



MIGRAINE WORLD SUMMIT

INTERVIEWS WITH WORLD-LEADING EXPERTS

# TRANSCRIPT



## MIGRAINE CHANGES IN OLDER ADULTS

GRETCHEN E. TIETJEN, MD  
PROFESSOR EMERITA OF NEUROLOGY  
UNIVERSITY OF TOLEDO



**Introduction** (00:05): Medications are much more dangerous — if you just stayed on the same dose as you move through life, it may have a different effect on you. So, if you're on a blood pressure medication, and maybe it was doing double duty — so it was keeping your blood pressure down, but it also was helping your migraines as some medications do, like beta blockers, for instance — when you get older, it may be that that dose was too high for you and you're going to have fainting spells because your blood pressure's not high enough.

**Carl Cincinnato** (00:42): Migraine may seem like a life sentence for anyone above the age of 60 who's had migraine attacks for multiple decades. You might have been told that migraine settles down after menopause, or denied treatment because of your age or stroke risk. We talk about these issues and more with Dr. Gretchen Tietjen, who's a distinguished headache specialist, a professor, and published researcher in this area. Dr. Tietjen, welcome back to the Migraine World Summit.

**Dr. Tietjen** (01:06): Thank you very much, Carl.

**Carl Cincinnato** (01:09): There are different definitions for seniors, but for the purposes of this interview we're going to define a senior as anyone 60 or above, but we certainly don't mean to cause any offense by that definition. So with that, what are some common changes in symptoms that seniors might experience after decades of migraine?

**Dr. Tietjen** (01:25): Well, it seems that oftentimes migraines get —the headaches get —less frequent with age. I guess that would be the main thing. The prevalence is only about 10% in seniors. That's still a lot, a high percentage, but it doesn't go down to zero, unfortunately; there are people that still get them even above the age of 85 — they've documented at least a couple of percent. But they do become less frequent. But sometimes people develop aura-like symptoms, which are frequently the visual symptoms that people will get as they age. And maybe those are less frequent than when they were younger, and then they get more frequent as they get older. So that's another thing. Oftentimes some of the associated symptoms like sensitivity to lights or noise get somewhat less. Nausea may get somewhat less. And also, as people get older, the studies have shown that the headaches tend to more often become bilateral, where they're both sides of the head rather than that one-sided head pain.

**Carl Cincinnato** (02:35): Does migraine tend to evolve, therefore, in most people over time?

**Dr. Tietjen** (02:41): There's a lot of fluctuation of migraine. I mean, if you look at frequency, some people, they'll have a lot of fluctuations and frequency over the course of their life. Interestingly, I know I've read that people that have migraine at an early age — they have an onset as a teen or even younger — those are the ones that tend to keep migraine longer in life. So if you meet somebody who's 80 and still has migraine and you ask them when it started, chances are it started in childhood or adolescence; people that start later, they tend to abate. So, that's one evolution in frequency. But yes, it's hard to know. We know that migraines can progress over time in people, but you know, the curve is generally that they become less prevalent with some changes. And luckily for a lot of people they cease [in women after they've gone] through menopause. But even for men, they will also ... the curve looks kind of similar. It definitely decreases after the age of 40 and tapers down.

**Carl Cincinnato** (03:55): For those that are experiencing more aura, for example, and perhaps less or no head pain, it sounds like that is not an uncommon transition that can occur, and perhaps sometimes it occurs with vertigo, as well. Is it a cause for concern?



**Dr. Tietjen (04:09):** I think it's a concern, in a young person or an old person, when they have aura, because it's my belief, based on my research and that of others, that there's a certain subset of patients with migraine that have their aura due to a little bit of ischemia — ischemia means lack of blood flow. And it may not be enough to cause a stroke, but it may be enough to cause cortical spreading depression, which is a physiological phenomenon of the brain, but that is what's believed to be the correlate of an aura. So if you get a little bit of ischemia — if you get a lot, you might have a stroke — if you get a little bit though, it might set off an aura. And so, I'd always wonder, is something going on? As a person gets older, you have more vascular disease, so are they getting narrowing of their carotid artery?

**Dr. Tietjen (05:13):** I've seen people with that, that are having spells that just sound exactly like migraine aura — exactly like it. And it is for maybe all intents and purposes, physiologically an aura that they're having. It's just what people sometimes call a secondary aura because the aura is coming because of ischemia to the brain. So, I think when a person, especially if they didn't have aura before, if they'd always had that exact same aura, I'd be less concerned, but if they hadn't had it before and they'd just start getting it as they're older, I would do an evaluation to look at their heart.

**Carl Cincinnato (05:52):** So, let's talk about stroke. It is a concern for a lot of people that have migraine and it becomes more of a concern I think when you start approaching that age of being someone at a senior level with migraine. What is the absolute risk of stroke in those that have migraine?

**Dr. Tietjen (06:11):** Well, that depends a lot on age. They've always said that, I think, in younger individuals, it was something like 17 to 19 per 100,000 had been estimated from some of the studies. In older individuals that had been in the Women's Health Study — and these were people with aura — it was more like 3.4 per 1,000. And so that would be more like 340 persons per 100,000. Now, it may not be all just because — number one, there's fewer auras as people get older, so it's an absolute risk that decreases a stroke being related to migraine — but they do have increased risk of stroke from a lot of other things.

**Dr. Tietjen (07:01):** So the importance of aura becomes less important as you age, proportionally, but any way you look at it, an older person is going to have more strokes than a younger person; they're just not as likely to be associated with migraine. So when we talk about migraine as a risk factor, we're really talking about primarily younger individuals. So, people under the age of 45 — actually it's people that look like they have healthier vasculature that are at higher risk of migraine-associated stroke. As people get older though, even like if you look at a study of older individuals — and by older I mean over the age of 45 and up — even in that study, which was a Women's Health Study, it was the group of women that were in the youngest stratification of that study: the 45- to 55-year-olds, they were the ones more likely to get stroke if they had aura than those that were older. And they were also the ones that were least likely to get heart attacks related to migraine. So really there's some, I think different mechanisms, going on in what causes the stroke as opposed to what causes a heart attack, for instance, in people that have migraine with aura.

**Carl Cincinnato (08:30):** So, it's interesting that the research found that the stroke risk is actually higher for younger people with migraine versus seniors with migraine, compared to the otherwise healthy population.



**Dr. Tietjen (08:43):** Yes. So, at least as a proportion as a reason for it. It's always a little bit confusing because they're not all looking in the exact same population. If somebody is doing the Women's Health Study and they're looking at older women, it's not like they're looking at the younger women in the same study using the same methodology. But study after study has shown that if you're looking at the population at highest risk of having a stroke, if they have migraine, it's migraine with aura and it tends to be women and it tends to be those that have a more benign cardiovascular risk factor profile. So they don't have a lot of other things like hypertension, high cholesterol, [diabetes], that would cause them ... to be at higher risk of stroke.

**Carl Cincinnato (09:38):** And so, if you take someone who has migraine with aura who's a senior versus someone who's younger, does the senior have a higher risk in a population of 100,000? Are they more at risk of a stroke?

**Dr. Tietjen (09:53):** There's going to be more strokes in that population, but the ones that are going to be attributed to migraine are less, because they're going to have other risk factors. I think that's sort of how I'd say it. If you look at an older population, they're always having more strokes. But if you look at migraine — I mean one other way to look at it is — if you look at the numbers, the percentage of strokes that are associated with migraine are small.

**Carl Cincinnato (10:21):** So it's not super common to have a stroke associated with migraine. It's not common actually at all. But there are risk factors, and there are people that are going to be listening that probably have some of those risk factors. What can people do to minimize their own risk of having a stroke, whether that's associated with migraine, or just because it's an increase with risk with migraine, they want to minimize?

**Dr. Tietjen (10:46):** So the question has always been: If you gave somebody a preventive drug to stop aura, like let's say you put them on topiramate, which is a migraine-preventive drug, and it's thought that in part it works by making the cortex of the brain less excitable — that might be one — not all the mechanism, but one of the mechanisms. Then the question would be that maybe they wouldn't get an aura or a headache if they had some ischemia, but are you really stopping the ischemia? Maybe in some people — at least a subset of migraine with aura patients — if they're getting it because they're getting a little bit of ischemia to the brain that sets off the aura, then just decreasing the amount of excitability doesn't necessarily mean it's going to stop them from having a stroke. And that maybe those people should be on an aspirin a day.

**Dr. Tietjen (11:45):** Now I'm saying that, maybe because that study hasn't been clearly done and we don't have proof of that. There have been studies that they've looked at women that were in a study where they're taking an aspirin — I think it was every other day — and they did look like they had — and it wasn't statistically significant — but fewer strokes. But interestingly, they had more myocardial infarctions. So I just never knew what to make of that. But I will say in my own population of patients that I cared for — and many of them coming in with migraine were younger women, at least younger than senior age — we found that just trying them on an aspirin a day oftentimes would take away their aura and they wouldn't get as many headaches. Now those were oftentimes women that also had like a patent foramen ovale, that little hole between the two sides of the heart that's been associated with an increased risk of stroke.

**Dr. Tietjen (12:46):** And there have been studies that have suggested that that is the case. But the problem is, when you look at all the studies that have been done — some are little, some



are a little bigger, the methodology's different, the anti-platelet agent's different — so no one can really say conclusively that an antiplatelet treatment is the answer. If you have migraine with aura, we try to get the migraines to calm down or something with therapies, and treat them acutely, and treat them preventatively if needed. The bottom line is that migraine is heterogeneous; it's like not every migraine person is the same. And the more we learn about migraine and the differences between people with migraine, I think the more that we'll be able to practice precision medicine or personalized medicine and give people what it is they need, and not just try to think that all these drugs are going to work the same in everyone. Maybe you need aspirin, but this other person would do better with topiramate as a preventive.

**Dr. Tietjen (13:53):** So, I think there's just things we don't know; you're always going to be exposing people to risk if you give them any medication. And seniors in particular, since as we get older, in that group there's more problems with kidney function, there's more problems with liver function, there's more problems with heart function, there's more vascular disease, and there's just more chances of interactions with other drugs or not metabolizing the drug as well. And more side effects. And so, you want to only give drugs to people who need them and try to be as safe as possible with them.

**Carl Cincinnato (14:32):** I want to talk about the broken menopause promise that a lot of people have received, but the promise hasn't been fulfilled and the audience here are that group of people who still have migraine in their senior years. Why do some women improve after menopause but others do not?

**Dr. Tietjen (14:51):** Well, I think that there are some women — particularly those that have menstrual migraine and maybe started when their menses started, with menarche, and always have headaches. Maybe that's not the only time, but they have headaches almost every time they have a period, and when they get pregnant their headaches get miraculously better. And you'd think in someone like that, that when they go through menopause, since there's such a strong estrogen component to their migraine, that it's going to get better. And that for the most part is the case. I will tell you, it's been the case for that group of people, and that's not everyone, but it's been for that group of people in my practice. Once, I think it was 2002, [there was a women's study] but when that study came out and suggested that hormones may be associated with a slight increased risk of breast cancer, a lot of gynecologists stopped prescribing them for women for menopausal symptoms and started to use other kinds of medications.

**Dr. Tietjen (16:05):** So, when they really cut out hormone replacement therapy for a lot of people, that's when I saw fewer and fewer older women that had migraines. And we do know that the type of hormonal therapy — so let's say you're a woman that is older, that is on hormonal replacement therapy containing estrogen and you need to be on that for either just horrible symptoms, or because it's treating something else that's necessary — there are different formulations, and they'd have to ask their doctor what's appropriate for them. When you look at men compared to women, migraine looks like it's about equal, actually it's a little bit more common in boys than it is in girls. And then as people age and after adolescents go through puberty, it starts to take off more in women than men.

**Dr. Tietjen (17:03):** The curve looks ... they're both at the peak at about the same age and come down after 40, slowly in both. But in women ... even though they may be totally out of estrogen, it never gets to where it is in men. At this older age, it's not like they're as likely or less likely than men to have migraines. We still have them more. So it's something besides just estrogen.



And that's why both for men and women, to be honest, some people have migraine, I hate to say it, until their dying day.

**Carl Cincinnato (17:38):** I think it'd be great to shift the conversation now to treatments, and Amy is someone from our community that asked if treatments should change as people approach that senior age?

**Dr. Tietjen (17:51):** Well, the sad part of it is medications are much more dangerous — if you just stayed on the same dose as you move through life, it may have a different effect on you. So, if you're on a blood pressure medication and maybe it was doing double duty — so it was keeping your blood pressure down, but it also was helping your migraines as some medications do, like beta blockers, for instance — when you get older, it may be that that dose was too high for you and you're going to have fainting spells because your blood pressure's not high enough, or it's going to cause some other side effects because you metabolize it differently. And you may be able to still stay on that drug, but you probably need a much lower dose.

**Dr. Tietjen (18:41):** And if you've developed diabetes, maybe a beta blocker, which could hide the symptoms of getting a low glucose level — if you're on a beta blocker, they say those symptoms aren't as obvious. And so, you know, you don't want to mask symptoms. Or if you have depression, there's some concern that maybe beta blockers worsen depression. And so, there's just things that can happen with a drug that might have been fine your whole life, but you need to change. I've always liked, just because it's so inexpensive, amitriptyline. But that's definitely something where there's real concern in seniors in taking that drug. And so, if somebody maybe was on 25 or 50 mg and it really worked for them, sometimes we'll decrease it to 10 mg or even have them try going off of it.

**Dr. Tietjen (19:30):** One of the things I think that has always vexed people the most, until hopefully recently now that we have some new drugs that could replace it, but acute medications like the triptans. Those cause vasoconstriction, which means any blood vessel in your body which has this type of receptor on it — the serotonin receptor of a certain type — if you had that drug in your system, it could cause some — potentially it could cause some vasoconstriction of your coronary artery disease. Now that is not common at all, but it's not unheard of. And so that's why with those drugs, once a person develops cardiac disease and has had a heart attack or has angina symptoms — which is sort of a warning for a heart attack — it's thought like, do not use that medication anymore. And so, this might have been somebody ... I've followed a lot of patients, prescribed it when they were in their 20s and now all of a sudden, they're in their late 40s or 50s and they notice when they take it they get some chest pain and we'll evaluate them. And they've had stress tests in the past that were fine and now they're not fine anymore — they actually need something done, either medication-wise, or stenting, or bypass — but you can't think that a drug is going to be safe all the way through just because it was safe when you were younger.

**Dr. Tietjen (21:01):** Now some of the new medications that have come out — like the gepants, which are small-molecule CGRP antagonists — but these are medications that in some cases can be used as preventives, but they're short-acting relatively and they can work acutely for migraine. Those are thought to be relatively safe even in a person that has cardiac disease. Another one, lasmiditan, which is a new type of drug called a ditan, it works on serotonin receptors but not the ones that cause vasoconstriction. And that is thought that in cardiac patients that may also be a safe drug to be used acutely.



**Carl Cincinnato (21:48):** So if you haven't had a history of stroke, are triptans still OK to take as a senior?

**Dr. Tietjen (21:53):** Well, that's hard to say because I could silently be having a lot of things going on in my body that's going to lead to — and it's not just a stroke, it's a stroke or heart attack, so it could be in either the brain vascular system, or the heart vascular system. But let's say my cholesterol's high and it's not treated properly, or I've developed some high blood pressure and I'm treating it but I still have it, and I've got a little bit of borderline diabetes. I mean, these are all things going on in your system that are not good for your blood vessels.

**Carl Cincinnato (22:30):** OK. And so you mentioned the gepants and the ditans were appropriate for seniors who potentially can't use triptans. And so, some of the gepants are Nurtec ODT, Qulipta, Ubrovelvy — people have maybe seen that advertised in the U.S. — lasmiditan, which is the ditan. What about the CGRP — the calcitonin gene-related peptides, the monoclonal antibodies? Are they appropriate for people or senior people with migraine?

**Dr. Tietjen (23:03):** I would say I'm not a hundred percent positive. I mean, they have done some studies with them like the erenumab, and I think the [eptinezumab], the one that's IV and then the other one subcutaneous, those have been in studies that looked at an older age group, but the older age group only went up to 65. So, they looked at all the people 60 to 65, they did not find any increased risk of MIs or anything like that in that age group. So that makes it sound like it's pretty safe. The problem is that what those drugs do, the [eptinezumab] lasts like three months, the other ones last a month.

**Dr. Tietjen (23:55):** They decrease the ability of the blood vessels to dilate by counteracting that CGRP, and whether that's any way how they work in migraine I think is debatable, but they do have that ability. I don't think they really cause a vasoconstriction per se, but they do cause an inability to vasodilate. So, there's always that concern, that if you were starting to have a stroke, or a heart attack, would it be worse if you had that drug on board than if you didn't? So maybe it's not causing it, but maybe it's going to be a bigger heart attack or a bigger stroke because even if they give you vasodilators, maybe they don't work as well. So, I won't say I've never put a senior person on one of those drugs, and I never have seen a side effect that was bad on them, but that does really cause me to hesitate. We can't just think, "Oh yeah, I've seen a bunch of people on it that seems safe; they haven't found anything." As these drugs are used [over] a longer period of time, sometimes you get more data and they do some of these post-marketing studies and they find that, "Oh, that maybe isn't as safe as we thought it was." And so, it really has to be at that stage. I don't have any data that says that these are unsafe. I just have the theoretical in the back of my mind.

**Carl Cincinnato (25:30):** What about neuromodulation devices, and are they contraindicated with anyone that has any kind of implants, like a pacemaker?

**Dr. Tietjen (25:37):** Well, I think for the most part they all say that they are, they say don't use if you have a pacemaker. As far as I know, I think most of them carry that. It's hard to say whether it would make a difference. But I haven't prescribed them in that population. But most people don't have pacemakers, and for those that don't, I don't think that there's a problem with using them in older individuals. It's just really unfortunate when people don't have access to them or maybe the companies could rent them out instead of making people buy them or something.





**Carl Cincinnato (26:19):** It's a frustration that's shared by our community, as well. Arlene has expressed that in saying that there's these amazing new treatments, but they all seem to cost around \$600 to \$1,000 per month when using Medicare, which is one of the biggest insurance providers for people living in the U.S., but it's similar overseas, as well. Doctors will often tell the patient that they need to switch if one treatment doesn't work, but they're switching to something that's out of reach, financially speaking. And Medicare in the U.S. doesn't seem to provide a lot of easy access to these new treatments. So what options do patients have?

**Dr. Tietjen (26:56):** I think that Medicare now covers some of the CGRP monoclonal antibodies, but the problem is that it depends how much your coverage is. And so in the U.S., what you'd have to have to get that covered if you had migraine would be to have a Part D for medication coverage. And Part D plans all have different drug formularies.

**Carl Cincinnato (27:30):** I would imagine the manufacturers of some of the newer treatments that you spoke about, the ditans and the gepants, would also be sort of lobbying insurers like Medicare.

**Dr. Tietjen (27:41):** I'm sure they are, because those drugs in particular are really going to be most useful in groups that can't take the other alternatives, like the triptans. And I will say, maybe they'll have some luck. The Alliance for Headache Disorders Advocacy group, that is one that had lobbied for Medicare to cover oxygen for cluster headache. They cover triptans but not oxygen, and it took a long time, it took years of going back and over and over and doing trials even in the trials that had been done showed it, but they weren't good enough. And there was basic science work that was winning international prizes showing why it worked, but that wasn't good enough. And so, they finally put together more trials and Medicare said OK. It's so sad that it takes ... and these were doctors and patients advocating together and going to Capitol Hill, and it just takes a lot of efforts like that for these things to happen. So if patients are out there and looking to join advocacy groups, they certainly can make a difference for these diseases. But it's a lot of work and it's a lot of time. It doesn't come quickly.

**Carl Cincinnato (29:10):** Yeah, the Alliance for Headache Disorders Advocacy is a wonderful advocacy group. And if we want to see gepants and ditans get added sooner, consider joining them. We can link to them in the show notes below. Are there any final thoughts you'd like to leave with seniors living with migraine?

**Dr. Tietjen (29:28):** Well, I would still say that I know it feels bad to be in the group of people still having migraine when the majority of people's headaches have gotten better, but it's so exciting that new drugs that are very effective in the studies and in the post-marketing use, don't have the bad cardiac side effects or other side effects that make them unsafe for a senior group. And yes, it would be nice to have more studies in seniors over age 65 and those that extend on, and I think, though, that there will be with time if these are drugs that prove to continue to be safe and well-tolerated. Because they are certainly effective — they're just as effective in seniors. And they look so far from the data that has been done for multiple trials, they look to be just as safe in seniors as they are in younger individuals, which means pretty safe. And so, I think that's something, and I think there will be some improvement over time on the neuromodulation pricing.

**Carl Cincinnato (30:45):** Well, thank you so much for generously sharing your time and expertise. We really appreciate it, and you joining us yet again on the Migraine World Summit.