CMEology

HAE – Hereditary Angioedema

Interview with “05”

June 3, 2024

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CMEology

Interview with 05 – Hereditary Angioedema

[START 05 6.3.24.M4A]

[IRRELEVANT MATERIAL OMITTED]

QUESTION: First question: what is your experience evaluating the HAE literature in terms of its implications for clinical practice? How do you approach the literature on HAE and what are you looking for?

05: For the medication?

QUESTION: Yes, or about the disease state, HAE in general.

05: I think we definitely need a little bit more information [phonetic] about the whole process. I'm always looking for new ways to diagnose the disease. I personally have, I would say, about a handful of people that are type III's, and these aren't opinions [phonetic]: like very clearly, when I give them a dose of a rescue drug, they get significantly better in the next 2-3 days, and then have repeat episodes later. So I am looking for new ways to diagnose in terms of new therapies, and looking for existing therapies; how many breakthrough episodes; how effective and how fast the therapy is.

QUESTION: So looking for information about efficacy, it sounds like.

05: Yes.

QUESTION: And then, as you said, new ways to sort of be able to diagnose people with a little bit more accuracy.

05: Yes.

QUESTION: Okay. When you are considering the implications of HAE research on clinical care, is there any format of research results that's more influential to you? So I'll give you some examples of what some different formats might be: abstracts; poster presentations; live conference presentations; academic detailing; tools such as UpToDate; or journal publications. What format for results tends to be most influential for you?

Commented [1]: Codes (1814-1842)
Literature review

05: I think journal publications. I think abstracts and case reports are nice to have in the background. Those are usually left-field cases that were approved by the journal, and it's usually, you know, there's a student there working with some attending that needs to publish, and so, they have an interesting case. I have plenty of them as well; I work in (Overlap).

QUESTION: Me too, me too.

05: Right, we all do. But I'm not sure whether those are great [phonetic]. I can tell you at the last allergy meeting, there were a ton of urticaria with angioedema slides: is it HAE, is it urticaria? It's supposed to be completely distinct from urticaria but doesn't stop people from having two diseases at the same time. So I'm looking for at least, and I know it's a limited disease, there are not that many, but I want a study that has at least, let's say ten or twenty patients in it that some therapy was given, it was peer reviewed by a few people, and not a one-off case; you can't treat, especially not these diseases, with one-off cases.

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Sample size

QUESTION: Yes, I have been the medical student or the trainee who has been there [phonetic].

05: We've all been.

QUESTION: Right? I mean, thankfully, right? I mean, those are great opportunities to kind of learn how to write and what the medical literature is all about, so definitely part of our development but difficult sometimes to maybe make conclusions from just—

05: Yes, and look, I think these cases, they're not useless, right? Sometimes, like I can say, oh, I have this one special case, [redacted] who says, well, they have one special case, [redacted] says he has one special case, when in reality, they're three of the same, right? So until one person puts it out there, the other two, or ten or 100, won't think that it's there. But I think that's what it's for; it's to find an identical other case that can be combined later for better research. And in reality, the true clinical trial has to be performed which requires blinding and all of that, which from an ethical perspective in this particular disease, you can't give them nothing, but you can give them standard therapy and see how much, how well you do on top of that.

QUESTION: Just out of curiosity, do you make it to national meetings? It sounds like you do.

05: Yes, I do almost all of them.

QUESTION: Which ones do you try to go to?

05: Mostly College and Academy from the allergy perspective. And then, the other ones are mostly by location.

QUESTION: So local meetings?

05: But I've been to all the College and Academy meetings in the last five years.

QUESTION: Oh, okay, all right. So you're a regular participant. You actually go to both in a single year?

05: I do.

QUESTION: Yes? Okay, all right. I mean, it is a rare condition. Have you seen any plenary sessions or other sessions that have been devoted to HAE?

05: Yes. To be honest, not that many, but yes, there are always some at the conferences. I think over the last five years, the only new thing has probably been Orladeyo, which was [phonetic] more of the same, but yes, we try to go to them because otherwise, locally, we're not going to hear much about it.

QUESTION: As regards to journal publications, tell me a little bit more about what motivates you to pull a publication or to do a search.

05: When I have a complicated case, I would want to do it; I'd want to compare, let's say, Takhzyro or Cinryze versus Orladeyo for patients who may not want an injection, or people who are not very compliant with doing stuff every couple of months. And then, for instance, Takhzyro: do we do every two weeks versus four weeks; at what point do we decide that once a month is enough for these patients?

I recently had one where I stretched it out and then she complained of hand swelling (Overlap). But usually, a case I have or if I'm skimming through the journal and there is something that looks good, an author that has already done a lot in the specific disease, then I would do more and just hit on [phonetic] the paper.

QUESTION: What factors are most important to you in interpreting the HAE literature and applying it to clinical care? You mentioned having an adequately-sized study population, for example. Anything else that you find that you need to possess in order to approach the literature in HAE?

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Professional Conferences

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Professional Conferences

Commented [5]: Codes (5613-5719)
Literature review

Commented [6]: Codes (5719-5781)
Literature review
Author reputation

Commented [7]: Codes (5781-5841)
Literature review

Commented [8]: Codes (6140-6340)
Author reputation

05: I mean, I like multicentered rather than one-center. I'd probably be interested in seeing some of the people that I know who have already done a lot in HAE; hopefully, they'll be somewhere in the authorship. And I would want to see a significant number of events in the nonstudy group basically because you need to see a difference, right?

QUESTION: Right.

05: And again, it's hard because it's a disease where they may not have a lot of attacks, and if they're not having a lot of attacks, then I'm not sure what to make of that then.

QUESTION: How about interaction with colleagues? Do you refer patients, for example, or are you the person to whom people usually refer their HAE patients?

05: I think it goes both ways. I don't consider myself a specialist here, but then again, if I were to refer to [redacted], whoever it is, it will be very difficult for the patients to get in anytime soon. I can expedite it, but in essence, the therapy is what it is. I will begin the process of getting it approved; if we can't get it approved, I'll ask the pharma people to sample it with a rare foundation or however it goes through, and then, that's it.

I think the only reason to ever really send them to an academic center would be if I need some sort of study that I can't get done or I'm worried about cost. So I've definitely had one recently where [redacted] wanted them [phonetic] to get genetic-tested, so the patient was very concerned about the bill; I was like, well, maybe we can ask one of the academic centers to see if they're going to do it, and then, I'll figure out a way to do it on my own.

So I think I have enough of these for a rare disease, I have enough of them that I can try at least something, and then, if it's a complicated case, then I will more likely refer to an academic enter.

But I think given the number of drugs we have and the knowledge we have now, I think overall, it's not that difficult, so as long as I have the time, I will treat it. I don't think this is like CVID where even if I treat it, I still want them to be followed by an academic person just because of more time and more interdisciplinary approach than I can have alone in my clinic.

QUESTION: So am I to infer then that you are in a private allergy-immunology practice then in the community?

05: Yes.

QUESTION: Okay.

05: Multispecialty, but yes.

QUESTION: Multispecialty. Are you the only allergist?

05: In my building, yes, but otherwise, there are four of us.

QUESTION: Okay, got it.

05: Well, we're all, so I work for [redacted] who is owned by [redacted], so if you include, and we're split among territories. [redacted]

[redacted]

QUESTION: Oh, I see, okay. And it sounds like you're busy enough or you've been in practice long enough to actually have seen HAE and develop some level of comfort with diagnosing and treating these patients.

05: Yes. For better or worse.

QUESTION: For better or for worse, yes, of course. Can you describe any barriers to incorporating research findings on HAE into clinical practice that you may have experienced? So I'll give you an example of what might be some barriers for clinicians. There can be patient-related barriers, health care provider-related barriers, practice-related barriers, or institutional barriers. Anything that you've encountered that sort of has made it more difficult to translate research into clinical care?

05: So I think insurance issues is huge; I know that [phonetic] from institutional as well. So [redacted] doesn't particularly prefer we have samples, doesn't particularly prefer we have, what is it called, MSLs or whatever it may be. So whether it's a type I, II, or even III, I've had type I's and type II's that are low but not considered low enough; or looking to, can we have it low C1 without a low C4, definitely have these cases.

And so, I have icatibant [phonetic], whether it's generic or brand, doses in my office; I'll give a dose and then follow closely with the patient. So I've had a number of these where it changes things significantly for a couple of these patients. And so, I haven't because I guess I didn't follow the rules, but the institution doesn't allow it, right? So without a sample, without an ability to get a sample, it would be really difficult to treat these patients.

And a lot of times, the only way to get it approved is to write a letter of medical necessity stating that there was a benefit from a sample which, in essence, creates two problems because the insurance is giving you the difficulty that the only way to do it would be to give a sample; but if you can't get a sample, then how are you supposed to approve it? In essence, you can't get anything approved without trying, but you won't be able to try because the institution doesn't want you to have samples in the office. So both of those are huge; it just makes things very difficult.

QUESTION: How about patient-related barriers?

05: I think mostly getting them in, getting them in and having them truly understand that this is somewhat of a chronic disease. A lot of times, they feel like because it flares and then they're symptom-free for six months or however long, that maybe they don't need to take anything, even though when they do get their flares, they're bad.

Having discussion between rescue therapy versus maintenance therapy is a little bit difficult with some of these patients. To them, it's sort of like, well, I can take my icatibant and I'm good for a couple

[redacted]

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Insurance/Prior authorization

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QUOTE
Avail of samples

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Avail of samples

Commented [14]: Codes (11131-11356)
Institutional barriers

Commented [15]: Codes (11459-11532)
Patient education

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QUOTE

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Patient education

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QUOTE
Patient education

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Patient education

QUESTION: Yes, it is difficult to convince patients who have intermittent attacks of anything, right, even asthma, that they should be on some sort of a preventative treatment. Yes, it can be very, very difficult. What do you think delays the introduction of evidence-based practices into HAE care?

05: I think mostly the ability to get the med [phonetic], and then, a lot of the testing is difficult to do. It's not so simple to send genetic testing on these patients. And then, a lot of times, you have a value, you want to repeat the value, it's hard to get the patient to come back. It's an intermittent disease, and that creates a very big issue.

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Testing

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Patient education

For those people, I would say when I was in Fellowship, we had the people whose throat was closing; they knew that they're very sick and they need it, right? But the ones who don't, who have like hand angioedema or abdominal angioedema, they don't find the need to, or if it's just lip but not throat, they don't find the need to get as much care as everyone else, which makes it hard to put any evidence behind there to show them that that's what needs to happen.

QUESTION: Yes. And statistics can be difficult for people to interpret, too, right? So you can say, well, the fact that you had a past attack and it was not an upper airway attack, you're still at risk for that, but that doesn't always resonate with people and translate into their wanting to do something about it. So yes, I agree it can be quite challenging to do that. Anything that you think could be done to overcome some of those patient-related barriers to getting diagnosed or having prophylactic treatment?

05: I think just more education to the patient. Again, as a private allergist, [redacted] much more difficult even though my staff translates everything and I can interact somewhat; but for them, it's sort of like, well, the problem went away, so I'm good. And then, they'll call and it's hard to get through, but I think if we can get better education about how it is an intermittent disease and that, yes, one attack is not going to predispose to the next, one attack may just be swelling of your feet, but then the next one can be swelling of your tongue.

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QUOTE

Commented [23]: Codes (14834-14880)
Testing

And then, better testing: C1 esterase and C1 is great, but it seems to vary a lot from one test to the other. I definitely had a patient with, his C1 esterase percent comes back in the 40s and the next one that comes back is 85, and I'm like, well, I don't know what to think of this. So I think testing could be slightly better as to why it goes down, and maybe better access to the genetic testing especially for, and I know some of the programs do this but it's still not as good for family members of people who already are clearly symptomatic.

Commented [24]: Codes (14880-14933)
Testing

QUESTION: What has been your experience identifying patients with HAE who would benefit from long-term prophylaxis? Can you describe what that's been like, if there have been any challenges in that? Sounds like we've touched on a few of them.

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Testing

05: It's really about getting the testing done. I work in two locations, in one location we draw labs, in the other one we don't; sometimes it needs to be left on ice and somehow that doesn't happen.

QUESTION: Oh, dear.

05: I know. So a lot of it is getting the test done; it's getting the patient to come in for the test. Seeing a positive doesn't automatically mean much. A lot of times, there is some question to some of the tests [phonetic] as getting Xolair approved through certain insurance companies for chronic urticaria requires ruling out bradykinin [unintelligible] which doesn't make sense but it is, and then you get a random positive and you don't know what to make of it; and if they are symptomatic, so again, maybe they have

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Testing

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Testing
QUOTE

both, but it becomes a question of do these people need preventative therapy or do we just have rescue for them?

And I think that there is no good answer. There is no good, well, if you have this many attacks in the last this-many months, that's what you should be on. It's left to the discretion of the doctor and the patient, and some people, you know, icatibant is a rather painful injection. Ruconest is even more difficult, right? A lot of people look at me like I'm nuts when I tell them they have to give themselves an IV drug.

So it's difficult. I think a lot of the barriers got better with the Orladeyo just because it's a pill, and hopefully, there will be a pill rescue soon. But as of right now, I mean, it looks like it's coming, but right now, it's not there yet. So hopefully, it will, and I think that would make things a lot easier. Until then, I would think that an example would be new inhaled or however, intranasal EpiPen coming, epinephrine [unintelligible] that would be, I think some people would be more inclined to actually use their epinephrine when they needed it, rather than just carrying it on them. But God only knows what happens.

QUESTION: Yes, absolutely. So actually, I'm a former pulmonary and critical care doc, and I did my training at a very prominent allergy-immunology center here in Denver, which you probably could name. But anyway, ironically, I have a son who's got food allergy, nut allergies, and he's pretty good about carrying epi around; but boy, mode of delivery certainly does make a huge difference, and having things that are more easy for people to self-administer or for someone else to administer obviously in an emergency, can make a big difference. Do you have many patients who are still on IV?

05: I like for them to have Ruconest, not for particularly outdoor or indoor use, but because I feel like if [redacted]

That being said, and I actually like people on both [phonetic] if I can get them, but last week, one of patients was denied for Ruconest on the argument that I had to select between IV versus IM or sub-Q, whatever it is, and I chose not to go the IV route because I think that's far more difficult for a patient to use. I don't think anyone is [unintelligible] I don't care that they've given them IV once [phonetic]; the bottom line is if they're going to need it, [redacted]ng to walk into some urgent care and the urgent care will put an IV in and give it to them. Well, that's going to impose a lot of issues. I'm not sure that the urgent care is always opened to giving meds, especially meds they've probably never heard of, and that's a hurdle for them as well.

QUESTION: Yes, that certainly is an issue especially in a rare disease like this. How do you gather and assess information about the impact of HAE on patient work, school, quality of life?

05: Sorry, can you repeat that?

QUESTION: Sure. How do you gather and assess information about the impact of HAE on a patient's work, school, family life, quality of life?

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Quality of life

05: I always ask that they keep a calendar of any events that they had, and any time they had to miss work or leave work or [unintelligible]. So I actually got one approved recently because the patient brought me

an entire log of her entire calendar of every time she felt that something was either hurting or swollen or something going on.

So I think just good records of it is important, and I actually ask the patient to keep a whole log of it because I think it makes a big difference. I think I need to decide, which is what I was mentioning earlier, if someone is on Takhzyro every two weeks, what actually determines that they can now go to once a month? It's easier to just say, well, they didn't have a big attack, but how do we know that they're not having small ones that they're sort of, when someone has a disease, they get used to it, so they sort of just kind of live with it and put up with it; and they're like, well, I'm better. And I always tell my patients better is not the same as being perfect, so I want to hear zero attacks; I mean, that's what we want. It doesn't mean [phonetic] we're going to get there, but we want it.

So I think absolutely they need to keep a log of everything, and then, if they're missing a lot of work or school or stuff like that, then we need to talk about what we can do differently. Now we have more therapies: do we need to change the therapy? No drug is perfect, right? In the pulmonology world, how many monoclonals for asthma do we have now? And again, these patients come back and say, oh, I'm much better. I'm like, yes, but I see that you still used prednisone last month. I work [redacted] owns the largest urgent care cent[redacted]n track these patients that way, a[redacted] you still use prednisone; what happened? They're like, yes, but you know, it wasn't that bad; I used [unintelligible] five times and now it's only one. So do we leave them alone, do we try another monoclonal in those cases; it's difficult.

And same thing here: if they're having, maybe they had a lot of attacks, they're having less attacks, or they had no attacks, I don't know. There is no direct study to show that Orladeyo is worse or better than Takhzyro or any of them. These are the main two I use; I don't use much of the rest. So I like, I prefer Takhzyro, but many people obviously don't want to inject; they want to use a pill. So I probably use them both, but it depends.

And so, I definitely want a full calendar. I want to know when they're having symptoms. I want to know how it's interfering with their family life, work, however it may be.

QUESTION: Are you aware of the fact that there are validated tools for assessing the impact of HAE on quality of life?

05: Yes, though I don't use them.

QUESTION: Okay. Sounds like they have been used mostly, or more often, in a research setting than they have in a clinical setting. But it sounds like you're really pushing for some objective evidence.

05: Yes.

QUESTION: More than just the, well, you know, how do you think it's been going, sort of thing. And your point about the fact that people get used to perhaps a certain level of symptoms and don't see it as being something that you would necessarily treat I think is important, especially with chronic diseases like this where these attacks, if you will, tend to be somewhat intermittent. And some of the symptoms, we've all seen patients with asthma who really can't go up a flight of stairs quite the way they should, but they think that that's okay because that's what they've been doing [phonetic].

05: Yes, and I think that a lot of it is once the diagnosis is given because a lot of them don't know what they have, but once you actually give the diagnosis, obviously, the patient is going to go home and read. And yes, if they're going to read online, they're going to see a picture of this, you go on Google, this

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QUOTE

Commented [30]: Codes (22566-22595)
HRQOL self assessment instruments

person's face is like super-swollen and the tongue is protruding and their lips are out there, and this person had to get a tracheostomy, whatever, the patient will say [phonetic], oh my God, well, I'm not at that level, so I'm okay.

But I always tell the patient, I'm like, the stuff you see online, that's not real-life; I mean, it is but it's always exacerbated. When I treat urticaria, I always pull up the pictures on Google, and the patient will go, I'm not that bad; I'm like, well, if you were, you would have been here sooner.

So no, I mean, bringing up these things each time is very important, and again, that's part of, one of the limitations of private practice is that we mostly won't have [phonetic] time for that each time. But my staff is pretty good, so they'll usually get a pretty good history about all these things before I come in, and then I'll just clarify it with the patient [phonetic].

QUESTION: How do you engage your patients in treatment decision-making about long-term prophylaxis? Can you talk a little bit about that and maybe what some of the challenges have been there?

05: Sorry, can you give me one second? I'm sorry.

QUESTION: Yes, sure.

[IRRELEVANT MATERIAL OMITTED]

05: I want them to know that they can either treat as needed or they can go on long-term prophylaxis. But at the end of the day, I will choose, I will in essence let them choose but I will tell them that if you're going to use your prophylaxis more than a certain number of times, like let's say once-a-month for three months straight, then you need long-term therapy.

QUESTION: Anything that you found that makes the process of talking to patients about long-term prophylaxis, anything you've found that helps make that easier?

05: I think it's just, I like to say it's good to be ahead of the problem rather than behind it. So why have a rescue that you may need to use when your chance of using a rescue becomes so much lower, right? So if you can live your life without any worry, and obviously they do worry, that makes things a lot easier and they can do what they're doing.

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QUOTE

Same thing as not the way monoclonals were meant for asthma, but if we're putting a cost [phonetic] on a monoclonal, your chances of needing to use your albuterol goes down. Nobody enjoys seeing their friends know that they have this thing, or having to step aside from a family event or any event for that matter, to go use your rescue. And in this particular disease, the rescue is not, well, like an inhaler where you take it and then in five minutes you'll be fine; this is one of those where you're going to use your meds and it's going to slowly make it go away over the next number of hours or days. So it's not a perfect fix, which means it's automatically once you have to use your rescue, you're probably not, you're in essence out of commission for a couple of days; that's just the way it is.

So I'll tell them, I'll say listen, if you go on one of these things, very safe, there's nothing there I'm that concerned about with the drugs, and then you will be able to do whatever it is that you're doing; you'll still carry your rescue but your chance of needing to use it will go down significantly.

QUESTION: How do you personally choose medications for long-term prevention or reduction of HAE attacks? How are you kind of, I mean, of course, you'll talk to the patient and see what they think about things, but what sorts of factors are you prioritizing when you're looking at the different options?

05: Really mostly that they're going to do it. I think especially the old-school drugs that were like every three days or every 48 hours, this was not viable, and they still exist, obviously, people will eventually give up or skip doses. I think some people are okay with taking a pill every day; some people are not. Some people prefer the injection. So I think it has to be in the discussion. But for me, it's what they're going to be most compliant with.

QUESTION: So you would prioritize what a person would be compliant with. Anything else that you are thinking about when you're trying to distinguish between agents?

05: I mean, efficacy definitely plays a role. So if you're going to be completely symptom-free with whatever it is, I'm going to go with that. But to me, I need to know they are taking it; I need to know that it works; I need to know that they're not going to have a breakthrough in the middle of the weekend where I'm going to get a call.

QUESTION: Right, of course. Acute emergent allergy consults are never a lot of fun; I see to remember that from my trainee days. Did you participate in any recent CME activities on HAE?

05: I think only at the conference.

QUESTION: Only at the conference you would do something like that? Okay, all right.

05: No, no, not that I would but I did at the conference.

(Overlapping Voices)

QUESTION: Oh, at a conference, you participated.

05: Yes.

QUESTION: Okay. Any thoughts about CME for HAE?

05: There's not enough.

QUESTION: There's just not enough, okay, all right.

05: I would receive from a bunch of them [phonetic] where we can go to, I don't think I've ever received any for this, not anything recently. I remember a bunch of them that was [unintelligible] not so much anymore.

QUESTION: Okay. Clinical guidelines are another way that research gets translated into clinical care, and I'm just curious as to what effect HAE clinical guidelines might have had on your practice.

05: I'm going to just follow them [phonetic]. I don't know if that's, I just follow the guidelines, but I think the guidelines leave a lot of choice to the physician. So I know the guidelines, I would say I mostly follow them, but I will choose what's best in my mind and based on the research [unintelligible] the guidelines [unintelligible].

QUESTION: Okay. I had heard of providers actually printing off the guidelines and sending them to insurers. Have you ever done that or used the literature when you've been trying to overcome some of the challenges with insurance authorization?

Commented [32]: Codes (27468-27548)
Injections/oral
Patient centered decision making

Commented [33]: Codes (27548-27688)
Patient centered decision making

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QUOTE

Commented [35]: Codes (29177-29518)
Guidelines

05: Yes. Yes. It works (Overlap).

QUESTION: It works, yes. Okay. And we're wrapping things up here, but I do want to ask if there is anything else that comes to mind as we're talking that you think would be good for me to know.

05: I think just from a perspective of clinical with what's not seen in research, is that every patient has a fear of something, and better addressing that fear tends to be kind of the way I go about this. So they're worried about throat closing and all this; I will explain that that's rather rare that it's going to happen but it doesn't mean it's impossible. A lot of people will be very scared, for instance, about, you know, mothers want to know if their kids have it, so that would be, well, you're a particular type, it shouldn't happen; but no, then we'll do genetic testing, something that I would normally not necessarily do. So I think just addressing the fears of the patient, what is their biggest concern, and then going from there more so than just what, you know, data is great, trials are great, but real-life it's not a trial. So something needs to be individualized.

QUESTION: Okay. Well, that really wraps up everything that I had on my plate to ask today, and I do again appreciate your time.

[IRRELEVANT MATERIAL OMITTED]

QUESTION: Again, thank you. Are you having a busy day in the office today?

05: Actually [phonetic] yes; it's very weird. I didn't think that I would. I thought May is over and that's it, but apparently no. But it's also because I'm doing an ad board at the end of the week, so I'll be gone for a bit [phonetic]. I guess because last Monday was Memorial Day, everyone has to make up their allergy shot this Monday.

QUESTION: Yes, I can understand that.

[IRRELEVANT MATERIAL OMITTED]

[END 05 6.3.24.M4A]