



MIGRAINE WORLD SUMMIT

INTERVIEWS WITH WORLD LEADING EXPERTS



TRANSCRIPT

AUTOIMMUNE DISEASES AND MIGRAINE: WHAT'S THE LINK?

PETER McALLISTER, M.D.



Introduction (00:05): So, migraine is a loop from the brain out to the peripheral pain nerves secreting this "inflammatory soup," and back into the brain. We know that autoimmune disease secretes all sorts of inflammatory bad guys — cytokines, leukokines, prostaglandins, leukotrienes — and there's an overlap there. So, we think that migraine has a strong inflammatory component, and we know that autoimmune disease has a strong inflammatory component. And I think that one of the keys there — this tendency to turn on and have somewhat of a limited ability to downregulate or dampen inflammation — is the tie between the two.

Paula K. Dumas (00:46): Immunity and the ability to fight disease have never mattered more than in the COVID era. The most frustrating part: Few experts understand what's really going on. Fortunately, we found a physician and researcher who does. Dr. Peter McAllister considers complex neurological mysteries to be challenges worth solving. Dr. McAllister, welcome to the Migraine World Summit.

Dr. McAllister (01:08): Well, thank you. It's a pleasure to be here.

Paula K. Dumas (01:11): Let's start off by defining autoimmune disease for those who may or may not know if they have it. It seems like an odd lot of conditions that range from gastrointestinal, to rheumatology, to neurology, and dermatology. What do they have in common?

Dr. McAllister (01:26): Well, you know, we all have an immune system that we would die without. This is how we fight bacterial infections and viruses, things like the flu, even COVID. When we have an infection [come] into our system, we make antibodies against it. Those antibodies then live in us in case we get reinfected, and they find that germ, and they kill it. Occasionally, these antibodies can go rogue. They mistake our own tissue for a foreign invader and they attack it. So the reason that so many different organ systems ... it just happens to be that's what that particular antibody is attacking. For example, if you have an antibody against a virus or a bacteria, and it goes rogue, and it attacks your brain tissue, we call that multiple sclerosis. And if it attacks your joints, we call that rheumatoid arthritis. If it attacks your bowels, that can be Crohn's disease or ulcerative colitis. So, it's the common denominator of an antibody that mistakenly saw "self" and attacked it, thinking it was foreign.

Paula K. Dumas (02:32): Rogue antibodies. That is the clearest description I have ever heard, so thank you for that. What are some of the most common autoimmune diseases?

Dr. McAllister (02:41): So, some of the ones I mentioned. Also, lupus is fairly common, at about 1.5 people per thousand population. Lupus affects 90% women, so men are very infrequently affected by it. When we get into the migraine link, we know that migraine preferentially affects women. Lupus also strikes women in their young years to middle-age, as does migraine. Rheumatoid arthritis affects about 1% of the U.S. population. A disorder in which you have dry eyes, dry mouth, joint aches, and nerve damage — that's called Sjögren's syndrome — about 0.2% of the population. When you take all of these, including autoimmune thyroid, myasthenia gravis, and the inflammatory bowel diseases, you add them up, it's about 12% to 18% of the U.S. population that has, or will have, some autoimmune disorder — which I find interesting because about 12% of the U.S. population has migraine.



Paula K. Dumas (03:42): That is interesting. So how much research is there on the link between migraine and AI disorders?

Dr. McAllister (03:49): Well, quite honestly, a bit. I think that we are very heavily focused on finding treatments and cures for diseases, and these epidemiological studies looking at association, there's just not that many of them. There are some, and there's some even in the headache specialty. Dr. Vince Martin is looking right now at allergic rhinitis, eczema and that sort of thing — atopic disorders. But I think there clearly needs to be more because there is, in my opinion, a strong association between autoimmunity and migraine.

Paula K. Dumas (04:27): Interesting. So, which autoimmune disorders do you see most often in your clinical practice among your migraine patients?

Dr. McAllister (04:33): The bowel disorders, I think are among the most common — celiac disease, Crohn's disease, irritable bowel, ulcerative colitis. We see one that may or may not — in fact, it's likely not a true autoimmune disease — but fibromyalgia is very comorbid. When we talk about a comorbid medical condition, that's two conditions in the same person that occur greater than what would be predicted by chance. For example, if you had a broken leg and a thyroid disorder, that's just coincidence. But we know that, for example, migraine has a whole host of things that tend to run with it. The more common ones that are not autoimmune would be things like anxiety — is very comorbid with migraine — depression with chronic migraine, post-traumatic stress disorder, sleep disturbance, fibromyalgia, etc. Among the autoimmunes, in addition to the gut, we do see the predominantly women's autoimmune diseases, such as thyroiditis, lupus, rheumatoid arthritis, and Sjögren's.

Dr. McAllister (05:41): And then there's one that's fairly rare, but almost always has migraine, particularly migraine with aura, and that's something that your listeners have probably never heard of: It's called antiphospholipid antibody syndrome. It's an autoimmune disorder that is characterized by clots — clots in the legs, clots in the lungs, even strokes in the brain, recurrent spontaneous miscarriages, and migraine headaches. Migraine, in fact, predominantly with the aura — the visual or the sensory half hour or so of something — followed by the headache. So, that one is a rather classic case of an autoimmune disorder that probably causes migraine.

Paula K. Dumas (06:27): Wow. OK. I want to come back to autoimmune disorders and how they relate specifically, whether they are causes, triggers, or comorbidities. But before we jump off of those — Lyme disease: It's very common in Connecticut where you practice.

Dr. McAllister (06:42): Yeah, it's actually quite common. Lyme disease was named after Old Lyme, Connecticut, which is just up the pike from me, because that was sort of ground zero when this was first discovered in the late '70s into mid-'80s. Lyme disease is from a spirochete bacteria. It's kind of a corkscrew-shaped bacteria, called *Borrelia*. And it's usually carried by a tick, a little tiny tick, of the *Ixodes* family. And that tick tends to hang out on deer mostly, but other animals as well. And all these pretty and beautiful looking deer in our backyards that we think are so benign and nice to look at, almost all of them in Connecticut — well over 90%, unfortunately — are carrying these type of ticks, and many of them are carrying the bacteria that causes Lyme disease.

Paula K. Dumas (07:37): So, Lyme is also an autoimmune disorder, correct?



Dr. McAllister (07:42): Well, Lyme can be thought of more as a primary immune disorder. So, the bacteria — the spirochete — gets into our system; most of the time, we don't have symptoms. Of those who get bitten by a tick, not all recall the tick bite — if you got bit on the back of your leg and you never saw it, that tick could have done its thing and dropped off you. And then you may not have noticed a rash, and then you have a whole host of interesting and sometimes awful symptoms, and that gets us into the more disseminated or more latent Lyme disease. And that's where we run into a lot of association with various types of headaches.

Paula K. Dumas (08:25): That is interesting. I know two family members that I have who have Lyme disease did not have the classic bite. They did not know that and so the whole process of getting diagnosed was really complex for them — very difficult to kind of tether out the symptomatology that could be associated with Lyme or could be associated with other things.

Dr. McAllister (08:44): If you think you have headaches that may be related to Lyme disease, it's important to seek out someone who has the skills and the training to diagnose you and make sure you're not just going down a path that winds up being incorrect.

Paula K. Dumas (08:58): So what kinds of certifications should people be looking for in a doctor that's going to treat Lyme or other autoimmune disorders?

Dr. McAllister (09:07): So, if you were going to seek out a Lyme specialist, I would look for an infectious disease specialist, particularly one at an academic medical center. Up here in my part of the country, Yale University and Columbia have outstanding programs, as does the State University of New York at Stony Brook. These are what we would call noncontroversial or legitimate programs, and you're likely to get an answer. I just don't like when patients come in to me with a whole host of nonspecific symptoms and say, "I was told by a Lyme-literate doctor that it's Lyme disease" — when really it's either migraine, or a sleep disorder, or an anxiety, or combinations thereof. So it's really important that you be very careful in who you choose and, you know, make sure you check your sources.

Paula K. Dumas (09:58): Well, that's universally great advice for people who are seeking medical care — to try to find the right type of specialists with the right credentials. So, if migraine is a primary headache disease, then would an autoimmune disorder be considered a trigger or a comorbidity?

Dr. McAllister (10:16): Yeah, that's a great question. So the answer, and I'll try to dive into it in more detail, is both. So, there are a number of autoimmune conditions that are comorbid with migraine — that is, the person with migraine is more likely to have these conditions than someone who is not wired for migraine, and those are the ones that we mentioned earlier.

Dr. McAllister (10:37): However, we know that there is an association; in fact, there is a reciprocal association between the autoimmune disease and the migraine. And I'll tell you what I mean: When someone has, for example, Sjögren's syndrome, if that condition — that autoimmune disorder — is out of control and not treated properly, it becomes in and of itself a trigger for worsening migraines in those genetically predisposed to migraine. Conversely, and this has been shown more recently, someone who has migraine — the disease — that actually adversely affects how they respond to their autoimmune disorder. It



either makes treatment more difficult — for example, many of the treatments that we use in autoimmune disorders, the number one side effect is headache. And if you are wired for migraine, for you, that [side effect] is a migraine headache. The classic one is intravenous immunoglobulin, which we use for some of these autoimmune disorders — the number one side effect is a really awful headache in nonmigraine patients, and a bad migraine in migraine patients. So, the two are associated very, very tightly.

Paula K. Dumas (11:50): That helps explain why so many people in our community are struggling with this and cannot seem to crack the code. Because we've tried to address this subject in previous years, but that is a great explanation. Thank you. And it saddens me, too, for those who are having that kind of effect when they're trying to deal with the autoimmune treatment. So, how well do researchers understand the link between AI disorders and migraine?

Dr. McAllister (12:18): Well, I think it's in its infancy. I think that we're getting there. When you think about what migraine really is — now, remember, 10 years ago we had just an inkling of an idea of what migraine is. The research, particularly on the CGRP medications, which I'm sure your listeners know all too well, has really given us an idea of what migraine is. So, it begins in the brain with either prodrome or an aura. And that turns on pain nerves in and around the head, in the lining of the brain, the meninges, in the eyeballs, the sinuses, the jaw, the upper neck, etc. Those pain nerves outside the brain — because remember the brain cannot feel pain — those little nerves are secreting lots of inflammatory mediators: leukotrienes, prostaglandins, CGRP, glutamate ... I could go on and on and on. So, it is an "inflammatory soup" that is being secreted by these pain nerves and that propagates the pain signal into the brain. So, migraine is a loop from the brain out to the peripheral pain nerves secreting this "inflammatory soup," and back into the brain. We know that autoimmune disease secretes all sorts of inflammatory bad guys — cytokines, leukokines, prostaglandins, leukotrienes — and there's an overlap there. So, we think that migraine has a strong inflammatory component, and we know that autoimmune disease has a strong inflammatory component. And I think that one of the keys there — this tendency to turn on and have somewhat of a limited ability to downregulate or dampen inflammation — is the tie between the two.

Paula K. Dumas (14:07): Interesting. So inflammation may be the tie. We talked before about there being a similar population — about autoimmune disorders and migraine both affecting women, and women in the younger 20s, 30s, 40s, 50s ages, correct?

Dr. McAllister (14:25): Yes, it's unfair. But migraine preferentially affects women. Autoimmune disease clearly preferentially affects women. And why is that? We think that because women have to carry the baby, which is part self but part nonself. So you're carrying something for nine months that's not all really genetically you, and the body's immune system has to be very careful to, for example, not attack that baby. So the immune system of a woman is different than that of a man because of that; therefore, the downside of that is, there's an increased risk of autoimmunity. There are very few autoimmune conditions that strike men more than women. I can think of a small handful, but overwhelmingly, it's women. Most autoimmune disease, like migraine, strikes in the prime work and child-rearing times. So these can be, you know, again, like migraine, very functionally disabling.



Dr. McAllister (15:26): And, like migraine, there's a variable expression of the phenotype. So, someone may have awful migraines and rather stable lupus; I've seen that before. But they do tend to follow one another. The common link to both flaring up, of course, is the state of the mind. Don't forget that the brain, and the mind contained therein, is an incredibly powerful organ. So stress, depression, anxiety, etc., lack of sleep — these would all be a common factor to flare up both migraines and autoimmune disorders. So, if you take a step back from that and you say, "How can we practice some positive strategies to help both?" Well, it will be just the opposite of what I said: It would be getting plenty of sleep, it would be relaxation, stress reduction, the proper diets, mindfulness, exercise. It turns out that that's not just good for all of us, but it would help both autoimmunity and migraine.

Paula K. Dumas (16:30): Yeah. I can see that those things would definitely help. It's not to say that either one would be "in your brain" as some doctors might allege — and patients are really sensitive to that — but that doing things that are brain-healthy behaviors are going to help both autoimmune and migraine. Is that right?

Dr. McAllister (16:50): Oh, yes. Right. So, to clarify, when I say "in your brain," by no means am I implying that it is somehow made up or fictitious; these are two absolutely real conditions. But the state of the mind has a lot to do with our body. And again, it's not just autoimmune conditions and migraine — it's a whole host of other conditions. We have a little bit of control over that. And if we practice good lifestyle, it's not a black and white — it's certainly not a cure — but it's a bit of a volume control. And we can turn down a migraine sometimes, and we can turn down an autoimmune condition if we try our best to do the right things.

Paula K. Dumas (17:30): Yeah. I think that's true. For me, it has made a huge difference when I finally started focusing on many of the SEEDS model of migraine management. Even though I don't have autoimmune disorders, it definitely did help me with my migraine. So, let's pivot a little bit more and dive into the care questions. Many people for migraine see a neurologist for their care. How can neurologists address the concerns of patients who have diseases that are not linked to the central nervous system?

Dr. McAllister (18:01): It's a great question. And to give a rather practical answer, it really depends on the neurologist. There are some headache specialists who tend to focus only on the headache and ask you to see a whole host of other specialists. We tend, here, to have a more kind of holistic and whole-person approach, which I think probably serves the patient best. I do treat, to the edge of my experience and expertise, conditions other than migraine. And I think that if you can be able to give advice or to treat more than one condition — if you can treat anxiety, if you can treat an autoimmune condition — along with the headache, I think the patient just feels more confident in his or her care.

Paula K. Dumas (18:44): Yeah. Does a compromised immune system put somebody at a greater risk for migraine?

Dr. McAllister (18:51): I don't think so, other than if your compromised immune system is being treated with certain medications that are known to trigger migraine — I think that can be the bridge there. But I don't think that a compromised immune system, in and of itself, would trigger more migraines in one who is wired to express them.



Paula K. Dumas (19:12): OK, great. Now, you mentioned inflammation, and you mentioned that inflammation does play a role in both migraine and autoimmune disorders. So from a care standpoint, what are some medical — or you mentioned some of the nonmedical and lifestyle things — ways to reduce inflammation? But can you expand upon that a little bit more? How do we deal with inflammation?

Dr. McAllister (19:36): Yeah, so there are ... now a lot of these are anecdotal, not all are approved to a very high level that a researcher like me would put his stamp of approval on, but I think they make sense. One of them is a diet that — while there is no one-size-fits-all anti-inflammatory diet — I think that we can get a sense that simple sugars and junk food is probably not good. I think that a diet that is — within the confines of your particular medical condition under the supervision of your doctor — moderately high in protein, fairly high in healthy fats, such as salmon and avocado and things like that. I think the brain tends to like these healthy fats, and to a lesser extent, proteins. So, that's one thing.

Dr. McAllister (20:29): The second thing is something I don't think is emphasized enough: Sleep is incredibly important as an anti-inflammatory-state inducer. So, I think that we are all running around doing a hundred things — taking care of kids, trying to work, doing Zoom meetings in a pandemic — and we sometimes don't give ourselves enough sleep. There was a study done a hundred years ago, looking at the amount of sleep Americans got, and we averaged 8.9 hours. And a hundred years later, we average 6.5 hours. And the upshot was, I think we've taken a collective hit by not getting enough sleep: weight is up, anxiety is up. And there's no direct complete correlation, but the idea is, sleep is a secret weapon that I think more of us need to use.

Paula K. Dumas (21:23): It took me a long time to prioritize sleep. And so we had Dr. Christine Lay talk deeply about sleep and about how sleep kind of helps your brain "take the garbage out" each night.

Dr. McAllister (21:35): I think "taking the garbage out" is an excellent way to say it. For those who may have a relative who has Alzheimer's disease, they may have heard of the plaques that get deposited in Alzheimer's disease — those are inflammatory beta-amyloid plaques. We know that we all make plaques in our brain and we all get rid of the plaques in our brain. And do you know when we get rid of the plaques? In deep slow-wave sleep. So insomnia is a risk factor for developing dementia later on.

Paula K. Dumas (22:05): OK. So less sugar and more sleep, just for starters.

Dr. McAllister (22:09): And the other one is that exercise, unless there's some contraindication, promotes an anti-inflammatory state. It also helps with sleep, it helps keep weight down. We know, just in general for migraine, increasing body mass index is a risk factor for chronification of migraine. All of these are easier said than done, and we all try and we don't have to beat ourselves up if we can't be perfect at them. But these are aspirational, and I think that if you concentrate on one or two of them and then incorporate a third, these are the things that really help keep our body healthy for the long haul.

Paula K. Dumas (22:49): Definitely. So, if somebody comes into your office with an autoimmune disorder and migraine, how do you begin to treat them?



Dr. McAllister (22:58): Well, you know, I want to get a good migraine history; I want to see where they're at. Migraine — the disease — has a very variable phenotype. Now, there are some very fortunate persons with migraine who have three or four a year. And then most of the patients at a tertiary care center like mine have 15 or more headache days per month. What I try to do — particularly if they're being treated with one of the new monoclonal antibodies for their autoimmune disease, or with intravenous immunoglobulin — is we talk about that two-way street between how well the migraine is doing and how well the autoimmune disease or treatment is going. These are people who I will really aggressively try to optimize their care. So we really emphasize the three buckets of migraine treatment, which is, the lifestyle/behavioral stuff that we were just talking about; we make sure that they've got a preventive that is doing what we want; and then we optimize acute care. We also give them a number of tools in addition to their standard acute care: We give them a backup and a rescue, when they are in their particular lupus treatment or their autoimmune neuropathy treatment, etc., so that they don't have to suffer a migraine in a response to their treatment.

Paula K. Dumas (24:19): Yeah. As you mentioned before, if some of those treatments can actually trigger a migraine attack, that's a really complex beast to try to work through. So, I'm sure it takes some time to get them optimized.

Dr. McAllister (24:31): Yeah.

Paula K. Dumas (24:31): Are there any other preventive or acute treatments that overlap between autoimmune disorders and migraine?

Dr. McAllister (24:39): Well, I think, here's one point that's come up at a number of lectures I've given: We're using more and more of what we call "biologicals" to treat all sorts of diseases. These are usually either intravenous, or they're EpiPen shots that you can do in your thigh, for example — lupus has them, rheumatoid arthritis has them, multiple sclerosis has them, we're studying them for myasthenia — so all these autoimmune diseases have their own, what we call "monoclonal treatments." Now interestingly, since 2018, we in the migraine world have our own monoclonal antibody treatment. Those are the anti-CGRP monoclonal antibodies that can be either given monthly, usually; or quarterly, some of them.

Dr. McAllister (25:25): And the question is, if you're on one of these biological monoclonal antibodies for your autoimmune disease — let's say you're on one called Tysabri, which we use in multiple sclerosis — can that person go on another monoclonal antibody for their migraine? It's an interesting question. And the answer is: 100% yes. The monoclonal antibodies that we use in headache medicine have been deliberately engineered to not play with the immune system. So they are little, sort of, engineered "smart molecules," and on the very top of that molecule, we put a structure that will direct it to wherever it needs to go. So my multiple sclerosis patients have one that works on their immune system, on their B cells; but we in the migraine world, our anti-CGRP monoclonal antibodies, they only work up around the brain, in the migraine centers. So though they sound like two big complex drugs, two different monoclonal antibodies, they can be used in the same person with complete safety.



Paula K. Dumas (26:30): So, if I'm understanding this, you're saying they are two very precise drugs that don't overlap, and that is ideal because they can each treat what they were meant for.

Dr. McAllister (26:40): Correct.

Paula K. Dumas (26:42): Very cool. So, we probably need a little bit more research to understand how the CGRPs actually work in a clinical trial, but at least in clinical practice, what you're seeing is, they are working effectively for that population.

Dr. McAllister (26:58): Yes. Even if you are on another biological, another monoclonal, for your autoimmune condition.

Paula K. Dumas (27:05): That is great news for many people who are listening. So, are there any other practical ways that we can boost our immune system against both autoimmune disorders and COVID that might also help reduce migraine?

Dr. McAllister (27:19): There is a lot of nonproved stuff. As a sort of "wonky research person," what I'm going to say has not been subjected to thousands of persons in a double-blind study. There's some anecdotal evidence that vitamin D tends to be healthy. There is even less evidence that perhaps vitamin C can be helpful. Personally — and I think the literature may support this, although I admit it is somewhat controversial — if you eat a very healthy, very clean diet, you may not need to take the vitamins that I'm just mentioning. It's always better to get your vitamins in through a very healthy clean diet. But if you're not the healthiest of eaters, some of these supplements may be helpful. The jury is still out.

Paula K. Dumas (28:04): Fantastic. Well, you've given us a lot of very practical information, useful information that we have never had before on the Migraine World Summit. So I hope everybody who has autoimmune disorders, or suspects that they might, has the chance to watch this. Thank you so much for this. Where can we learn more about you and follow your work?

Dr. McAllister (28:23): Well, the website is www.neinh.com — that stands for New England Institute for Neurology and Headache. And if you like Instagram, we've got a really fun, informative one, and that's @headachedocs. So jump on; we'll be happy to interact with you.

Paula K. Dumas (28:41): Fantastic. And if somebody is in another part of the country or another part of the world and they want to consult, are you guys doing telehealth?

Dr. McAllister (28:49): Yes, actually we've been doing it all over the country and outside the country before it even became COVID-fashionable. So yes, if somebody wants to contact me, I'd be happy to speak with them.

Paula K. Dumas (29:00): Wonderful. Are there any resources that you would recommend or offer to our audience?

Dr. McAllister (29:05): Well, I think the ones that your educated audience is certainly aware of — the American Headache Society, the International Headache Society — those are just great clearinghouses for information on migraine, the disease.



Paula K. Dumas (29:19): Fantastic. Dr. McAllister, we are so grateful for your expertise and joining us today on the Migraine World Summit.

Dr. McAllister (29:27): Thanks. It's been a pleasure.