week spot in the world of neurology. We found that a lot of people who were trained, they didn’t have the capacity to look at language and sort of break it down and say, “This is where it may be a problem.” We kind of learned that, with dementias, some couldn’t even decipher the difference between delirium and dementia. We kind of learned that, with dementias, some couldn’t even decipher the difference between delirium and dementia. So I need to go through and just define what dementia is. Like, what exactly does dementia mean, and how do I determine dementia versus delirium? And if somebody’s delirious, what are the causes of that? Because the worst thing you could ever do is try to treat somebody for dementia when they have acute onset delirium, because they have a urinary tract infection and they’re an elderly person. That would be a very bad thing to do, right? So we’ll go through and we’ll define some of those things.

So, I want to take some of the cellular mechanisms, apply them to clinical syndromes. So you’re not going to see me get as cellular. I’m going to do some of that at the beginning, and I’m going to talk to you a little bit about calcium homeostasis within a cell. But we’re going to get into the clinical stuff, and then know the details, really of each syndrome. Break them down. I’ve got so much redundancy, really, of that in this section. And the reason why I made it redundant is because I want it to be redundant. I need you to see it over and over again so that you can start to identify, “Man, this is clearly this neurodegenerative disease.”

Be able to diagnose, recognize each pathology. And then again, look at severity and prognosis. You saw the lady earlier. Here’s what’s going to happen to her: She is going to continue to probably neurodegenerate and have problems. I don’t know how long she’ll stay as functional as she is. But right now, they’re happy that she’s doing better. I would say that, for someone that has, like, Alzheimer’s disease, every day that is an improvement is worth a million dollars, maybe. I don’t even know. It’s invaluable, in other words. You give somebody back a day with their grandkids, you give them the ability to go on one more vacation, you help their brain have the capacity to do something that they weren’t doing for six months, like tell time... I mean, think about it. If you can’t tell time, it’s going to be a pretty rough day. So there’s little things I think we take for granted, but that’s why I like this stuff.
And then, really what I’m going to be progressing into is learning how to be multi-dimensional on treatment, and multi-dimensional as far as treatment plan is concerned, because I think that those are the… That’s what really separates great clinicians from clinicians that just know the material, and that is, how… you know, what really is involved here? What am I going to treat first? What am I going to treat second? What do I stack together? And then, how do I start to put this together in an order that makes sense? And it’s a lot easier to learn that when you see somebody do it, and you see how somebody thinks. And that doesn’t mean that I’m trying to get you to think exactly like me, but I want you to see the process of it. Because we give you these localization forms, we do all these things, but then I might say this: Like, we had somebody last night at the hands-on deal, and there was lots of neurological signs and all these things, and what it boiled down to is, the individual had an anemia that, you know – because we were asking questions about the heart and all these different things – there’s an unresolved anemia. Well, that has to be resolved, then you can activate the brain.

Guys, if you have an anemia, and you’re not carrying... Let’s just make it simple: where you’re not carrying oxygen to tissue, and if you don’t carry oxygen to tissue, you don’t make ATP. And if you don’t make ATP, you’re activating a system that literally doesn’t have any energy. I don’t really know how to pull that out of this material and tell you that it’s safe to go out and start treating people and never run a CVC. I know you heard me say that earlier, so I don’t want to sound super-redundant, but it really is one of those things that... it is kind of something we have to pay attention to.

Now, we’re making these localization forms, and then we’re making these sort of conglomeration forms, where it shows examination findings and applications. And I want to reiterate again, because I know somebody will go off and not catch it. Do you see the applications section? It is not a hundred percent complete. We will add things to these. These will grow. We will make charts – we’ve already got one made for the vestibular system next module that is really, really, really good. Okay? The hands-on section for next module is three hours straight of vestibular tests and how do you do them. I think that it’s going to be kind of difficult to learn all the material. I would say that I would want everybody there, because you’ll learn a Hallpike. You’ll learn and Epley. You’ll learn how to do all the, you know, the stuff that we’re going to be teaching in the Module. You’ll learn the hands-on, and it’ll make a lot more sense to you when you go through the lecture. So, really planning out how all these forms are going to grow, and how we’re going to add these. These are the things that are the most time consuming for us, because we have to sit down and make sense out of this, and then somebody has to put it together, and it has to be organized, and really done in a way where we think that people are going to grasp it.

So, we’ve already kind of done the early neurodegeneration. Now we’re kind of at the neurological differential diagnosis. After this, Dr. Kharrazian’s going to go more into the cellular mechanisms. And then tomorrow we do treatment of cellular mechanisms, and treatment for neurodegeneration, or the functional neurological model.

So, the way it’s going to kind of work now is, the first couple of hours will be review, Saturday will be learning new material, and then Sunday will be learning the applications of the new material. And there’ll be questions at the end of each day, so that people don’t feel sort of left behind. And we’ve gotten pretty good feedback so far that answering questions has helped people, because if you’re on the other side of the planet, and you have a question, you don’t really have a platform whenever you send it in and somebody answers it. We feel like that helps.
Now tomorrow, what’ll happen is, each one of these boxes will be filled in finally, and we will work through an entire case at the end of the day. So you will finally see... We were giving you a way to think You will finally see how each box is filled in, and you can use it as a way to strategically say this: “Okay, look. I know where the problem is, and I know what their chief complaint is. And I’ve localized it with my intake forms and my physical exam.” And then you’ve looked at things like memory, speech, cog... whatever it may be, you’ve looked at it. And then we finally localize it. Where is it? Where are the regions, and how do they related to each other? Is there more than one condition that’s not related? So they’re separate, but they actually end up impacting each other? Okay?

So for instance, if you have neurodegeneration and you have diabetes, could a polyneuropathy end up affecting your brain? It’s a decrease in feedback, or information into the somatosensory cortex. So you don’t stimulate your own brain. That on top of the fact that the diabetes itself is going to perpetuate neurodegeneration, in all likelihood. So it’s like you’ve got one genetic condition, and another genetic condition, and now they’re colliding together to create a scenario where, if you don’t pay attention to one, the other one is really not going to do anything.

And then this section right here, we’re going to be identifying exercises, identifying pre- and post-synaptic pools that will be affected, the regions – this is what we’re going to be adding into future modules. You’ll have those, like, those compilation forms up, but then we’ll overlay pictures of the vasculature, and then if there’s a specific vascular bundle that’s damaged, it messes with that whole area. So then you’ll know if there’s a stroke to this area, it’s related to this part of the vasculature, and you’ll be able to trace it all the way down. So every time we add material, those forms will continue to grow.

Well, then we go down here, and it’s “Identify the metabolic factors that impact that region.” And I can’t tell you how much this has changed my practice. Between just doing neurological therapy, and then doing neurological therapy at a rate in which the patient can tolerate it, and their brain can say, “Yep, I’ve got the energy and the endurance and the mitochondrial function, and the glial cells are not inflamed, and the cell membranes are stabilized.”

This stuff we’re going to be going through for this afternoon. You’ll understand. And then, we’re making case-specific exercises, and pretty soon what’ll happen is, we’ll put up a case, and you guys are going to start making treatment plans, based upon all the information we’ve given you. So it’ll go from “here’s the regions; need to understand it,” to “here’s everything brought together; you need to understand it.” “Here’s a list of exercises; you need to understand them.” “Now, let me give you the entire thing: You put it together.” That’s the process. And it’ll be like, “Hey, you give some supplementation. What would you give?” And then it might even be like this: “Hey, here’s some medications. Does this make sense or not?” That’s reality. We have to make it reality. How many patients that are elderly, with neurodegeneration, are on meds? Virtually all of them, right? For one thing or another. Maybe it’s blood pressure or maybe it’s a blood thinner. Maybe it’s something else.

This is what we’re going to be looking at right here. Now, I’m not going to go through all the brain tumors, because I don’t want to make you... That’s not what we’re here for. I mean, if you think somebody has a brain tumor and you find it, please refer them out. We’re not making anybody oncologists here. And even most neurologists are not oncologists. They’ll send them off to somebody that specializes in neuro-oncology, or just regular oncology, or whatever the case may be.
We’ve already went through the early neurodegeneration, or the mild demyelination. Excuse me. Or the lack of plasticity and integration. So I’m going to go through all of those really hard-wired neurodegenerative diseases, and so we’ve got neurodegeneration, and right here is the neurodegenerative disease part. So this is where we’re actually building up to. I have animated what tau does perfectly in the pharmacology lecture. I have animated what amyloid does. And these are terms you may not even be familiar with yet, but you’re going to be by the end of the weekend.

In other words, what are all the intracellular and extracellular processes going on that are messing with the brain, and then is there any nutrients, supplements, or functional neurological mechanisms that actually make it better, or reduce the probability? And they’re coming up with all kinds of things. Some of it makes sense to me; some of it doesn’t. Like, when you make these oligomers, they turn into amyloid, and then it messes with the cell, and it stops the synapse. They’re trying to make vaccines for that stuff. I mean, you... They’re coming up with all kids of things, alright? I don’t know that any of it will work. I think a lot of that stuff looks good on paper. In reality, sometimes it doesn’t work out so well.

Okay. [You saw] this slide already earlier, but I want to go over it again, because this is kind of the basis slide of what we’re going to be doing. So, in dementia... Dementia is this: It’s not rapid onset. But delirium is. Now, some things that can cause delirium: dehydration, medications, infections. In other words, there’s a lot of things that happen where there’s a rapid onset of a decline in neurological function that’s not something that insidiously happens over time, like, “You know what? Three weeks ago I couldn’t find my keys; six months later I can’t find where I parked my car; six months later I don’t know the names of my family members.” But you still probably need to check out the anatomy of some of these patients, meaning imaging and things like that.

So the biggest thing is, just forgetting stuff you recently learned. That’s short-term memory. “I just don’t remember what I was just told.” But then it gets a little bit more aggressive, and now it’s like you’re forgetting dates and appointments, and things that are really important, like anniversaries and birthdays. I know every guy in here is like, “Oh crap, I’ve got Alzheimer’s disease.” Nope. You probably don’t. But memory lapses in the middle of conversations, like, “What was I saying?” I mean, and you see it, when people are tired and they’re fatigued, and they’re like, “I just totally forgot what I was going to say.” Okay, it happens. A senior moment. And the biggest thing is forgetting locations. So, thank God for the, you know, like the automatic car, like, ding-ding-ding, so you can find your car.

But I’ve had a couple of instances where, like, I’m walking out of Wal-Mart, and you see some lady wandering around, and you’re like, you can just see it. You’re like, “Hey, you okay?” and she doesn’t want to say it, and you’re like, “You can’t find your car, can you?” And she’s like, “No.” And then it’s like, “Well, what does your car look like?” And I always ask this, the first thing: “What color is it?” “Uh, I think it’s green.” You’re like, “You got a green car?” “No, I think it’s read.” And you’re sitting there going, “Wow, you don’t even not only know where you’re at, you can’t remember the color of your car.” “What kind of car do you have?” “Mmm, I don’t know. I think it’s a Corolla.” And you’re going, “I think it’s time to take your keys away. Do you have a phone?” I mean, there’s been some... How many of you have been through situations like that, where you just see that person wandering around? It’s not so good.

With Parkinson’s disease, we want to think this: Motor. With dementia, not as much motor, and some types we’ll see it, but it’s really highly cognitive. Now, when these things advance, they go across their borders
of symptoms. Like, a Parkinsonian condition will start out motor, but it may progress to cognitive changes. But Alzheimer’s disease will start out with cognitive changes, and it will progress maybe to motor. Multiple systems atrophy will be much more autonomic, but then will progress into cognition. So I’m going to show you how these things start, and then how they end. And the end result is this: A lot of them look very similar.

But you have to be able to go back to how it started. Okay? Frontotemporal demise: A lot of language and a lot of behavioral disturbance before the actual memory loss or the dementia occurs. Alzheimer’s does not start that way. So when you go back and you’re like, “Hey tell me a little bit about what’s the first thing that went in the patient here?” And as they draw out the timeline – and here’s what I suggest you do: Everybody get dry-erase boards or pencils or something like that, and you draw a timeline out, and then start etching in: What is the first thing that occurred, and where are they at now? And that will tell you how for down the pike have they gone, where did they start, and then you can start saying, “This looks a lot like this condition, not like this condition.” And then the further down that line they are, the less likely you are to make a huge impact in their condition. Catch them early. I’ll show you some stuff about that in a minute.

Now, cerebellar degeneration. We’re finding a lot of things degenerate the cerebellum. There are genetics, SCAs, spinocerebellar atrophies. You need to know the difference between a SCA and a Friedrich’s ataxia and a Charcot-Marie-Tooth disease. I will show you those three things today, and I hope that you get those three things. And a lot of kids get these. And the cerebellum is one of those areas that can be deafferentated, meaning you’re sedentary, or you have cervical myelopathy, so the pathways that ascend up to it are not there. But also with inflammation and autoimmunity, this area gets slammed a lot. So you have to kind of say to yourself, if you see cerebellar damage, “Is it vascular? Is there infectious disease? Is there autoimmunity? Is it deafferentated? Is there something like, you know, a Chiari malformation?” And then another thing is this: There’s really quite often tumors there. It’s a pretty common place. So when we look at this, we’re like, “Hey, can I simply tell the difference between a cerebellar problem, a Parkinsonian problem, and a straight dementia?” So let me stop here and give you a couple of easy things.

Cerebellum. Doesn’t have much to do with cognition directly, but it will indirectly go to the contralateral frontal lobe. But these are people... cerebellum is very, very, very involved in this: telling the cortex how to do things. Like, “Hey man, let me give you programs. Let me make this nice and smooth for you.” So things go so rapidly, you start and stop so quickly, that it moves smooth. So when you’re... with a cerebellar lesion, you’re just sitting here and you’re fine, but as soon as you go to move, and you need to push those programs through to the cortex, they’re so delayed, it’s kind of like I said last night to some people: Have you ever had a really slow internet connection? And you’re like, “This think won’t even load.” That’s kind of like when the cerebellum is damaged, it won’t load things into the cortex very well, so it’s like this: The more intention, or the more finite the movement gets, you see it break down and it becomes very evident. But it’s not so much cognitive, even though the cerebellum, they’ve proven, does show involvement in cognition. But it’s not the main symptom. So if you see that person with that wide-based gait, and they are a little bit floppy or hypotonic, and they have a little bit of intention issues, or kinetic or postural titubations... We’ve got a whole lot of things we’re going to show you about the cerebellum with eyes and stuff like that. If you start seeing those things, you have to say to yourself, “Okay, wait. This looks highly cerebellar to me. Which cerebellar condition is it?”

So, here’s my... Here’s how I’ll work through it. “Do you drink?” Because if I see it in your legs more than your arms, and you have busted petechiae on your face, and you’re getting very thin legs with a
protruding abdomen, I may say this: “Do you drink?” “Um, a little bit.” “No, no, wha…” And you know, the three-question rule. By the time you get done talking to them, they’re drinking, like, a bottle of whiskey a day. The problem is, is it really destroys the anterior lobe of the cerebellum, and so what happens is, the anterior lobe of the cerebellum controls the legs. So their heel-to-shin is really terrible, and it’s way worse than their finger-to-nose, and rapid alternating movements. But they start to break down. Now, when that happens, please do me a couple of favors. Check their labs, and check their thiamine levels, and make sure they don’t have some sort of really multi-dimensional B-vitamin, you know, deficiency issues. Because it can wreak havoc on the brain. One area that suffers tremendously is the cerebellum. If they don’t have that, they may need some genetic testing. Here’s the only problem with genetic testing: You have to sell a kidney to afford the genetic tests. Because some of the spinocerebellar atrophy tests, and the genetic tests, can run anywhere from ten to twenty thousand dollars. So it would be better if you knew how to just diagnose it clinically. Some people want that tangible information though, because they want to know if they have a genetic condition, because they want to have kids. So it’s important to them, okay?

Do they have thyroid disease? Do they have Hashimoto’s? You heard Dr. Kharrazian earlier talk about TPO. It goes right to astrocytes in the cerebellum, and creates a load of problems with astrocytes. And one of the problems with astrocytes is the amount of glutamate that can be released, and the amount of other inflammatory byproducts. And it creates a situation where the cerebellum may be overfiring, or it can’t summate at all. So maybe it takes just a little bit of activation. It fires very rapidly and then fatigues, and we call that, you know, some of the past lingo has been TND or transneural degeneration. In other words, it’s very fragile. Okay?

So with Parkinsonism, it’s this: The on-off switches are messed up. So with cerebellum, it’s the “let me give you the information so that as you’re trying to do it, it’ll go correctly.” With Parkinsonism, the basal ganglia, which is what says start and stop, Just at rest, and when you’re going. You’re just sitting there, and now it’s unbalanced, so you may have an oscillation, or you may have firing of one system over the other, and now you see a tremor at rest, but when you move, it’s slow, but you see it go away. So you may have them sitting there, and they’re doing this, and then you bring their hands back up like this, and then it’ll start to reemerge; after ten or fifteen seconds you’ll see it come back. Versus cerebellum, they’re fine, they come up maybe not so bad, but then as they reach for something and grab it, you see their movement break down just a little bit as it becomes more detailed.

So these are the three categories: Is it straight-up cortical dementia? Like Alzheimer’s, hippocampus frontal, and then little slips in different areas? Is it frontotemporal demise? Is it corticobasalar degeneration? Is it multiple systems atrophy? Or is it Lewy body dementia? We’re going to go through each one. I know I said five or six different things there. We’ll break it down nice and slow. But the bottom line is this: The frontal lobe may… will probably be involved in all of them. If the cerebellum gets damaged through something called diastasis, the contralateral frontal lobe will break down. We may get depression. We may get difficulty concentrating. There’s a lot of people that they’re like, “I’ve got adult ADD,” and you start looking at them, and you’re like, “You know what? You’ve got adult ADD because you’ve got adult neurodegeneration.” And then they take certain medications, which I’ll talk to you tomorrow about. How do the pharmacokinetics work? Why does the brain get better? Or, why does it look like it gets better, and what does that tell you as a functional provider?
So, focus and attention, working memory, brain endurance. Really, when brain endurance goes down, and cells start to die, and certain regions start to become dysfunctional, we see, very commonly, depression, focus and attention, working memory, and all this stuff goes down because brain endurance is not there, so these people go through their day, and they’re like, “Man, by the end of the day I’m functionless. I can barely do anything.” And you’re like, “Wow, that’s endurance issues. That’s a metabolic component that we maybe need to enhance before we start doing therapy.” And there’s some patients that come in, and I’m like, “I know for a fact if I do therapy at 4:30 on this patient, after they’ve done X, Y, and Z, they’re going to fail on all of their therapy,” so I don’t necessarily do therapy at that time period. Some people are different. Okay?

Here they are. So let’s take a look at these real quick. There is vascular dementias. Why in the world would a vascular problem create dementia? Just picture it like this: In order for me to have a city to function, I have to have a four-lane highway. It now turns into a two-lane road. Can’t get materials in, can’t get materials out. There’s not enough oxygen to get in and get out. There’s not... I mean, everything that you need to make the brain really happy, you’ve just reduced all of the building products. The oxygen, the micro- and macronutrients, they’re not getting there. Listen: When somebody comes in with neurodegeneration, you literally have got to run lipid panels.

Let me explain to you what I mean. Run LDL, HDL, total cholesterol. Those things actually do matter. I run apoenzymes, and I’ll talk to you about that tomorrow when I talk to you about treatment. But I also run homocysteine, and I also run fibrinogen, and I also run inflammatory markers. Just some basic inflammatory markers: CRP, and, you know, ferratin, which... Ferratin is not normally an inflammatory marker, but it can go up, because iron is utilized by macrophages for immune responses. So look: it’s called a, you know... You can also overdo that with Fenton responses. Somebody comes in, and their cholesterol is way too high, their homocysteine’s way too high, their fibrinogen is way, way up, their triglycerides are at 600, and they have abnormal insulin problems, and they’re diabetic, and they have poor capillary refill, and they’re starting to get cold limbs, cold nose, cold toes – ears, nose, hose, and toes – those things... it becomes a problem. There’s not blood getting to the distal extremities. And so when you look at that, if it’s not getting to your hands and feet, it’s not getting to your head. Over time, the brain starts to break down and starts to decompose, and then whenever you do MRIs, you start seeing things like this: patchy white matter disease. Now, how many of you have seen patchy white matter disease on an MRI? Well, it’s so common, that radiologists are like this: “It’s just a normal variant for age.” That could be demyelination because of multiple sclerosis, it could be demyelination because of gluten reactions, it could be demyelination because of small vessel disease and ischemia. You have to look at it and then correlate it with other things, because some people will get quite a bit of it.

Infectious disease. We’re finding a lot of correlation with spirochetes and neurodegeneration. Certain types of virus. Had a patient come in, twenty-three years old; he couldn’t remember how he got there. So I’m like, “Wow, this is not good.” And he started getting a foot drop, and had a massive neuropathy. Ran an RPR test on him, and an HIV test. The guy ended up with syphilis and HIV-positive, and it was attacking his brain, and he was getting decimated from infection. So he was going through what looked like early onset dementia, but he had infectious disease. So you’ve got to realize, “Does this make sense for the age or not?” It’s not normal for a twenty-three year old to say, “I don’t know how I got here, man.” You know, do they have a spontaneous bleed? Something happen to them? Did they have a stroke? Do they have inf...? You know, he didn’t have any of those things. So you kind of have to boil it down here: I’ve got to look for infectious disease. And if that’s the case, they need to go where they need to go.
Demyelinating disease. Well, like MS can cause problems. And endocrine problems. One of the things that we’re really seeing is this, in females, and I just want to kind of throw this out there. If you go through menopause, and you have ovarian letdown, ovarian drop, and you’re starting to lose your estrogens, and you have bad adrenal function at the same time, you don’t have that adrenal capacity to kick up the estrogen levels to support it. So if you have bad adrenals, and you go through menopause, and your estrogen levels drop rapidly, dementia can start pretty quickly. I’ve seen it start within a couple of months of this happening. So, keep that in mind in your patients, okay?

I can’t begin to explain how important it is to just understand TBI. We have a whole module on TBI, so I’m not going to get into it too much here, but of course somebody can add traumatic brain injury, and that starts off a neurodegenerative process, and we’ll talk about that in the cellular mechanism section.

But really, [B vitamins] are a big, big deal. So people who have, like, low stomach acid, or they have pernicious anemia, or they are drinking, or maybe they’re, you know, have a certain type of diet or lifestyle, they may not have the B vitamins to just have a really awesome nervous system, so sometimes it’s just as simple as giving them some B vitamins and then activating their brain, and they just do way better. Methylmalonic acid. Great marker, along with some of the other specific B vitamin markers. Methylmalonic acid for B12. Really good.

Autoimmune of the vasculature. You won’t see that a whole lot, but it happens. Toxicity does occur. The biggest one is alcohol. It really is. Alcohol, over time, will start to do bad things to a brain. It’ll just make it shrink. It hits the cerebellum, and the cerebellum hits the frontal lobe, and then the person gets depressed, and they start to neurodegenerate fairly rapidly, especially when somebody is allergic to one of the components of the alcohol, so now they’re being inflamed to the alcohol, and they’re having a toxic reaction to the alcohol itself. That’s a bad combination, okay?

And then some of the other things, like hydrocephalus after injuries and so forth. We won’t get into all of these. We’re going to stick with the main ones. But you’ve seen this slide a thousand times, and that is, guys, we still have to have oxygen. You can’t be anemic. We still have to have glucose. You can’t be diabetic. You still have to have stimulation. You’ve got to get up and move. You can’t have oxidative stress. You’re going to lose a percentage of it after the age of twenty-eight, thirty-nine, or twenty-eight to thirty-two. So with anemia, with poor circulation, with dysglycemia, lack of activity, any inflammation – whether it be from a virus, a bacteria, an infectious disease of any type – autoimmunity, all the way down to some of your environmental toxins, it’s going to create unhealthy neurons and you’re going to go downhill.

Now, if you’ve already got a genetic neurodegenerative disease, and then you have these things on top of it, there’s the possibility of it escalating the decline on the amount of progression that you’re going to have in this disease. So this right here, straight of the paper, Nature Reviews, right here. So this is the early stage, and we start getting synaptic loss. This is where you want to recognize it. When you start getting synaptic loss, you haven’t necessarily loss cell volume yet. So by doing things to reduce the triggers, reduce the things getting in the way of synaptic capacity, and then activating that person, you can re-establish synaptic connectivity, and not always lose cell volume. But when you start getting down here to where you really get neuronal loss, it’s very difficult to make neurons grow back. I mean, if anything, that’s the future of medicine in the world of neurodegeneration. How do we get stem cells to do what they’re supposed to do to grow brain matter back? But here’s the thing: Let’s say that I inject... or, I get a stem cell to grow? Does
that mean it’s going to synaptically connect? Does that mean it’s going to immediately go back in place and regain all the memory and all the function, and everything that you’ve learned over a lifetime?

So, it’s not just as simple as saying, “Yeah, we’re going to give this person stem cells and regrow neurons. Okay, cool.” You regrow neurons, they’re not connected. They don’t have the same memory. They don’t have the same capacity as the ones that were there. So it kind of makes you start thinking. I’m not so sure that in our lifetime this is going to work out. I think the best thing to do is, recognition, early prevention, get rid of all the factors, and try to live a clean life and activate the brain. Does that make sense? That’s what we have right now. Okay?

And then once we go down here, it’s just functional deficits, and that’s when we start to really see it. And that’s why we wanted to go through the early things. So we put right here, right after the area of prevention, you start getting symptoms. And you have this window of opportunity, and this window of opportunity is right about here. Once you start to get right here, and you get on a rapid decline, you’re all the way down to the component to where you’ve actually lost neurons, and even sometimes activating them can exceed their metabolic rate so bad that they lose neurons faster.

So, I’ll just give you the rule in our facility. You know that scale you saw, like, stages one through seven? In six and seven, we don’t treat. Five maybe. Three and four is where I really feel like I can do something to maybe prolong the five, six, and seven. I love getting people in one and two that have a family history, and then I can say this: “Look man, you’ve got a family history, and you’re showing some early signs, one and two. We need to start doing some stuff right now while you’re thirty-eight or forty, so that when you’re sixty, you don’t end up at stage five and you can’t work.” Do you see how that... It’s really... that’s the name of the game. Not everybody that walks in... Some people will walk in, and they’ve already kind of reached it. But these are the things that we need to be looking at.

So, Dr. Kharrazian I think, is probably going to go through this really well, and that is the cellular mechanisms. And I don’t want to get into it too much. But let me just say this: Any time you create a couple of things, all hell’s going to break loose. If I have sustained inflammation, because the inflammatory cells have decided to be turned on and not turn off, you’re going to have a landscape of neurons that is going to be destroyed. And these are called microglial cells. So, what are the glial cells? And I’ll say this briefly without stealing Dr. Kharrazian’s thunder on this. There’s astrocytes, there’s microglial cells, and there’s oligodendrocytes. This is way back from biochemistry school days, right? It’s real simple. Oligodendrocytes make myelin. Astrocytes have certain cellular functions; they deal with blood-brain barrier.

And then we’ve got microglial cells, and they’re considered this: the immune surveillance cells of the central nervous system. And they look at things and say, “Hey neuron, you’re too weak. You gotta go, man. You can’t stay here and die. Become a debris field, and then all of a sudden we make an antigen-antibody response to neurological tissue. You gotta go.” So they go through a process of removing and clearing things out. The problem with microglial cells is, they’re a bit paranoid, and when you tick them off, they tend to stay ticked off. So you get that one head injury. And they may stay on for two to four weeks, because they’re like this: You know, your parents are out of town, and you had that party, and you’ve got to get everything cleaned up before everybody gets home. They just want to clean everything up before the next head injury. But let’s say that you have another head injury while they’re still in the process of cleaning things up. They just get even madder. So now they stay on for six to eight weeks. And then you have another head injury during that
six- to eight-week time, and they’re like, “You know what? If this is going to be your lifestyle, here is what we’re going to do. We’re just going to stay on.” And so they’re going to produce things like interleukin 1B, interleukin 6, TNF-alpha, all the things that are inflammatory and create apoptosis or cellular destruction. And so now you start losing cells that aren’t necessarily problematic, because there’s global inflammation. And when this goes on long enough, it’s called chronic traumatic encephalopathy. Now, how many of you have heard of that? Listen, when you’re in the NFL, every freaking football play, every play is pretty much a head injury. When you have somebody six-foot four running full speed at you, and they hit you, even if you don’t get knocked out, it still is not good for your brain.

Some of the studies also show this: If you’ve been knocked out, your chances for having complications later on are higher. So listen: Repeated head trauma, bad deal. Microglial cells making inflammation, bad deal. Look at this: Here’s resting microglia; here’s microglia as they start to get angry. They phagocytize things, and then they start making all of these things that destroy either cell bodies, myelin, the blood-brain barrier, the outside immune system comes in, everything starts to get confused, and now outside inflammatory events can come into the central nervous system and start creating a central nervous system inflammatory event, even though that’s not where it originated. So I ask you the question: Is it possible for somebody to chemically re-concuss with no head injury? What if they have a celiac event? Or what if their thyroid antibodies go way up? Or what if they get an infection? Or what if they get the flu? Anything that creates inflammation, and it gets through, and you’ve got a sensitized microglial system, you have to get a little bit worried. And this is on... this is a lot of stuff that Blaylock and Maroon started, way back whenever they were looking at NFL football players, and they were looking at CTE about a decade ago. Okay? Pretty well-referenced information, even though it changes quite a bit, because the technology coming out, especially for testing it, is getting better and better.

So when we have all these things, we have to remember that all of these neurodegenerative illnesses have that as a cornerstone, and then they have another thing, and that is letting calcium in. Now just real quick, let me tell this story. I’m a cell. And I’ve got an NMDA receptor on me. And you guys have heard me tell this story before, but I’m going to tell it again very quickly. There’s receptor activation, or there’s a hormone, or there’s a neurotransmitter. Something docks on the cell that activates it, and the cell says, “This is great. I need to be activated, because to be quite honest with you, I have to be activated so that I can activate a gene response, and when I make a gene response, I make proteins, and when I make proteins, I make structure, carrier molecules, neurotransmitter vessels, neurofilaments.

In other words, everything that’s made inside the cell is activated because the cell is activated. Is that cool? That’s very cool. And it does it through a bunch of different receptors on the cell surface, one of them being NMDA receptors. And I picture an NMDA receptor is like a really famous person, and it’s got, like, a posse with it. You know, all the guys that run around, and they’re like, “Yeah, that guy’s cool!” Those are called ampa receptors. And ampa receptors carry an action potential from one cell type to another cell type, but when they’re activated, they also activate the NMDA receptor, and it says this: Let’s let some calcium in. Let’s move magnesium out of the way, let’s let calcium in, and calcium will come in and activate mitochondria to make energy, activate the gene to make proteins, and when we do that, everything will be cool. The cell structure will be good, the bilipid membrane will be good, and we’ll be very, very happy. When there is inflammation, or when the microglial cells are ticked off, or when there’s a problem going on, those NMDA receptors, and voltage-gated calcium channels, and the endoplasmic reticulum, all decide to dump calcium out at once, and the whole thing reverses, and you get nothing but free radical damage within the cell, and
every cell goes boom. I put a great paper in your notes that talks about calcium buffering inside the cell. Not extracellular calcium, but intracellular calcium buffering as the cornerstone of all of these diseases.

See, you may make amyloid, you may make tau, you may make synuclein, but if you start losing energy, and you start having an influx of calcium, you trigger them, and they may trigger at different ages. So your head, boom! Now whatever genetic condition you have, really gets nasty. You don’t want neurodegenerative disease along with trauma or energy failure-induced lack of neurological function. When you combine the two together, you start expressing things in a very nasty way.

So, as we do this, and we go through, we have to realize that this oxygen, glucose... and you saw this slide earlier, but when we look at this, when there’s brain damage, and there’s cytokines, and there’s inflammation, and the brain is going downhill, it’s possible for us to have a decrease in hormones. It’s possible for us to have abnormal adrenal function. It’s possible for us to have a decrease in TSH and T4, not an increase in TSH and a decrease in T4, like with a primary hypothyroidism. Sometimes you see brain patterns. And, you know, of course the autonomic nervous system will change, and you saw Dr. Kharrazian talking earlier about how sometimes the vagal system is actually a pathway from the guts back up to the brain to create problems, which can be a problem as well.

So, this is the first thing I want to talk about as something that will really screw with the system, and that is, insulin. Now guys, if you have type 2 diabetes, here’s what’s going to happen. Let me just put it to you this way. Remember that calcium story I just told you? If you have blood sugar dysregulation, it allows the calcium store to be dysregulated. If you have too much insulin, it allows things that promote things like Alzheimer’s disease to escalate. If you don’t have enough insulin, then you don’t have the capacity to utilize fuel appropriately. So one of the things we want is this: I want my C-peptides to be normal, I want my blood sugars to be normal, and I want my glucose, oxygenation, and the ability to get the fuel – fuel! – into the system appropriately. I don’t want to be anemic, and I don’t want to be dysglycemic. Does that make sense?

Like, the two things I would tell all of you: If you want to do something for all of your neurodegenerative patients, do this: Make sure they’re not anemic, and make sure they’re not dysglycemic. It’s like, just start there. We don’t have to make it rocket science. And make sure if they have an anemia, you help them. Or find somebody that can. And then if they have uncontrolled blood sugar, you have got to do something to get it under control. Insulin is just as destructive as blood sugar. Some people have normal blood sugar, but nobody measures their insulin. And insulin, when it’s really high, it goes up and just beats the crap out of the brain.

And so, what are some signs and symptoms? So the patient comes in, and they’re like this: “Look, I’m starting to lose facts, figures, short-term memory, and by the way, I fall asleep every day at three o’clock after I eat.” You’re like, “Whoa, let’s check your insulin.” You look at it, C-peptides way up, blood sugar’s normal. You say, “Hey, congratulations. You’re having insulin surges, and this is actually starting to make your brain go downhill.” Another person comes in, they’re losing weight, they’re not hungry, they’re skipping meals, their blood sugar’s at 63, and they’re like, “Every time I miss a meal, I can’t, like, remember where I’m at.” You go, “Congratulations, you’re hypoglycemic. That’s one of your big problems.” Do you see how easy that is? It’s really not difficult. Somebody else comes in, they have paleness, they’re tired, their heart rate’s up, they’re tachycardic. You look at them: they have zero iron, they have a heavy menstrual cycle, and you go, “Congratulations, you are anemic. You literally are not carrying oxygen to your brain, and your brain’s going,
‘What are you doing to me, man? Please fix me. I need some iron, and you need to make my blood volume loss go down. I can’t lose all this blood, because every time I do, I’m losing my iron, and every time I lose iron, I don’t have mature red blood cells. When I don’t have mature red blood cells, I don’t carry oxygen to the brain, and when that happens I don’t have any energy, and the brain dies.’

So the two things: anemia and dysglycemias. Rule them in and out. Have we given you details on that yet? The answer’s no, but [this is] sort of a preview of what’s going to be coming down the pike right here. The other thing I want to say is just this – and this, I said earlier that stress destroys the hippocampus. Well, here’s a paper, right here. I mean, this is, you know, right out of the literature. “Stress induces the release of corticotropin releasing hormone, adrenocorticotropic hormones, leading to the release of glucocorticoids,” and these corticosteroids, they modulate synaptic plasticity within the hippocampus. So, I would keep them normal and level if I was you, oh ye of the neurodegenerative disease treaters. It’s important. Hey, don’t expect somebody to come in who already has a little bit of neurodegeneration, and is already expressing disease, and they’re going through the most stressful time period of their life with a divorce, and, you know, doing whatever it is, this, that, and the other, and there’s a death in the family... Don’t expect their brain to become stellar during that time period. Like, you are going to have to support them. And you are going to have to say, “Listen, your stress hormones are getting you, your blood sugar is getting you. You need to control your lifestyle. You’re overdoing it. You’re starting to lose brain function, and I’m scared that this is going to escalate rapidly to the point where you have volume loss, and then there’s not as much I can do about it.”

Okay? So this is an important concept to understand. And testosterone and pregnenolone are important [too]. We use some of these things in people who... Listen. If you’re a guy, and you come in, and your testosterone is at 89, and your estrogen is higher, that’s a problem. But I had a guy who came in the other day; his estrogens were at 5. Well, it’s neuroprotective for them too. You want optimized hormones. You want optimized blood sugar. You want optimized insulin. You don’t want to be infected. You don’t want to have spirochetes. And you don’t want to have anemias.

Are you starting to see how the list is growing? Because I’m fixing to just give you the differential diagnoses between the conditions, and that part’s going to be fairly easy. The thing that’s going to be difficult is saying, “What do I look at to help all of these differentiated conditions?”

Alright. Testosterone reduces neuronal secretion of amyloid-peptides. Now, okay. I’m a cell. And I [have] all these receptors. And there’s a thing called a secretase, and it snips these things off and trims them down. If I have a mutated secretase, it starts to cut these receptors off at a rate that’s just bizarre. So they all come off, and instead of being a monomer, they bind into oligomers. And these beta-oligomers come together and make something called amyloid. And then amyloid activates microglial cells to make cytokines. So now you’re inflamed, and the amyloid sticks onto the cell, and then it goes to the synaptic cleft and blocks it, so you don’t actually make transmitter go across the cleft. The amyloid activates the onset of tangles inside the cell, and now you’re globally inflamed. That’s how your brain starts to go like this: sssllllfff.

We have nutrients to stop or help amyloid, we have nutrients that help with oligomers, we have nutrients that help with tangles, and we have nutrients that help with neurotransmitter conduction. So does that make sense? Sometimes that’s very, very, very necessary whenever you’re saying, “Look, I want to activate his Papez circuitry, I want to activate short-term memory, and I want to drive frontal systems as
a neurological mechanism.” But there’s amyloid everywhere, and there’s tangles all over the place, and there’s complement everywhere, and there’s inflammatory cytokines everywhere, and you’re sitting there trying to do this neurological activation dance around this neurochemical environment that’s looking at you, going, “What are you doing? Like, there’s no way what you’re doing is going to work!” That’s why the combination of the two is pretty cool.

I just had... I’m not going to read this to you. I put it in your notes. This is right out of a paper that basically describes everything a functional neurological provider does in a paper that doesn’t care about what functional neurological providers do. I mean, look at this: “…the modulation of synaptic function involves the facilitation of synaptic plasticity. Plasticity, by strict definition, is a change in synaptic strength in response to a brief increase in neuronal activity.” I mean, these dudes, in this paper, just described what we do to a T. I like it. That’s why I threw it in here.

So, we’ve got Alzheimer’s we’ve got to go through. We’ll get it. We’ve got Lewy body dementia; we’ll get it. We have Parkinson’s; that’s great. You’ve already talked about protein folding. We’ve got multisystem atrophy, frontotemporal dementia. That’s the main ones. We’ve got a couple of other ones here: supra... progressive supranuclear palsy; that’s kind of like Parkinson’s on steroids. Corticobasalar degeneration; really easy to differentiate from the other ones, maybe, until it’s end-stage. Huntington’s disease; not going to talk much about it. Cerebellar ataxia; I’m going to talk about it.

Listen: Any time somebody has a movement disorder, you need to check serum copper. You can overload somebody with iron, and it’s not good for the brain. These guys, don’t worry about. Now, if you have somebody with a prion, they’re just unlucky. Okay, I mean, what have they, been in the cadaver lab? Or what’s been going on? Prions are extremely dangerous, and by the way, cook your food if you’re going to eat meat. Down where I live, I’ve had several cases of worms burrowing into brains because of people eating uncooked pork. Not cool. Not a pretty picture.

Now, I put this in there. This is not in your notes. Feel free to snap a picture, whatever you want to do. It’s nothing important, it’s just something I wanted to throw up here and say, what is the difference between delirium and dementia? Look at the very first thing: Acute versus insidious. That’s the biggest thing. If you... There’s no such thing as rapid onset dementia. That’s called delirium. Delirium has a different mechanism of action than dementia. You understand? Again, an elderly person with a fever, in the hospital, with a catheter, and it’s dirty, and now they get a urinary tract infection, they can become delirious very, very easily. What’s the source of their problem? Their fever. Okay? But then you’ve got some things that are pretty common, like, they can both have hallucinations. Their perception can be altered. I mean, things can be impaired in regards to orientation and memory and stuff like that. But just remember this: Rapid onset dementia is not a very common thing. By definition. People don’t just become... They don’t get Alzheimer’s in, like, five hours. Like, “This person was totally fine yesterday, now they have Alzheimer’s disease.” You might have to question that diagnosis just a little bit.

So I made [this] slide for you. And what this slide does is, I put down here the breakdown: forty-seven percent of Alzheimer’s disease, and then then there’s a mixed pattern. There’s some vascular stuff over here. Frontotemporal is only five percent. And then Parkinson’s that goes all the way to supranuclear palsy is probably at a lower percentage than all of them. So what I just did is, I just gave you a flow chart that you can read later on. But this is a list of all, right here. Oops.
Frontotemporal dementia. What does it look like? Alzheimer’s disease. What does it look like? I tried to put little single things in here that would help you distinguish one thing from the other. And that’s going to be probably the most important part that we’re going to talk about.

So right here: Alzheimer’s disease. Well, cognitive impairment, vascular dementia, cognitive impairment. They may be a stroke risk. Their labs may be really high.

Dementia with Lewy bodies: Now, these are people with... they’re this: They look like an Alzheimer’s patient, but they’ve got all the symptoms of Parkinson’s disease. A tremor. Rigid. Stiff. Their voice gets quiet. So when you look at this, you’re like, “Man. Extrapyramidal signs and hallucinations and sleep disorder? That’s all dopamine. Short-term memory loss. Visuospatial activation. That’s all acetylcholine.” Now do you understand how the nutrition and the pharmacology is going to come into play, and then you understand the brain region localization form and how that’s going to come into play. We’re bringing this together into one symphonic orchestra that makes sense. But you need to know where you’re playing.

Frontotemporal dementia. Look: aphasia first thing, and then they become behaviorally disturbed. So they don’t talk right, their behavior’s different, then they get the dementia. Whereas Alzheimer’s disease, it’s not the language first, it’s the short-term memory loss and the visuospatial loss, then they get the language changes and the behavioral changes. It’s the order in which it progresses. The net result is the same. They’re demented, they can’t function, they’re lying in a hospital bed, and they’re right there knocking on death’s door. What is the process they got to? You know, you need to go back and find out again: On a piece of paper. “Where’d you start? Where are you at? Where’d you start? Where are you at?” So now you’ve got this person that comes in, and they’re like, look: they started out with this speech disorder, and they were acting super bizarre, and they don’t have any executive function, and then as time went on they started to become demented. You might say, “Wow. That looks a little fronto... – you know – ...temporal demise. And I’ll go through some other stuff that will add on to that.

This is what we were talking about earlier. Olfactory function and olfactory testing being a big, big deal. It goes first. The enteric nervous system goes, the olfactory bulb goes. Some of your biomechanical and gait stuff becomes disturbed, anywhere from a decade to fifteen years before these diseases start to manifest symptomatically.

Okay. I didn’t define this very well, but since I’m going to talk about dementia, I want to go ahead and talk about these.

Working memory. Now, working memory is the ability to actively hold information in the mind needed to do complex tasks. Reasoning, comprehension, learning. Well, these are parietal. I mean, there’s ways you can test this.

Declarative memory. Now we’re going put to the temporal lobes. And really, this is facts and events. So I can say, “Hey, I can give you a list of facts and events,” or, “I can give you some complex tasks, reasoning and so forth,” and have you repeat them. Now, I can do these in different orders with vestibular stimulation, and make it therapeutic. Are you catching me? I can make you visualize things, and then give you a list of things, and then use vestibular stimulation as a firing pin into all of these regions, and they summate temporally...
and spatially. Meaning, one pathway fires over and over and over, and then I’ve got other pathways coming in to fire into it, so that neuron says, “Alright, cool. I’m activated. Let’s make some plasticity.”

So we start getting a multimodal approach into stacking our therapy. That’s literally the first thing I’ve said to you about treatment since we started. I will give you spatial and temporal exercises. I’m firing one pathway over and over and over to see if it works, and if it doesn’t work, I’m going to start adding other things in that I know come in to it. And sometimes it’s a very odd combination of treatments that finally makes it fire. Okay.

So, we go down here to procedural memory, and this is cerebellum, and this is, you know, the ability to have, you know, flying an airplane, to reading. A lot of these things are automatic, that you would just do as an efferent copy mechanism.

And then short-term memory is hippocampus. This is what our patient had earlier. You can tell her something five minutes... You can tell her something, in five minutes she won’t remember it, but she can remember stuff from twenty-five years ago. Now, you’ve heard me say this before: One of the interesting things I like to do with my Alzheimer’s patients is say, “Okay, look. What’s the girl’s name at the front desk?” Because I will always have the front desk person introduce themselves and say their name, and make it very clear and say it two or three times. Kind of almost obnoxiously. That way it’s one of those things where they should remember it. I’ll say, “What’s her name?” “I don’t know. I can’t remember.” “Okay, what’s your kids’ names?” “You know, Jimmy and Tommy.” “Okay, what’s your grandkids’ names?” And let’s say this person ahs a grandkid that’s eight years old, ten years old, and seventeen years old. They know the seventeen-year-old name, but they don’t know the other two. And you can go back and say, “Man, the disease started during that time frame, right around ten years ago.” You can literally trace it back to the years that they don’t remember. Very, very interesting.

This is where we start doing what this whole section is about. Here’s Alzheimer’s disease. Guys, I just told you the story of amyloid. You have amyloid plaques and oligomers, and it makes neurofibrillary tangles. Picture this: amyloid comes, snaps on the outside of the cell, and it screws with the intracellular function, and it’s just like this: You ever watch the show Hoarders? Well, that’s what the inside of the cell becomes. It looks like Hoarders. You get all these tangles, and nothing can move or transport where it’s supposed to go, so you lose intracellular function and it dies. So, that’s the bad thing about Alzheimer’s disease. Now, it’s... Here’s what you need to remember: Alzheimer’s disease is hippocampus and cortex. And it’s the Meynert system. And it has a little... picture it like this: It starts right up here, short-term memory, and it slides right up to the frontal system, and there’s little bits of it that go in other areas, so that you can remember things, and remember where you were at when you did it, and how you can get to point of where you were at when you remembered it. If you start losing all those things together, like visuospatial, with short-term memory, and some facts and figures, and you’ve had some depression, you have to start thinking to yourself, “Whoa, whoa, whoa. This looks like Meynert system, and the amyloid production of tau and tangles is starting to become a problem in this patient.” That’s going to look marginally different than Lewy body dementia, which I’ll get to in a second. Okay?

So, did we give you an area for the hippocampus on the brain region localization form? Yes. Did we give you frontal lobes? Yes. Did I show you earlier, how one was really bad and then you could see it going into the
frontal system, and then minimally into the temporal and parietal system? The intake forms will literally trace it right through for you, if they have the capacity to fill it out appropriately.

Now, which neurotransmitter deals with acetylcholine? I mean, Alzheimer’s? There you go. That’s my fatigability right there, and it took approximately sixty minutes. No, Alzheimer’s disease is acetylcholine. There’s a cholinergic system. Now, Lewy body dementia: dopamine. So when I say dopamine, you say movement. When I say acetylcholine, you say short-term memory and some autonomic. But now, instead of the hippocampus, which is the subcortical thing that’s getting screwed up in Alzheimer’s, now we have the basal ganglia, the substantia nigra that makes dopamine. So now these people start having things like, okay, these are Lewy bodies that are made. Now, is the cortex going to get screwed up when the hippocampus is messed up? Yes, because there’s projections that go to it. So when one dies, the other one secondarily dies with it, and there’s some other mechanisms.

Same thing here. The substantia nigra, which lives in the top part of the brainstem, when it doesn’t make dopamine, the basal ganglia becomes messed up, but you also have frontal lobe projections that are dopamine. So now the cortex goes away with it too. So you have to say this: “This guy’s demented. He’s got cortical problems. But he’s also got dopamine signs and symptoms. It’s not Alzheimer’s.” You see the difference? If you know the neurotransmitter, and you know the area that’s being screwed up, and what the neurotransmitter does… Dopamine deals with this: hope and movement. It really does. Okay?

Now, Parkinson’s disease, just by itself, it’s a Lewy body also, and maybe it’s synucleinopathy, protein misfolding. Substantia nigra becomes damaged. One of the things that can become the difference between Lewy body dementia and Parkinson’s is, a lot of Parkinson’s patients don’t become demented. They just don’t move well. They’re completely cognitive, they just start to get hunched, they get a little bit slow, but they can still hold great conversations and remember things. Okay?

Vascular dementia. Well, these people have small vessel disease. You see it on imaging. You see it in their labs. So, I’ll give you some other things that will help you differentiate them real quick. I’m just outlining the ones that we’re talking about real quick.

Progressive supranuclear palsy. So again, basal ganglia, midbrain. So this is Parkinson’s that has spread all the way through the brainstem, and then all the way up. And this looks a whole lot like, kind of like Pope John Paul before he passed away. You guys remember how he was super camptocormic, very slow, very deteriorated? There was lots and lots of brain matter, unfortunately, that was damaged in that progressive condition.

Now, corticobasal degeneration. This is a whole different type of intracellular process. But this again is cortex and basal ganglia.

Now, I’m going to show you the differential findings between these in just a second. And then we’ve got multiple system atrophies.

So let’s stop for a second. We have Alzheimer’s disease. Okay? And then we have Lewy body dementia and Parkinson’s disease. And then along with that, we have multiple system atrophy. And then we have corticobasal degeneration, and then we have vascular dementia. I need you to know those things. Because
when somebody walks in, and they have signs of dementia, I want you to have the confidence to go [snap] and just rattle it off and say, “I think this person has vascular dementia because of this.” Or, “They look like they…” and we’ve got a couple more that we have to go through. Or, “They definitely look Parkinsonian.” Or, “This is definitely Alzheimer’s disease.” Alzheimer’s disease may be difficult to determine from corticobasal degeneration, but we’re going to try to give you ways to go around that.

So here it is. I put this in here for you specifically – and by the way, this is right out of a textbook. Right here: Alzheimer’s. Language, delusions, hallucinations, executive function. If you come over here, they have some personality changes. Remember I told you about the different types of memory? They lose their declarative memory first. They may have some language stuff. Now, what was the language difficulty that our patient had earlier? Were they fluent? Yes. Were they receptive and comprehensive? Yes. But they couldn’t find words, because they can’t remember them. When you can’t remember words, and it gets so extreme, it looks like an aphasia.

So I’m sitting there, and I’m like, this person comes in, they’ve got… they don’t have personality changes at first. They have visuospatial changes, some cognitive changes, but progressive neurodegeneration typified by memory impairment first, executive dysfunction, then you might go to motor problems and then eventually you can’t talk right because you can’t remember what you need to say. It’s so bad that in the middle of the conversation, you can’t remember the first part of the conversation, so you can’t answer the second part of the conversation. It’s like, “Hey, I was going to go jump into the car,” and they’re like, “I was going to… go into that thing… uh… that has four wheels…” And you’re like, “The car?” and they’re like, “Yeah, that thing.” You’re like, “Whoa.” They are forgetting… their memory is so short-term, they’re forgetting pieces as they go. Okay.

Now, Lewy body. Cognitive, declarative, but these people have falls and syncope. Now, why in the world do they have really bad delusions? Dopamine deals with hallucinations and delusions. Dopamine and catecholamines also deal with blood pressure. So these people can become syncopal, fall, they very commonly get depressed. But look at this: There’s one thing I want you to see here. Some people come in and you’re like, “I don’t know if it’s Alzheimer’s, and I don’t know if it’s Lewy body dementia.” Check this out. Are they rigid and masked? Did you see the patient I showed you earlier? She had zero masked face. She’s like, “Hey!” She was just smiling, happy as she could be. “Where are you at?” “I don’t know.” That’s different than this: “Where are you at?” “I don’t know.” You’re like, “Whoa, that’s dementia, but that’s not the cholinergic tau, neurofibrillary tangle one that I know with Alzheimer’s. That looks more like Lewy body dementia.”

It all boils down to this: Two different genetic issues, two different neurotransmitters. You following me? Now, wait until I start talking about pharmacology and the interaction between acetylcholine and dopamine. Guys, you do not want to give acetylcholine to somebody who has already lost dopamine, because it inhibits it in the basal ganglia. In fact, if I’m giving you medication, L-dopa, to drive up your dopamine, if it’s getting too high and you’re getting hyperkinetic, I can give you different types of cholinergic medications to regulate that on top of it. So now it becomes a seesaw between “which one do I make higher” – “which one do I make lower” in order to get the extra… not the extra pyramidal findings, but the hyperkinetic stuff from the actual drug, from overdosing, how do I balance that out with cholinergic medication? So you see how, if you don’t know the difference between Lewy body dementia and Alzheimer’s dementia, and you start augmenting the wrong neurotransmitter, how you can actually escalate the issue?
Just hang on to that, because I’m going to go back over that again tomorrow.

Okay, so these people have terrible Parkinsonian symptoms, and they basically look like this. These people look like an Alzheimer’s patient with Parkinson’s disease. So I’m just going to put it to you this way: You don’t want this one. You don’t want any of them, but you really don’t want this one.

Here’s Parkinson’s disease. Well, it’s this: It’s Lewy body dementia, but you know what? You don’t get the cognitive changes as much. Okay? So you can always be like this: “I’ve just got Parkinson’s. I didn’t get Lewy body dementia.” It’s one of the worst.

Vascular dementia. Cognitive loss, looks like Alzheimer’s. Do the imaging. Here’s some labs for you. I just threw it out there. Do fibrinogen. Do your lipid panel. Do homocysteine. Differential diagnosis is imaging with other issues of small vessel disease. They may have both Alzheimer’s disease and vas... sorry about the vascular misspelling there. And vascular dementia at the same time. That’s an overlap. So there’s a high percentage of these neurodegenerative conditions where it looks so overlapped they just really don’t know, so it’s multifactorial dementia.

Multiple system atrophy. If somebody comes in, and they have massive autonomic damage, problems with urination – almost all symptoms are autonomic, like Shy-Drager or something like that – and they’re getting signs of cognitive deterioration with all these autonomic changes, you might want to start thinking of something like multiple system atrophy. Lots of information out there about it being autoimmune. Lots of information about it being inflammatory based. I’ve got to be honest with you: This is a tough one to treat. Very tough to treat.

Front... okay. So here it is. Frontotemporal dementia. What’s the difference: frontotemporal dementia and Alzheimer’s? What I want you to be able to do is, you’re at the bar tonight, you’ve had three drinks, you’re destroying your anterior lobe of your cerebellum. Some of you will be doing that; that’s cool. If you do better with alcohol, then you probably do have a cerebellar lesion. But look: Some... Could you sit there and say this: “Let me tell you the difference between frontotemporal dementia and Alzheimer’s disease.” And of course the person sitting next to you is like, “Okay, great. Go ahead.” And you say, “Look, this whole thing started with an altered, bizarre personality, and they had speech and language problems, and they were very apathetic, and then it turned into disexecutivism.” Because it goes in the temporal system, comes around to the frontal system, versus being in the frontal system and then coming around to the temporal system. So they start getting these bizarre behavioral changes, and these aphasias, and then as it wraps around, you start getting things like all of these impaired planning. So not Alzheimer’s. It does have more motor systems up front, and then speech loss, and then you become... A lot of these people, here’s their behavior changes. Aggressive.

How many of you have been to a dementia unit in a hospital? And there’s just some people, it’s like, “Don’t go near old man Rivers. He will punch your face off.” It’s like, “Why?” “Well, he’s got neurodegenerative illness. He doesn’t have a gating mechanism. He’s like a limbic monster walking around. He’s like, “Eh! Psht!” So, I mean, look. This is one of those things where their behavior and the way they come across, this stuff, along with language, starts changing before the “what day is it, what’s that word?” But eventually, Alzheimer’s disease and frontotemporal dementia will start looking very similar as they progress, and more common areas of the brain degenerate together. Okay?
Corticobasal degeneration. Pretty rare. Pretty rare, I’ve got to tell you. It looks like Parkinson’s disease, but it has dementia. Here’s the deal: They can’t move their eyes well, and their speech is slurred. So I have a great chart here in a second that shows you all of the ocular findings in one paper, with every neurodegenerative disease, proven, researched, and done statistically. Not any of this, “Well, this is what it is, this is what it is just because I say it is.” I don’t care that you know that. We have one whole module on eyes. I will eventually teach you how to differentially diagnose all these, by the way an eye moves. But you can only learn so many layers at once. Right now I’ve just got to get you familiar with, hey man, frontotemporal dementia looks a little bit like Alzheimer’s disease, but what’s the difference?” How does Lewy body dementia really differentially... I mean, what’s the difference between Alzheimer’s disease and these other ones?

So, corticobasal degeneration is one. This is progressive supranuclear palsy. Looks just like Parkinson’s disease, but it’s got, of course, the cognitive changes.

Corticobasal degeneration: These people have alien hands. Fifty percent. Fifty percent have an alien hand. So, have you guys ever seen Spies Like Us? You know the part where they’re in the desert, and, you know, he goes up and he grabs the girl, and he has, like, an alien hand? It’s just like, things happen. The hand will do things. They’ll fight with each other. They can’t control their handedness. Okay? Bizarre things happen. The alien hand goes, and Exner’s area is right next to Broca’s area. So it starts to deteriorate, so handedness changes, the understanding of handedness changes, and speech output changes. So what you see is an alien hand, with language, with the progression of dementia, and profound early speech delay. And then you end up getting asymmetric motor loss. Why is it asymmetric? It typically happens in the left hemisphere. So you end up getting, usually, dominant hand, language hemisphere, handedness goes with speech, and the person ends up with cognitive decline with those two things together. Not easy to diagnose. I’m just telling you right now. Okay.

ALS. This doesn’t have as much to do with cognition as it does with what’s going on with them, in the periphery. Remember, this is ventral horn cells dying. Now, there’s parts of the brain that will die as well. I had a vet; guy came in and he sits down, and he’s like, “I got in a car wreck.” And I’m sitting there looking at this guy, and I’m like, I see his shirt kind of moving around a little bit, and I go, “Hey man, I need you to take your shirt off.” He takes his shirt off, and it looks like little firecrackers going off underneath his skin and everywhere. Little pops. And immediately my heart just sank. Benign fasciculations happen in one muscle group repeatedly, in the same muscle group, and it drives the person crazy. When you start getting ALS and ventral horn cells die, remember I told you this for the peripheral nervous system component. When the ventral horn cell dies, the entire muscle fascicle spontaneously fires, so you can see it. If an individual fibril is denervating, you won’t see it unless there’s a needle in it. So you see these things popcorning everywhere, and their hands are starting to rut, and you start doing, “Oh my God, this is ventral horn cell disease.” And he walks in and he goes, “I got in a car wreck.” And he goes, “Now I don’t feel good.” And I see this stuff everywhere, and I’m like, “You have...” I mean, I told him. I said, “You’ve got ALS.” I mean, we went through the process. I examined him. You have to be pretty sure of yourself before you start telling somebody they have ALS, because you’re basically telling them they’re going to what? They’re going to die. We went and saw him, and he’s... now speaks with his eyes. He can barely move them. And he can’t lift anything. He’s just there. He’s just in existence. And that was a year ago, and now he’s not here anymore. It goes fast.

Why do you want to know? What happens if you don’t tell that person, and they’re out at the mall, and they all of a sudden can’t move, they can’t get around, and they can’t breathe? They need to have their affairs
in order. Okay? Know what you’re looking at. Now, by the way, here’s what a lot of you will say: “Well, I’ll just, you know, send them off to another neurologist.” Well, he had been to the VA neurologist three times. Nobody said anything about it. Okay? So, it’s important to know.

Multiple sclerosis. Demyelinating disease. The very first thing is this: One of the very first things you’ll see is,… People don’t… they see colors differently between their eyes. They get double vision, or… One of the biggest things is this: They get pain behind their eyeball. Pain behind an eyeball, especially when they move it. They’re like, “Ow, crap, it’s killing me.” And all of the reds turn pales, and their optic disk gets pale, and then all of a sudden, next thing you know, they have, like, sensory changes, then motor changes, then they have double vision. It’s a twenty-eight-year-old female that moved from the north to the south. I mean, those kinds of things, okay? This isn’t really the neurodegenerative diseases that we want to talk about right now; this is more in the autoimmune realm of diseases, but it still can mimic some of the other things.

Okay. I want to jump to right here. Psht. These are the three things I want you to know. This is important. The cerebellum. Okay. We have spinocerebellar ataxia, Friedrich’s, and Charcot-Marie-Tooth. These are the three things I need you to learn to differentially diagnose. Now, spinocerebellar ataxia, they’re all going to give you this: gait issues. So you can’t just say, “Ah, you got an abnormal gait. It’s this, this, or this.” It doesn’t work that easy. I’m fixing to give you a golden nugget, right here. Spinocerebellar atrophy versus Friedrich’s ataxia. They both have gait changes. They can both give you all kinds of problems. But in one you have a foot deformity and one you don’t. See, in spinocerebellar atrophy, you don’t have high arches and hammer toes, but you’ve got all the other cerebellar findings: the dysarthria, the gait changes, and all those things. But then you’re like, “Take your shoes off.” They take their shoes off, and you’re like, “Those arches just look beautiful, and there’s no hammer toes.”

Well, now you have this person, they come in, and they have gait ataxia, dysarthria, changes… they’ve got nystagmus, all these things, and you take their shoes off, and they’ve got this way high arch and hammer toes, meaning they’re curled up, and you’re like, “This isn’t SCA. This is Friedrich’s.” And you’ve already ruled in or out alcoholism. And then you’ve already looked at their thyroid to see if they have a goiter, thyroiditis, if they have high TPO antibodies. You’ve already done that. Do you see what I’m talking about?

So you go through this, and you’re like, “Wow.” Now, Charcot-Marie-Tooth disease is in the peripheral nerves. Now, watch this. This is so cool. With SCA, no foot deformities. With Friedrich’s, foot deformities. With Charcot-Marie-Tooth, it’s nerve damage, so they get atrophy. With the other two, you don’t get atrophy. And they lose everything. They get pencil knees. From here down, they lose their peroneal muscles, and they lose their gastrocs, and they start to get a slappage gait that is a little bit ataxic, versus a wide-based ataxic gait with high arches, versus just a wide-based gait with no muscle loss and no high arches. There you go. That’s the cerebellar game. Ninety-nine point nine percent of all neurologists will not walk through it that fast.

Do they have arches, or not? Do they have muscle loss, or not? If both of those things are gone, it’s just SCA. If it’s not SCA, it’s alcohol. Do they have autoimmune disease that’s going up there and attacking it, if all that other stuff is not there? You can work through it pretty darn simple. And I’ve got it right here for you. By the way, guys, this is right out of a paper. That’s why I like taking these and clipping them out and then putting the references in there, so that you have it. Okay?
Alzheimer’s, Parkinson’s, frontotemporal dementia. I put this chart in here so you could say this: “Here’s what’s happening. There’s plaques, Lewy bodies, or whatever. It’s tau, and these are some of the locations and the mutations. Dr. Kharrazian’s going to talk about these in detail when he starts talking about nutrition and cellular mechanisms. I’m just trying to get you in the ballpark. Like, “Hey man, this looks like frontotemporal dementia.” Okay.

Here’s diagnostic criteria for progressive supranuclear palsy. And I kind of put these in there for you. Here’s the difference between progressive supranuclear palsy and corticobasal degeneration. So, as you go through this, both frontal, dysarthria can happen. Now remember, apraxia of speech, fluent versus non-fluent language changes. If you have Parkinson’s disease, guys, you have fluent speech. But if the dementia starts in the cortex first, you might start having some speech changes that are either word finding problems, or a lack of fluency repetition or comprehension. Parkinson’s doesn’t start that way.

I’ll go through eye stuff a little bit later on.

Frontotemporal dementia. Now this right here kind of describes all of them together. Frontotemporal dementia, corticobasal, progressive supranuclear palsy, all the way up, and it just strongly goes through what are some of the differences. Everything that I just pretty much told you. Now, here’s the most beautiful chart I’ve found. Alzheimer’s disease, vascular dementia, Lewy body dementia, and frontotemporal demise. Look at this, right here. I told you: Frontotemporal dementia: behavioral changes that eventually goes into language impairment, which eventually goes into memory changes. Lewy body dementia: hallucinations, dopamine, spontaneous Parkinsonism, dopamine, visuospatial will be last, memory will happen. These people have extrapyramidal findings first. Vascular dementia: okay, verbal memory better preserved than the other ones. That’s one of the things that will give you a difference, okay? A lot of times these people who’ve had a stroke, and after the stroke they’re just not the same, and they start getting dementia. Alzheimer’s disease is this: short-term memory. Spatially disoriented. If they have short-term memory and they’re getting lost, it’s Alzheimer’s disease. That’s their first symptoms. Normal aging; they can do everything; it’s just not like it used to be. Congratulations, you’re getting a little bit older. That’s the perfect person to optimize, do some nutrition, do some brain-based therapy.

So, I had to give you a little flow chart that would give you the way to break this down, and then give you this summary here where it’s like this: Vascular, tremor, hydrocephalus, progressive supranuclear palsy, all the way down. It gives you the changes in history, signs and symptoms, imaging, and comments. Now, here’s what I’m going to do. Not in your notes. I’m going to take this in the member section, and I’m going to post it up during the next section, so you can just go right on there, pull it off. Because I think this is very nice. I found this during lunch, and I wanted just to throw it up there because I thought, “You know what? This is a pretty cool chart.” Alright?

So, we have a couple minutes left. Look at this. Supranuclear palsy. Dopamine. Basal ganglia. See the lid retraction? This person cannot look vertically. Where does the nigra live? In the midbrain. Where to the vertical eye movers live? And the interstitial nucleus of Cajal live? Midbrain. They all go together. So the person does this, and then when they have to look up, they go [leans backward], and they have a masklike face. When you see that, you’re like, “That’s not Alzheimer’s disease. That’s mesencephalic dopaminergic. I don’t know if it’s Lewy body dementia, progressive supranuclear palsy, or just Parkinson’s disease. Let me go ask them some questions.” If they’re cognitively out of it, it’s probably beyond Parkinson’s disease. Great
picture. This right here is what the person looks like all the time. They didn’t just see the scariest thing or the most wonderful thing ever.

So guys, here’s the early signs. We’ve already talked about them. Look at this right here. I’m giving you a nugget of what’s going to come. With brainstem lesions, here’s all your ocular findings. With cerebral cortex, here’s all your ocular findings. And by the way, we will have a Friday night workshop that will be nothing but these things right here. You don’t want to miss it before we do it, because if you do, it’s going to be difficult for you to be sitting at home, testing your own eyes, stuff like that. It doesn’t work out very well. This is right out of Current Neurological Neuroscience, 2010. Nice paper.

Hm. Okay. So, Alzheimer’s disease can deal with tangles, synaptic loss, inflammation, compromised all kinds of stuff, metabolic substrates, essential fatty acids, antioxidants, trace minerals. And when you boil it down, here is a slide that Dr. Kharrazian already gave you. And then I put in a couple of things here that just kind of outlines what these look like in paragraph form. So here’s Alzheimer’s disease, here’s corticobasal syndromes, and then last but not least, the most beautiful thing, look at this: Parkinson’s disease; bradykinesia, rigidity. These respond to dopamine therapy. Look at this: Dementia with Lewy bodies; hallucinations, fluctuating cognition, and they can’t sleep. Progressive supranuclear palsy; they can’t move their eyes. Corticobasal degeneration; slow, alien hand. Cerebellar signs, with multiple system atrophy along with autonomic signs. So here’s Shy-Drager, along with autonomic stuff.

All the way... these are all the Parkinsonian ones, or the ones that are more dealing with dementia with Parkinson’s. So these are the differential diagnoses of all of those. Now, let’s go to... and I’m almost done right here. These are the ones that just deal with dementia. We have metabolic, vascular, Parkinson’s, frontotemporal demise. Look at this: disinhibition, aphasia. Alzheimer’s disease is episodic memory deficit. And then some of these overlapping ones that are atypical; that’s where you have, like, maybe a frontotemporal dementia and a little bit of dopamine and a little bit of cholinergic component with Alzheimer’s disease.

This right here are the summarizations into something like this: Patient comes in, slow moving, apraxic, alien hand, and rigid. What do they have? Corticobasal degeneration. Very good.

A person comes in with cognitive impairment, patchy white matter disease, poor capillary refill, abnormal labs. What is this? Vascular dementia.

A person comes in, cognitive impairment, non-fluent aphasia, behavioral disinhibition, progressive, speech went first. Frontotemporal dementia.


Boom. There’s your dementias. Listen, okay. I just need to summarize this. What I just gave you was a pretty good summary of the big guys that are involved in the world of neurodegeneration, like the stuff that’s going to walk in the majority of time. I want you to be able to say, “I think it’s this,” or “I think it’s that,” so that the cellular mechanisms will make sense. And so tomorrow, when we take the cellular mechanisms, and say, “Here’s the nutrition,” and then we take the neurological exercises and say, “Here’s the functional neurology,” it makes sense because you know which one it is. So if I give you temporal stuff and frontal stuff,
that’s drastically different than if I just give you hippocampal stuff. That’s drastically different than if I give you dopaminergic stuff. That’s drastically different than if... you know... we do something else.

So, I think you’re understanding the differential diagnosis. It’s not that hard. You just have to know the anatomy, know the intake sheets, know a little bit about neurotransmitters, and know how it all connects together. And then we’ll start overlapping treatment, and you’ll get it. The treatment will teach you the differences between these, and then I’m going to, tomorrow, teach you. Thirty minutes a day for thirty days, and you don’t forget any of this. That’s your study time.

Alright. Fantastico. You guys did good. Thanks for hanging in there.