CMEology

HAE – Hereditary Angioedema

Interview with “13”

April 12, 2024

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Interview with 13 – Hereditary Angioedema

[START 13 4.12.24.M4A]

[IRRELEVANT MATERIAL OMITTED]

QUESTION: This, as you know, is about hereditary angioedema, or HAE. The first question is: what is your personal experience evaluating the HAE literature in terms of its implications for clinical practice?

13: I think it's pretty good. When I was at [redacted] I did academic medicine for 20 years, and so, it had a pretty big, they have a fairly decent patient population there.

QUESTION: And are you a specialist in allergy and immunology?

13: Yes, ma'am.

QUESTION: And you were at [redacted] in an academic setting?

13: I was until about a year ago. I spent 25 years there and said, no, no; now I'm in private practice solely right now.

QUESTION: Ah, okay.

13: Twenty-five years, maybe it's time to move on.

QUESTION: Okay. Well, that's a big transition to make, isn't it?

13: It's fun. They allowed me to do private practice part-time at [redacted] part-time for 17 of those years.

QUESTION: Oh, okay.

13: So it's kind of neat. So then, I became full-time and now I'm just private practice.

QUESTION: I see, okay.

13: It's fine. It's a little bit more laid back, so I like that.

QUESTION: Are you in a group with other people then?

13: Right now, I have my own practice right now.

QUESTION: Okay. So you're truly in a solo practice?

13: It is. I've got people wanting to join and some stuff with nurse practitioners happened, working on that, and some other associations I'm looking at. So it'll probably a group within a year or so; we'll work on that [phonetic].

QUESTION: Okay. Well, it sounds like a new challenge.

13: It is.

QUESTION: Sometimes, I was in [redacted], I guess you would say, allergy immunology center, and anyway, it's interesting to make a transition, I think.

13: Was that [redacted]

QUESTION: No, no, no, it was [redacted] Does that give you any clues?

13: Oh, yes, [redacted], yes.

QUESTION: Yes. [laughter]

13: Oh, they're renown, no doubt about it.

QUESTION: Oh, yes, yes. I mean, I loved, absolutely loved working there. But I think there also is for many people, there's a time where they feel like they just need a new challenge, whether that's the subject matter—

13: Exactly [phonetic].

QUESTION: —or maybe it's the business end of it or doing something different in that regard, and I think it's a good thing. It's a good challenge for everybody who wants to take that on. So okay, I'll ask you a couple questions, and it's helpful for me to know your background and the fact that you were in academia. Can you tell me a little bit about your experience with the literature in HAE?

13: I just try to keep up-to-date on it and do the CMEs. I've posted a case study, gave a practice, did something years ago on one of our patients we diagnosed with it years ago, but it's just trying to keep up. It's interesting, through the American Board of Allergy and Immunology, you have to do questions every six months and answer three questions on ten articles, and they show up there. Then they show up on CMEs; I need CMEs for my hospital staff. So you selectively do that, plus you browse through, they still send me the old-fashioned Annals in Journal of Allergy in the mail, believe it or not.

(Overlapping Voices)

13: And so, you kind of peruse through that when you get it.

QUESTION: Okay. So you try to read the hard copy if you have a chance?

13: You do, and you glance, okay, you look at the summary first, and if it's something you're interested in, then you follow up with more details, yes.

QUESTION: And then, it sounds like you're using UpToDate then as kind of an onsite practice tool?

13: Yes, you always run stuff by UpToDate. The author [phonetic] actually provides it for us, that, too, on that. Or if it's interesting enough, you can just Google the article and say, hey, with that, have something like this, and eMedicine sometimes has something to look at and that type of thing. And of course, again on these CMEs, they are quoting articles and sometimes you'll look at some of that stuff and go, wow, where did they get that?

QUESTION: Are there particular questions that you are most often looking for when you go to the literature?

13: What I'm looking for is to me, it's fascinating, I treated this before we had it, I remember giving danazol out, and tranexamic acid. In fact, I've still got one person on it. They do well with it and it was nontoxic [phonetic], what the heck, on that, and to me, you're looking at this and saying, okay, you get the C1 esterase inhibitor, great, now you're looking at bradykinin-2.

Commented [1]: Codes (2898-2936)
CME

Commented [2]: Codes (3164-3250)
Prof society updates or tests

Commented [3]: Codes (3674-3704)
Literature review

Commented [4]: Codes (3898-3899)
Expert opinion/Up To Date/Google/Medscape

Commented [5]: Codes (3899-3932)
Expert opinion/Up To Date/Google/Medscape
Expert opinion/Up To Date/Google/Medscape

Commented [6]: Codes (3932-3933)
Expert opinion/Up To Date/Google/Medscape

[redacted]

QUESTION: Yes. And it's like a lot of other areas in medicine now, right—

13: Oh, it is, you know?

QUESTION: —where we're really much more targeted, targeted therapies, and that's always interesting to me because we all recognize that in a complex disease like HAE or whatever else, asthma, allergy, right, you name it, we know that there is more than one receptor or more than one substance that is the driver for these things.

13: The other nice thing about us is we're a boarded, you know, allergy is conjunct between internal medicine and pediatrics, and this is obviously a hereditary disease, and a lot of it's hereditary, not always, but it's neat where we do get to see pediatrics and adult, which is kind of neat for us on that, whereas opposed to the cardiologists love to look at adult versus pediatric in some ways.

QUESTION: So how does that being able to see the pedes and the adult side of this for HAE, clearly some of the newest agents aren't approved down for pediatrics yet. Are people thinking, well, it sometimes happens in pedes, well, should I be trying to use this off-label in a child or is it like, well, we'll just wait until they've done the appropriate studies, or how does that go for you?

13: It's like everything else in the world: everything, it's judgment, and historically, you're using adult medications in pediatrics although we are using nebulized Pulmicort in adults on that. So you like it, or they do have these things now down to age six on that, which is nice. So that's changed that equation, too, on that. And I usually don't see them below the age of five or six.

QUESTION: Yes, that's pretty little. True, okay.

13: So that's cool to watch this now, too, and you're thinking it's okay to get it down to age 12, that makes you feel a lot better, too. And so, it's interesting watching that. And on the other hand, it's like everything else with risks and benefits, and this can be a pretty brutal disease.

QUESTION: Absolutely.

13: The swelling [phonetic], it's not like you're going to give them a shot of epinephrine and they get better in two minutes. So that does factor into a risk-benefit equation.

QUESTION: Yes. One of the things I was taught as an adult pulmonologist is that, and there is some physics about this, obviously, right, but if you have airway swelling in a child where their airway is so small to begin with, it's a much more critical situation than when you're dealing with a 6'2" man and they have some airway swelling, right? You have a little more surface area volume to work with there than with a small child [phonetic].

13: Well, it's just pure terror either way.

QUESTION: Oh, pure terror, right, absolutely, yes, totally.

13: I'm not a pulmonologist, so yes, you're right, it's just pure terror. I can take your hand swelling up all day, fine, but there's nothing that scares you more than that.

QUESTION: Absolutely, airway stuff for sure. So when you're thinking about the implications of HAE research on clinical care, is there any particular format of research results that's more influential for you? So for example, do you prefer to get information from an abstract; poster presentation at a conference; conference presentation, symposium, that sort of thing; academic detailing; sounds like you do like UpToDate; you do have some journals; but what kind of a format do you like to see things in?

13: To be frank with you, I don't make a whole lot out of poster presentations at the meetings. To me, it's more like the Fellows get to do, and it's nice in that you can walk around and look at them; I don't make a whole lot of that. Sometimes a good detail does give you, points out, it's interesting enough, it is kind of interesting it will point out more of what's wrong with the other guy than theirs, that type of thing. CMEs are quite helpful, too, to me. And then something, and I guess I'm biased, if something is coming through in the Annals or Journal of Allergy, you're much more likely to see it. I don't have a subscription to New England Journal of Medicine or AMA; I guess there is a bias there on that. The other thing is word-of-mouth.

QUESTION: Sure. So from like your colleagues?

Commented [7]: Codes (9573-9712)
Collegiality

13: Yes. [redacted] with angioedema is a sharp guy, and he's a nice guy to ask, hey, you know, what's your experience here on that? [redacted] was brilliant in that; that guy's an MD/PhD pharmacology guy. And boy, when he said something, people listened. He passed away.

QUESTION: So follow-up question for you on that: when you say CMEs, can you tell me a little bit more about the format of the CME that you tend to use the most.

Commented [8]: Codes (10049-10401)
CME

13: It's one, you hate to say it, you need for allergy, if you're not going to a conference that year, I think you need, is it 25 or something you need? And then, the state requires something. Our hospital I think has lowered it; you need like 50 CMEs over a period of time. You've got all these recommendations. [redacted] used to require like 100 every two years.

QUESTION: Oh, my heavens, okay, wow.

13: It was brutal on that. I think they've cut back on that, but you needed a lot of CMEs.

QUESTION: Yes.

13: And you have different timeframes, too. You've got the hospital, the state, the American Board of Allergy plus the boarded term [phonetic], and so, it feels like you're always doing them. And so, once you can get a hold of, I'm blanking on the one I use a lot of, if it shows up there, you're more likely to do it on that. And there are a couple of them I go to; I'm trying to think of the one I go to the most. I'm blanking. Medscape—

QUESTION: Medscape, okay.

13: —is one, and if it shows up there, I'm probably doing it.

QUESTION: Uh-huh, okay. So do you get like an email from them?

13: I usually ignore the emails. Usually [phonetic] when you're looking—

QUESTION: Or you just go there?

13: —for something, when you need these credits. Like my [redacted] is due at the end of the year on that, and so, you'll start looking for more CME. I think it is a good factor, and again, the American Board of Allergy, they have angioedema questions and if it shows up there, you're definitely doing them, one of their articles.

QUESTION: Right. Okay, great. Thank you. What factors are most important to you in the process of interpreting the HAE literature and applying it to clinical care? So it sounds like you have experience maybe curbsiding a colleague or someone who is influential in the field—

13: Oh, yes.

QUESTION: —being able to ask like, this is a weird situation, what do I do? Are there any other factors that are important when you're looking at the literature? Do you feel like you're pretty well prepared to analyze the data that you're seeing?

13: Well, I will give the American Board of Allergy credit on that one. They force you to regularly do this. And I don't know if you're still boarded in medicine; you have to do that every four months now where they give you scenarios.

QUESTION: Yes, yes, yes.

13: And so, sometimes you've got to find stuff quick on the internet.

QUESTION: Yes.

13: And so, a quick, I think one of the things it teaches you to do, and by the way, it's very interesting for me to treat a brain aneurysm or subarachnoid hemorrhage for an hour [phonetic], so it's kind of fun in keeping up on a test at least, but to me, it does force you to find some reliable sources and not look at the junk, quick; you get the junk out of there. So you know where you can find some of the stuff and be able to do it. And so, always with studies, you're always looking at: did they compare it, how many people did they do, how many people dropped out, that's another huge one on that type of thing. And the side effects is interesting, too, because the thing that makes you nervous with hereditary angioedema is giving something that can cause anaphylaxis; that always makes me a little bit nervous, too.

QUESTION: Yes, of course. I mean, anaphylaxis is a very real thing for allergy immunology. It's not a theoretical construct.

13: No, it's not.

QUESTION: Yes, which I think I didn't really appreciate quite so much until I started doing my training at [redacted] was training in pulmonary but had a lot of interaction with allergy colleagues, and I would cover the acute observation unit, and yes, it just makes you respect things like allergy shots and first doses of monoclonal antibodies even more.

13: And that's something like [redacted], if they come out with a study, you're going to look at that one. You hate to say it, and there are other organizations to come out with something that, hey, you're going to take a close look at this from that institution.

QUESTION: Yes, exactly. So being able to look at, do a quick scan of the author list or the [unintelligible].

13: Yes, if you see an author like [redacted] [phonetic] in allergy—

QUESTION: Of course.

13: —if he says something, you're going to look at that a little bit more closely.

QUESTION: Yes. Okay, fantastic, thank you. Any barriers that you find incorporating research or the literature in HAE into practice?

13: Oh, it's the insurance companies.

QUESTION: Yes, yes.

13: The costs and preapprovals, and it's that.

QUESTION: Mm-hmm. Do you have help? I mean, you're by yourself now. I mean, how do you handle that because that can be complicated?

13: I have one person that does preapprovals in that and just kind of works through stuff. And that's a nice thing is you have very limited preapproval medications on that, but the monoclonal antibodies is always an issue.

QUESTION: Right, of course.

13: Sometimes it goes right through and sometimes three months later, you're still haggling.

QUESTION: Yes, yes. And that's something that sounds like you might have to get involved with if it's taking a lot of time [unintelligible]?

(Overlapping Voices)

13: Oh, yes, it depends with monoclonal antibodies. They're pretty good about, okay, Xolair for urticaria, we start learning that. But some of these other nuances, it's a little bit difficult, like Xolair for straight angioedema that's not hereditary angioedema is a little bit more problematic.

QUESTION: Have you encountered any issues or barriers specifically with HAE treatments?

13: It's basically, yes, no one wants to pay for a monoclonal antibody on that for any of them with this. So it's an issue. But once you start doing it, you just kind of realize, okay, and some of it's gamesmanship on that which shouldn't be: they send you over here and it's finding the right person, and finding out the right wording that they want, which is you have the scenario but you didn't use the proper noun that they like. And so, even in [unintelligible] like, well, that's a dumb way of describing it but it's true, but is that what you want? Okay, fine.

Commented [9]: Codes (13928-13999)
Source of the research

Commented [10]: Codes (14115-14175)
Author reputation

Commented [11]: Codes (14490-14519)
Insurance/Prior authorization

Commented [12]: Codes (14895-14941)
Insurance/Prior authorization

QUESTION: Yes. How about patient-related barriers?

13: Most patients are just thrilled that one, they get somebody finally getting to the bottom of this. And obviously, anything with injection sites isn't fun with that. But on the other hand, you see less of that than you would for something else because again, this is a terrifying entity that this occurs, or they go to a dentist or something, and again, it's interesting how you get less pushback on that.

QUESTION: Okay. Any other, it sounds like you're now in your own practice, so maybe there aren't any institutional barriers to—

13: No.

QUESTION: —doing things at this point. You've cleared some of those away.

13: Yes.

QUESTION: Yes. Okay.

13: But interestingly enough, you learn a lot by doing that, so you were actively involved in the preapproval process, and interestingly enough, some of my nurses who used to work there now work for me, so there is a lot of learning that you get from that. So it's not like starting anew; you do get a lot of learning.

QUESTION: Right, exactly. Okay. Why do you think it is that evidence-based care gets delayed in practice when it comes to HAE in particular?

13: One is I think there is a sense out there that it's flooded in that whereas like, well, gees, you have a plasma inhibitor and it's a C1 esterase-based disease, and you have a C1 esterase inhibitor, or plasma recombinant whatever, and so, you have that; and the second issue is, well, look, this is a lot better than danazol we used to give [unintelligible]. But I think the point is that that kind of pathway, you know, it's fortunate, [redacted] and it's a much more complicated pathway, and this idea that it's just one little thing, you know, in the human body, there is so much feedback and there are [unintelligible] concurrent loops that it's an oversimplification. And I think to say, okay, hey, is it an inhibitor deficiency, no, it's more complex than that and there are multiple loops and there are feedback inhibitors which are important. But on the other hand, sometimes that message, I don't think it's translated as quickly as it should be.

QUESTION: Okay. Yes, there is kind of a bind there, right? Companies have to talk about their mechanism of action.

13: Exactly.

QUESTION: They can't overstate what they're doing. They have to be pretty conservative.

13: That's the promise. Here it is, it's a C1 esterase inhibitor deficiency, and that's what it is: either acquired or just an inherited one, and that's the test you get. You get a functional one, you get a total one. And so, all of a sudden, it's simplified for them. And in some ways, I wish we had another test that we could give, and we don't have that piece of paper that comes in and says, oh, no, your C1 esterase inhibitor level is two where it should be, or your percentage, your functional level is 35%.

Commented [13]: Codes (16346-16395)
Patient anxiety/concerns

Commented [14]: Codes (17347-17570)
Excess choices

Commented [15]: Codes (18853-18900)
Testing

And so, you can see that number, you can quantify it, and I wish we had something else to say, well, no no no, your bradykinin-2 or your something else is that low, your kallikrein or something else to say, oh no, look at this number. But a lot of us and I believe, yes, I'm a believer where yes, there are multiple things working together, but I think that message does get, I don't know if the complete message gets across to some people.

QUESTION: Okay. So it sounds like there may be some hesitation about oversimplifying the mechanism and getting someone to say, oh, well, yes, that clearly would be the best treatment.

13: Optimal way of treating.

QUESTION: Yes, optimal way, especially when there are other products on the market that are, perhaps you have more individual experience with, or they've been on longer. Obviously, there are pluses and minuses to any kind of treatment that's out there. How do you think that some of the delays or the hesitation could be overcome?

13: One, it would be great to have a second number. And again, you're going back to you've got a bad number you want to fix, like if somebody's potassium is low, you give them IV potassium, something like that, that would be nice. It's just more education. In some ways, you'd wish that, I guess the way it's referred to on that, it's a pathway or it's called a pathway type of thing, I'm not up [phonetic] on that, it's just trying to get people to understand the complete picture.

QUESTION: Okay. I'm assuming at [redacted] you guys probably had allergy immunology rounds or something where you would get together and talk about what's currently going on in the literature or the like. How about now that you've made this transition out into private practice? What are your sources?

13: Not as much. I'm very much more reliant on the journals. You still know these guys, a lot of people, and so, the people in the community here, you can still call, pickup and say, hey, what do you think about this? It's not a total isolation. And unfortunately there, allergy is so spread out there that they have pediatric allergy, adult allergy; they have eight different locations. And so, sometimes the rounds in particular, some of the attendings are not as well attended on that. So it's more of talking with people; it's more looking at the literature, too. It remains important.

QUESTION: Okay, all right. What's been your experience in identifying patients with HAE who would benefit from long-term prophylaxis?

13: You've got to look at the severity of the disease on that, too. And it's interesting, too, you'll see people, if the test is not the greatest, too, because you'll see people, if that serum is not immediately processed, sometimes the numbers come back artificially low. And also, it's the airway. And also, people forget about this, these people get some pretty severe abdominal pain which interestingly enough again, it's a spectrum, but it's interesting to see how those bowels get in angioedema, essentially in the bowels, how much people would benefit from that part of it, too.

Now, again, this stuff is always in the airway, but that's a part that people do forget about. And also the fear of, you know, I had a person, she's swimming and sure as heck, just decided to jump off the pool and hit her neck on the edge of the pool, that type of stuff. And so, taking away some of that fear is quite helpful.

QUESTION: Okay. And so, you're talking about the patients having fear of another attack?

13: Yes. Oh yes.

Commented [16]: Codes (20869-20914)
Literature review

Commented [17]: Codes (20918-21070)
Collegiality

Commented [18]: Codes (22435-22491)
Promoters of translation/ prophylaxis

Commented [19]: Codes (22507-22579)
Promoters of translation/ prophylaxis
Fear of episodes

Commented [20]: Codes (22579-22580)
Promoters of translation/ prophylaxis
Fear of episodes

Commented [21]: Codes (22580-22597)
Fear of episodes

QUESTION: Yes, okay. It's so unpredictable—

(Overlapping Voices)

13: Any trauma like jumping off of a pool, or just having some fun, or all of a sudden, you just wake up and you're [unintelligible] you look like a club. You look like you got mad and punched a wall or something, you know what I mean? It's just people don't understand, it looks like somebody hit you or something. And in trying to explain that to the population, their neighbor is now waking up [phonetic] on that, it just did this [phonetic].

QUESTION: Okay. So you're really kind of looking, you're balancing out severity of disease, obviously whether or not there are airway issues, and then, if the patient is experiencing severe abdominal issues or just the unpredictability of not knowing whether they're going to have another attack, those would be some of the things that you're thinking about in terms of [unintelligible] prophylaxis.

13: Exactly.

QUESTION: Okay. Honestly, when I was doing a deeper dive into HAE, I thought to myself of every person I've ever seen during my training in the emergency room who had severe abdominal pain, and you end up going, oh, well, we don't know what it is, right?

13: Exactly.

QUESTION: And that's not an uncommon scenario, right, in the acute care emergency setting [phonetic].

13: You wonder how many of those had their appendix taken out, you know?

QUESTION: Oh, for sure.

13: With abdomen, boom, you know?

QUESTION: Yes, exactly.

13: They gave them some steroids, so the white blood cell count is up.

QUESTION: Yes, it really is an underappreciated condition, and of course, it's rare as well, so it doesn't get thought of as much as it should, and diagnosed as much as it should as well. So when you're evaluating a patient, as you may know, there has been kind of a renewed emphasis on looking at the impact of HAE on quality of life. How are you going about evaluating impact on daily activities, work, school, et cetera? How do you do that with your patients?

Commented [22]: Codes (24261-24306)
Primary care misdx or no knowledge

13: Basically, okay, what symptom are you having of HAE? And then, they'll say it and a lot of times, they'll pick up and give you an anecdote with this: oh, yes, well, I'm fearful; or, oh man, it's was awful, people didn't understand why my eye was swollen. You know what I mean?

QUESTION: Mm-hmm.

13: Or my hand is swollen. They'll say something and when they're giving the symptom out, they'll usually put some type of anecdote in that and why that was important to them. And to me, that's how I pick up on that.

QUESTION: So listening to what happened, what their symptom was, and then how they felt about that or how it might have impacted [phonetic]?

13: Or how they even talk about it: look, my hand is swollen up, it hurt; look, my stomach is hurting. They just don't say, yes, I had angioedema; look, it was swollen there and I'm in this situation. And you're just calling it angioedema on that, but when they tell you that, they'll describe it to you.

QUESTION: Okay. So you get a sense a little bit then of what this means to them in terms of limitations in their lives; and obviously the unpredictability, I think, for some people is really very hard to live with as well. You may or may not know there are some validated questionnaires for quality of life that are out there. Are you using any kind of validated tool, or did you use any validated tool when you guys were practicing in the clinic at [redacted]

13: We had an urticaria index that we used. We had to use it and sometimes you have to use them; I'm blanking on which one it is. One of the insurance companies required that for preapproval for Xolair—

QUESTION: Oh, interesting.

13: —for hives on that. But I mean, yes, I do think that in medicine in general for conditions, I do think quality of life stuff is underutilized.

QUESTION: Okay. Anything that you think might help people use those tools more often?

13: I think more discussion on them, more differentiating one. And you're right, 20 years ago, it was just your judgment, and now it's nice to have a number. I do think that you're going to be seeing more in your EMRs on that. But yes, I see that in the next couple years becoming a much bigger, much more important than we're putting emphasis on. Now, it's like we're describing their quality in life and giving a numeric value. But yes, it's something that we are working on.

QUESTION: Yes, and it would be a little easier if you are dealing with an EMR. Hopefully, you would be able to pull something up, or your EHR would help you, right?

13: Well, it's nice, the ACT Score, I guess in some ways, that's quality of life but that is automatic, and it's nice to see it and okay, they're indicating this person's ACT is 21, the lowest one has some nocturnal issues. Yes, I think it would be, and the other one is the nuances between the two, between the ones, and they're all in the literature. In some ways, you're like, then they'd give you three different ones: which one do you use? That's something, and it's something that I do see it's going to become a much bigger role in medicine, and hopefully, we can start incorporating that like we do our ACT Score in the EMR, which would be great.

QUESTION: Yes, okay. And I think you raise a good point, too: there are a number of different tools for quality of life. I think there are at least two for HAE that, if I remember correctly, and clearly, many of them have been used in a research setting more than in a clinical context. And I think it's natural to question because we all know that clinical populations and research populations are different, and the whole process of being in a research study is different. Some of those things, it sounds like, might need to be discussed a little bit more before a clinician who's in regular practice would want to embrace using a tool of that sort. I think also there sometimes is a perception that it just takes too long to use a tool. But on the other hand, being someone who did a fair amount of work in asthma, I can actually say I think ACT and ACQ and those sorts of things save you time in the end.

13: Oh, yes. That one is nice.

QUESTION: You've got to get used to it.

13: Well, there are five questions there that you don't have to ask.

QUESTION: Oh, it's so easy, right?

13: And when you're looking at this, you can say, oh, the person is a 25, having no shortness of breath at night.

QUESTION: Yes, it does.

13: You know? It almost dictates itself on part of that.

QUESTION: Yes, exactly. How are you talking, when it comes to treatment and you've got a patient who has HAE, how are you engaging the person in decision-making when you're talking about long-term prevention.

13: Well, the first issue is long-term prevention, acute episodes, which way do you want to go? Obviously, the frequency of events has something to do with it.

QUESTION: Sure.

13: And basically, you say, look, this is the older way and these are the new things that have come out in the last 5-10 years, which is on that. So you just break it down between, okay, you get acute attacks and then you have more prophylaxis.

QUESTION: Any challenges that you've run across with patients when it comes to talking about long-term prophylaxis?

13: Well, it's the frequency of events. And it's like any health condition: if you're feeling good, you're going to live your life. You know what I mean? Just put it in the back of your mind. It's just like any other condition; it's like bad cholesterol and high blood pressure. Look, you're living your life, you're working, and it's not until, okay, you start getting some fluid backing up, or your chest starts hurting when you do something, or you can't hike anymore. So it's human condition that if you're doing well, there is much less of a propensity to do anything about it.

QUESTION: Okay. So a patient who is having more frequent or severe attacks might be more open to the option—

13: Absolutely.

QUESTION: —of doing a long-term prevention versus someone who is maybe just having a very rare—

13: It's also rare in severity and where they are.

QUESTION: —okay. When you are currently thinking your way through all of these different options for treating, especially when it comes down to prevention, long-term prophylaxis for HAE, how are you, I mean, I know you want to get your patients' input, right, of course, but how are you choosing or going through that in your mind at this point?

13: Again, it's frequency of attacks; two is you start looking at some of the side effects; three is you've got to start looking at what's covered for them. And four, hey, you can say this although interestingly enough, a lot of times, they do take cues: a lot of times you're like, look, you give me eight different options, just pick one, but you do like to always give two or three options and say, look, this is what we could do, and look, this is an oral pill, that's cool. But oh yes, look, it's not the greatest thing, the IV. And so, some people are petrified of IVs, and so, you've just got to look at the patient and take a look at all this, and you've got a ton of options now.

QUESTION: Yes, there are definitely a lot of options, okay. You did participate in the CME activity—

13: Uh-huh.

QUESTION: —on HAE. Can you tell me a little bit about how participation in that activity might have influenced the way you think about translating evidence into care?

13: It's a nice review, I mean, just seeing the expanding levels of stuff coming in, and gee whiz, you're looking at all these phase 2/phase 3 things coming in. My goodness. And now, you're looking at, gees, you've even got an IgG-1 thing coming in, and you remember seeing this in theory. I mean, look at the different mechanisms, absolutely incredible how, which is the magic bullet. The other question is one of these days in life, you're going to have the classic Advair type of thing, or inhaled steroid long-acting bronchodilator; I mean, when is this going to come out? And so, I don't know, it's impressive on this, and wow.

QUESTION: Was there anything in the activity that you felt would encourage you to change something that you're doing now?

13: I think it's pushing me more to look at some of this newer stuff coming out. And I do think yes, again, all these studies keep on telling you about quality of life things: that hits home and I think it makes things even more complex.

QUESTION: To think about quality of life?

13: No no, quality of life for me, all these different mechanisms coming out—

QUESTION: Oh, I see what you're saying, uh-huh.

13: —and options. It's like, you've got to do some more work on this.

QUESTION: Yes, okay. So it sounds like it was kind of eye-opening for you?

13: Eye-opening on this type of thing as, wow, this is about ready to change and I better be ready for some of these newer mechanisms, and again, it's just not as simple as, oh, this can replace the C1 esterase, anymore. So that's thought-provoking.

QUESTION: Sure, okay. All right, thank you.

13: They gave a lot of information about some of the new stuff, too, so I'd investigate [phonetic].

QUESTION: Yes. Well, that is part of when you construct CME, you have to present things, and hopefully, we do this, we have to be fair and balanced, which means you can't just talk about one thing.

And it's natural to talk about things that are in phase 2 or are still in phase 3, and it kind of does put things on people's radar, right? Like oh, there is something that's new that's coming out; I should probably at least in the back of my mind say, oh, there is a new mechanism of action that I need to kind of think about. Whether or not that agent will ever be approved for use, who knows, but it does, I think, it makes people realize that there are new things that are out there; it's not just what we had five or six years ago.

13: Exactly. It's just this simplification, again, I keep repeating on that where it's just, oh, it's a C1 esterase property, it's C1 esterase, and that thought in looking at the complexity of this and seeing even some of the stuff we have now is which is the better one?

QUESTION: Yes. And that will be a challenge, right, because there will never be—

13: Exactly, yes.

QUESTION: —there are never going to be head-to-head trials probably; it's a rare disease.

13: Oh, you can't, yes.

QUESTION: Right? So even in asthma, right, and asthma is not uncommon, there is actually a lot of people with severe asthma out there and we're never going to have head-to-head trials on those, either.

13: It's tough, or just no treatment, placebo-controlled? It's hard. And also, too, this is someone, a heterogeneous disease like everything, every disease in some ways is like that, but not everybody presents in the same way and it's almost you're looking at them on this [phonetic]. And again, we're getting different oral stuff. I mean, it's really cool to see; really cool to see.

QUESTION: Okay. As you may be aware, there are clinical guidelines for HAE, and that's one way that research gets translated into clinical practice.

13: Uh-huh.

QUESTION: What would you say the influence on your practice has been? How do the guidelines influence you?

13: I think you look at them, you're aware of them. The problem is you've got rapidly-evolving therapeutic options, and so, is there delay in translating the guidelines to some of the newer current stuff? You've always got to keep that in the back of your mind. But yes, you always like staying in the guidelines. It also makes things very easy, easier for preapprovals.

QUESTION: Right.

13: You shoot that back at them.

QUESTION: Yes, if the guidelines actually mention the new agent that you would like to use, and as you mentioned, that can be a challenge because clearly, there is a lag, right? It takes, not only does it take expert panels and people, time to make all these things but then it takes, journals are not fast, so it takes another 6-8 months to even get it into print.

13: Exactly, yes. They're nice to have though because when you're trying to get a preapproval, you're like sending them the guidelines. If it's on there, boy, that is helpful.

QUESTION: Yes, exactly. Anything else as we're wrapping here, anything else that comes to mind that you would like me to know about HAE, or your thoughts on it?

13: No, it's a great drug. I mean, it's just amazing to see in five years how we're going to be dealing with this. This is really, really cool to see. And particularly, somebody who was treating this before we had most of the stuff where you were getting danazol, and that type of thing, and what do you do before they go to the dentist? So it's really neat to watch the evolution of this with that, and it is kind of neat when you get, I think this was a very well done CME; I really liked it.

QUESTION: Oh, good.

(Overlapping Voices)

QUESTION: Oh, that's fantastic.

13: You did a very good job, and that does help with this when it's well done.

QUESTION: Okay. And I imagine, just one last quick question, when you were [redacted], you were probably getting referrals from people practicing in the community—

13: Yes.

QUESTION: —with complicated patients with angioedema—

13: Uh-huh.

QUESTION: —as a consideration, HAE as a consideration. What were the gaps that you were seeing the most in the previous care that people had before they came to your tertiary-quaternary care center?

13: One is that I don't think they considered this on this. Two is I can't tell you how many times people would just get a total quantitative C1 esterase inhibitor and not get a functional.

QUESTION: No? I see, okay.

13: So you're going to miss about 15% of that. I can't tell you how many times where this serum, we had problems with his blood draw, so he had an artificially low one, too. I guess the message and again, what we tried to do, and I think [redacted] does a very good job on it, they did a very good job, is trying to get the message out, hey, to get angioedema without urticaria, you've really got to look at this, that that's the message.

QUESTION: Right, okay. Well, that's really helpful. I appreciate your time very much today.

13: Appreciate that.

QUESTION: If you have any questions going forward, you should [redacted] fairly quickly.

13: Okay.

QUESTION: And if you have any issues, please just [redacted] who was in touch with you previously; she is fantastic and she'll help you get set up with things if you have any issues. But again, thank you very much. I'll let you get back to the busy world of practice and seeing all your patients.

[IRRELEVANT MATERIAL OMITTED]

[END 13 4.12.24.M4A]