

INTERVIEWS WITH WORLD-LEADING EXPERTS



CONCUSSION & CONTINUOUS POST-TRAUMATIC HEADACHE

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Introduction (00:05): What's been proposed is — many of your people in the Summit are aware of a chemical called calcitonin gene-related peptide, CGRP. It's huge because that's what we're treating with all of our injectables and our antibodies and our gepants. Well, it is believed and has been shown that there's a burst, a release of CGRP that occurs at the time of head injury. And could it be that that irrevocably changes the working of the head and of the coverings of the brain, like in the dura?

Kellie Pokrifka (00:41): Has an injury impacted your migraine? Why does it feel like so many of us get a concussion and then suddenly our migraine is transformed? It's chronic, it's hard to treat. It seems like we have no options. Why does it seem like every treatment continuously fails us? Do we have any reason for hope? To help us get to the bottom of this is Dr. Alan Finkel. Dr. Finkel, welcome to the Migraine World Summit.

Dr. Finkel (01:03): Thank you. I'm really glad to be here and honored by the opportunity.

Kellie Pokrifka (01:08): I'm so happy to have you here. So, what is post-traumatic headache?

Dr. Finkel (01:12): So, post-traumatic headache occurs in the clinic in a person like you, in a person like me. If it's not a personal injury — that being something involving another person where a legal injury has occurred — and if it's not a worker's injury that occurs on an occupational setting, it leaves the rest of us. And that doesn't — when you think about it, how else do we get injured? We fall on the ice, we trip — you know, getting in a fistfight maybe — but those kinds of injuries that the CDC lists all lead to headache. And so post-traumatic headache is the experience that the person has of head pain. And what differentiates it, in my mind, from all the other headaches that we see, what we call primary headaches. And I know the Summit will have a lot of stuff about the primary headaches, migraine, and cluster, and tension-type headache — and those wonderful ones like SUNCT. But in fact, post-traumatic headache can take any form.

Dr. Finkel (02:17): We tend to see from the studies that it is more migraine-type, and that's what we use. We usually use a modifier: migraine-type, migraine phenotype. And even to the point that the most common, as published by Jim Couch in the VA from Oklahoma, migraine with aura. Shocking, totally shocking to think about it in terms of the prevalence of migraine with aura in the population. You know, when you think about 2% of males perhaps, 10% of females in the population, you know, we say 20% of 20%. So maybe 5 or 6% of females with consistent migraine with aura. Well, holy kamoly, some studies are showing migraine with aura in 40% of people. So that's the first thing that post-traumatic headache is. It's a little bit different.

Kellie Pokrifka (03:09): Let me interrupt real fast. Does it have to be from a concussion or brain injury? Or can other injuries result in post-traumatic headache?

Dr. Finkel (03:17): OK, so that's really — that may end up being something that is very important to the Summit — because there's another headache that's going to be talked about, I'm sure: COVID headache. And COVID headache is a new daily persistent headache. And you're going to have people talking about new daily persistent headache. So, post-traumatic headache is a form of new daily persistent headache. Because one day you didn't have it, and then the next day, if it ends up being constant and daily, I would say that it's fair to say it is a new daily persistent headache. But there is no other thing that we should call post-traumatic headache except that which involves concussion or higher grades of TBI — traumatic brain injury — because some



people with very severe injuries also will have headaches. Which is, again, another interesting area, how to compare people with milder injuries as to those with more severe injuries.

Dr. Finkel (04:14): So yeah, we would want to narrow it down, let the other sessions at the Summit kind of pick away at what we do when we see somebody like this. Because your question is even better than that, Kellie. What about the person who shows up in my clinic who says, "Twenty years ago I had a car wreck and I've had a headache ever since," do they have post-traumatic headache? I think, you know, late at night after our meetings, we'll sit around and talk about this stuff. And the answer is yes. I think I would have to say a person who lost his leg 20 years ago still is an amputee. I would have to say somebody who didn't have regular headaches or may have had migraine infrequently, who then at the age of 25, gets in a club soccer injury and she or he may claim having headaches, and I'm seeing them in their 40s. So yeah, those are the granular things that we may not have time to get into, but those are the real questions for the clinician and the researcher. But more for the patient, because that person is going from clinician to clinician, evaluation to evaluation, for years being told they have migraine. And your next question is, why doesn't anything work in post —

Kellie Pokrifka (05:32): Why doesn't anything work? Exactly.

Dr. Finkel (05:36): Because it may be two different ways of thinking about it. And again, I'm trying to cover everybody's knowledge base, because we probably on this Summit have the most brilliant headache people in the world. Not just patients, but people who understand headache from the inside out. Whether they're clinicians, or people with migraine or headache disease. So, if a person experiences migraine-type headaches, then the question is: Are they going to respond to migraine-type medicines, specifically triptans or even our newer medications, gepants? And to speak to the experts who want, or even the academics, who want us to make sure that the studies are pristine and well done.

Dr. Finkel (06:28): That's another complication of treatment, and actually evaluation, because there's nothing that we can do, it seems, to really get good studies done. So many studies have been done and the pharmaceutical industry has been trying to look at the indication of post-traumatic headache of the migraine type, mostly because, again, that's an analog that we could use for moderate-to-severe headaches. You can use the same kind of metrics that you would use in a chronic migraine study. So that's first and foremost.

Kellie Pokrifka (07:00): Mm-hmm. And you are seeing that in your data? That a lot of patients with post-traumatic headache — migraine treatments aren't really working for us.

Dr. Finkel (07:09): They work incompletely. If I gave an observed anecdotal example, Botox treatments for chronic migraine. One of our publications from the Army was about using Botox in a small study of 65 patients — actually, still the largest study of Botox in post-traumatic headache, which is crazy. And a recent one — again, it was a controlled study — came out, which again showed similar results, that it does help, it seems to help. Ours was a very poorly designed study. We felt as a group that it was being used so regularly in the military that we had to try to get it published. And we did. We got it published in *Headache*. It was an important thing to do. But people with Botox treatment in chronic migraine, oftentimes — and again, I'm sure that this might be discussed — it doesn't last a full 12 weeks. But in people with post-traumatic headache, in my experience, it's even shorter in terms of before it wears out.



Dr. Finkel (08:09): And the same thing might go for something like a triptan. It may work, but it may not take the headache completely away. And that brings up the next question in post-traumatic headache for the person who has the disorder or disease, or the person who's trying to treat it. Which is, oftentimes they will have a second headache or a headache that's constant, that grows and mushrooms into a migraine-type headache. And what we did in our study was try to differentiate that.

Dr. Finkel (08:40): And now more studies are coming out — including one published last year by Metti who was the first author on our paper — looking again at a group of soldiers returning from redeployment, just to try and figure out what they're telling us about migraine or migraine-type headaches. And it ends up being that their response to medicine is probably based on the fact that it's not migraine. And I know I keep saying that — but it is a migraine type. So, they are coming in that way, Kellie. And they're also coming in — like my COVID headache — was recently published. And again, that study from 2021 that we were referring to before, where the returning soldiers were giving a lot of information in an epidemiologic study. So — wasn't clinical-based — was that "continuous headache" is the term. Some people might want to use the term "constant headache" or "always there" headache.

Dr. Finkel (09:39): And asking the question for the clinician is very difficult. And this is something I tried to teach for the last 30 years of how to ask questions about headache. If you say, "Do you have a headache all the time?" They might say no. If you say, "Do you ever have a day without a headache or an hour without a headache?" And that's what I would do with our soldiers. I would say, "Do you have a day without a headache?" "No." "Do you have an hour without it?" "No." "Do you have a minute?"

Dr. Finkel (10:05): So we coined the 24/7 is really 1,447, which is all the minutes of a day, seven days a week. So that continuous headache is vexing to the individual because it's never there. And you can ask the question lots of ways: "Is it there when you wake up, is it there when you go to bed? Is it a zero ever during the day?" But that's where the trouble begins for many patients. Their clinician will say, "That's not possible for you to have a headache all the time," and the person's going, "Well, I do. And then it gets really bad." So, there's the constant headache — continuous — then there's the headache that we want to name.

Dr. Finkel (10:48): So name it a migraine. Name it migraine with or without aura. Name it cluster, cluster headache. Who'd a thunk that we would see the kind of rates of cluster-like headache — a unilateral or a one-sided headache, extremely severe — associated with the things we associate with cluster headache? That being runny nose, runny eye, change in the face even. But sometimes they don't respond to the cluster-type medicine, but many times they do. And so that, again, is how the clinician asks the question. Because if they say, "Do you get bad headaches?" "Yeah, I got a headache every day." "OK, well, must have migraine. Here, take this." But in fact, you have to say, "How long is the severe pain?" You know, does it, and it's not going to be typical, right? We don't like it when a cluster headache lasts more than three hours.

Dr. Finkel (11:41): Patients with cluster-like headache after an injury will say, "Oh my God, it'll last a half a day." So I have to say, "Does it go away?" Because when cluster headache goes away, then it comes back. So, anytime we phenotype the headache — whether it's a paroxysmal hemicrania, an indomethacin-responsive headache — those headaches, like the hemicrania continua, was one we published also: that half of the headaches that we put in the autonomic category we called hemicrania continua because the person had [pain] on one side of the head.



But understanding, too, that they may have been blown up in a Humvee that rolled over twice, and they banged their head a few times against the side of the battle truck.

Dr. Finkel (12:22): So, my patients from there are not typical and their headaches may not be. But all the other publications, including from veterans and also from civilians, are beginning to show these other headache types. But they're usually broken down: migraine, not migraine. So why don't the treatments work? I think the treatments don't work because the injury is more complex. I don't want to say that migraine is an injury. Migraine is an event, and actually, concussion is an event. It's not a diagnosis. It's forces being imparted into the brain.

Dr. Finkel (12:53): So, just to follow that in a way, if people are interested. We believe that what happens at the time of injury — so, a little bit about concussion: If I hit you with a baseball bat, the forces that are coming through — the weight, moving at that speed that hits your head imparted into your brain and your skull and the soft tissue and the nerves. But what was interesting about the blast injury is that nothing touches them. The blast injury is just a sound wave. So, if you go to a concert — a rap concert or a heavy metal concert — and stand in front of the big speakers, you can get a concussion. But again, that's the extreme.

Kellie Pokrifka (13:37): One of our viewers, Gemma, asked: What actually happens during a concussion that makes this post-traumatic headache so bad? What is happening, and why do some people just not seem to be able to get on, get over it?

Dr. Finkel (13:53): If we look at animal models of concussion — and there's some issues with those — but we look at humans, what's been proposed is — many of your people in the Summit are aware of a chemical called calcitonin gene-related peptide, CGRP. It's huge because that's what we're treating with all of our injectables and our antibodies and our gepants. Well, it is believed and has been shown that there's a burst, a release of CGRP that occurs at the time of head injury. And could it be that that irrevocably changes the working of the head and of the coverings of the brain, like in the dura? And then also migraine with aura. That's a brain injury.

Dr. Finkel (14:39): So, when we talk about TBI, there's different injuries, and I just listed them: head, skull, bone, tissue, nerves, brain, the dura, that site that we really do believe so many of the migraine things come from, including the pain. And then the inside-the-brain things, which we would call the concussive symptoms. Those are the dizziness, those are the problems of sleeping, changes in personality. Those are also vision changes that are very well documented and really important to my patients. Because when Gemma asked that question, she's asking, "Why can't I sit at the computer for more than 20 minutes?" And the reason is, is because the concussion may have weakened the connection between your eyes and your brain. And therefore, the stress and strain, like any stress and strain that could occur on the head or brain or body, may trigger off or worsen the headache.

Dr. Finkel (15:36): So, the reason that they're as refractory as they are is: First of all, they may begin with a mechanism that changes things so the brain and the head can become more of a migraine-type head and brain. And then the difference is that for a person who has migraine in the family, what is it that's really triggering their migraines? That's very, very different, right? We don't really know.

Kellie Pokrifka (16:03): And you keep mentioning aura — does that seem to be more prominent in post-traumatic headache?



Dr. Finkel (16:07): It is uncanny how frequent it is being published as occurring in people who never had aura before. And that goes back to your first question and to Gemma's question. Most of the people who I see in different contexts, in different environments, are male. Interesting, because in headache clinics, females are more prominent and prevalent. And also, we know that the prevalence of migraine is much lower. So it's less likely that a male will have migraine before they're injured. But if they do have migraine before they're injured, it's a negative. It is definitely a predictive factor, right? But so, there are those who had headaches before, those who didn't have headaches before; there are those who had concussions before, and those who didn't have concussions before. And all of those factor into that whole idea that the headaches are different.

Dr. Finkel (17:10): So the prevalence of migraine with aura being that high for me also does two things: One, it tells me that there really is an injury and that the brain has been changed. I think people would want to know, what would we do for the different people who come along? The person who is really, really, really having difficulty will, by the time they come to see me, have had several evaluations, because oftentimes they're seeing concussion specialists or neurologists, not necessarily just headache people. And they will sometimes have detailed testing, scanning of the brain as indicated. I think in a person who doesn't get better — because you're looking not for brain damage so much as you're looking for other changes that could occur, including things that will be talked about in the Summit — like low pressure or high pressure, if a person months and months later is still having persistent symptoms.

Dr. Finkel (18:05): And so they should have some imaging. They might want to have some testing of their brain power using things like neuropsychological testing, or even just going to a speech therapist to have some basic testing. Because so many people will say, "I just can't remember things. I'm constantly losing things. I can't remember simple things that in the past were very easy for me," and that's a whole other subject. But again, all of those things that can affect a person's, what we call "headache hygiene": the sleep, the diet, the regularity of the days, light exercise if possible, these are all the things that we encourage anyway for my patients with headache disease. But in post-traumatic headache, it can be extremely important also, depending what the goals of the patient are.

Dr. Finkel (18:51): Then there's the sleep. And that for me is probably the most vexing of the problems that people who have a concussion will bring to me. Because if they don't sleep, their brain doesn't rest. And if their brain doesn't rest, it's getting ready for the next headache. Whether that's a migraine headache, or a cluster-type of headache, or any other kind that the brain can generate. So sleep becomes extremely important at the very beginning and also throughout the course. Those other symptoms which come from the brain: vision problems, balance problems, speech issues, and then changes in the personality which a person can't account for, really have to be attended to, otherwise the patient can't get better. So putting the headache in isolation oftentimes is a discredit to the person who's been injured.

Kellie Pokrifka (19:40): Yeah, that makes sense. So, what about different treatments? You were talking about the CGRP increasing during the concussion. Are these patients more likely to respond to the CGRP treatments than they are to previous migraine treatments like triptans, etc.?

Dr. Finkel (19:55): Well, again, both. As we know from the Summit, we treat migraine and headaches three different ways: I call it the preventive way, the acute way, rescue way. So, from the preventive side, we are using every single thing we can. Topiramate or Topamax has —



which is the old brand name — has been used, and it challenges me to give a 16-year-old soccer player who's a learner, topiramate. But sometimes we do. And sometimes it can really help.

Dr. Finkel (20:25): So, all the way down the line, because some people will develop problems of dizziness and fainting. Things like what we call POTS-like symptoms or problems of losing their blood pressure. They would do with a beta blocker, like many people. And we used a lot of beta blockers in our younger soldiers because we could deploy them on beta blockers. It wasn't a mental drug.

Dr. Finkel (20:45): We do use SSRIs. We do use the antidepressants that are used in migraine as well, if a person does have other things that that might be helpful for. But when you come down to the newer therapies — Botox, the gepants, the CGRP antibodies — there are some studies, unfortunately, that have not been of the highest grade. I think probably two of the better studies were published in the last — in 2021, our study that we published together from the Denmark group — and that showed again that people who were using one of the — they were using erenumab, or Aimovig, because of the time, it was when it came out, it was not a choice. And it was a consecutive patient study of a hundred patients or so. They completed somewhere in the range of 90 to get them through a general trial. It was not placebo-controlled, but they did show that the benefits in terms of number of days reduction in migraine-type headache was similar to what you would see in people with chronic migraine. And that was very encouraging.

Dr. Finkel (21:57): The companies across the board have pulled out. There was a study that was sponsored by Teva, which was a very brave study, and they worked as hard as they could to get the numbers. And again, that study was terminated as completed on clinicaltrials.gov. But again, the data showed improvement. It just was difficult to get the numbers. They couldn't really get the numbers. Across the whole class, people have entered into this area and pulled out for very important reasons, Kellie. The reason being is people who have had head injuries may not be able to participate the same way people with migraine — chronic migraine — can. They forget to fill out their diary. And if you don't have good data, you can't publish it. And that's what happened with almost every study, whether it was a drug study or other treatment studies.

Dr. Finkel (22:39): Now, other things. By the way, just because there's interest out there, what about the stimulators? So, by the way, I'm giving them and I'm giving them and I think they're making a big difference in people's lives. The newer drugs, I think, have such a low side effect profile and are doing really, really well. Also as — hopefully people will be talking about in the Summit — in combination, Botox and an antibody. Botox and maybe one of the others, as long as we can get them covered or as long as we can try. Because I think the safety is there and that's great for our patients with post-traumatic headache because they have other complications. They have pain in other places that may be complicating, and their other medicines may make it difficult.

Dr. Finkel (23:26): So, these are great because they mix and match very, very well. I can't give you evidence yet to say that any one of them is better than the other, but it's incumbent upon the clinician — and this may sound a little bit wrong in the '20s — but we don't do enough for our patients when it comes to it. We give them lip service: "Oh, well, I think you'll get better." And then the person who's five years out, we say, "Well, I think you're done." We should give each one of those as we would a person with an untreated chronic migraine, the kind of due diligence that they deserve.



Kellie Pokrifka (23:58): I definitely agree with that. Do we still have hope if we're five years, 10 years, 40 years out?

Dr. Finkel (24:05): I think we do. I think we do. There have been studies — again, coming from different areas — that stretched our understanding of persistence. Like, how long would a person have these things? And what are the things that happen over the years? So, the best studies really go out to five and seven years. There's an 11-year study, a 14-year study. These are hard to do well, but they really do show that if you have it at three-to-six months, you are likely to continue to have it. And unfortunately, that's bad news. But it also means that we should get in there as early as possible, try to reduce the absolute number of symptoms and headaches that we can, without subjecting the patient to the kinds of things that medicines can do. Which many people on this — at the Summit — know how bad these medicines can make people feel just for the hope that they're going to get better with their headaches.

Kellie Pokrifka (25:01): All right. So, correct me if I'm wrong. Is this what you're saying that you tend to see with post-traumatic headache patients? They tend to have a lot of aura. They tend to be very refractory. They tend to be continuous. Am I missing anything?

Dr. Finkel (25:15): No, and again, I think it's important that we place the aura in context. Because it's such an extraordinary event for us to see it in the numbers. But it's not like everybody with post-traumatic headache has aura. I think more people — your second point about continuous headache — as the publications are coming out, it's being acknowledged. I think that there's more than we thought. The original publication, I think one of the original publications looking at people in car wrecks was about 7%. Ours was 70%, but those were people coming to the clinic. It rides in there about 20 to 30%. But when I think about what that means in terms of the numbers of injuries per year, and whether or not the simple question, "Is it there all the time?" is being asked correctly. Because if it is, then that person needs very different attention, I think. Not more or less, they just need different attention. Because there, they might use medicines that are more like a tension-type medicine. Like things like amitriptyline to help them sleep. Or things even like light muscle relaxers that could be taken as needed. I like to use baclofen a lot.

Kellie Pokrifka (26:23): So, first of all, we can't just be treating this headache in a silo. We need to look at all the different symptoms that they're experiencing, or we're not likely to make progress. And then also it's not just, you know, people in the military, athletes, intimate-partner violence. It can be everyday people just getting in car crashes, slipping on ice, and all of these people need to know if there's differences in these injuries and they all need attention.

Dr. Finkel (26:52): And you bring up two things which I don't — I think I would be remiss if I didn't highlight what you just said — is that we didn't even talk about domestic violence. And that's a very important part of what we do both in military medicine and in nonmilitary medicine. And also, I think that the Summit does something very important, like so many of our advocacy projects: is empower the person to not be afraid to speak to their clinician. And tell them because if they — if the clinician is not hearing something, then it's not there.

Dr. Finkel (27:32): And so, they're going to ask specific questions: "Are you dizzy?" But sometimes the person says, "No, I'm nauseous." And they go, "Well then they'll give you something for your nau" They go, "No, but it's in my head. I'm nauseous in my head." Things like that that people will say. But yes, it is very important: What happened? What was going on at the time that it happened? What was your first contact with medical care or any other kinds



of care? And then, how long between the time of injury and adequate treatment? That's most important.

Kellie Pokrifka (28:01): I love that. So, speak up, say your symptoms, and know that you deserve care.

Dr. Finkel (28:06): Exactly.

Kellie Pokrifka (28:08): Dr. Finkel, thank you so much for being here.

Dr. Finkel (28:10): My pleasure.

Kellie Pokrifka (28:10): How can we follow your work?

Dr. Finkel (28:12): Well, again, right now most of my work is still in our private practice at Carolina Headache Institute. But again, I would like to make myself available to anybody around the world. And my email, again, can be distributed. But it is FinkelA: F as in Frank, I-N-K-E-L-A, at "chi" — like our energy — C-H-I zero nine dot com. And please avail yourself of me. I'll provide you with any of the sourcing or even any kind of simple advice I can do without getting particular with any patient information.

Kellie Pokrifka (28:46): Thank you so much. I think I may personally take you up on that. So I appreciate this. Thank you so much for being here, Dr. Finkel.

Dr. Finkel (28:52): OK. And again, congratulations on a wonderful event.

Kellie Pokrifka (28:55): Thanks.