International Symposium on Usher Syndrome

Transcript from the Usher Syndrome Family Conference, Saturday, July 12, 2014

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# Session I: Diagnosis
# Presentation by Dr. Margaret Kenna

MARK DUNNING: Okay, guys, we need to get started. If everyone would please take their seats.

I'm glad to hear so much talking because this is when this day is all about; this day is about making connections and making friends. And getting to meet other people who are part of the Usher Syndrome community. So I strongly encourage you to take every opportunity that you can to introduce yourselves to others, and to -- to make friends, and to make connections. We have a number of the leading researchers in the world are in attendance here today, as well. And I know that they are very happy to help out with any questions that you may have.

I have some housekeeping stuff to do, but before I do that, I just want to make sure that I say my name is Mark Dunning; I'm the Chairman of the Usher Syndrome Coalition, and we are very happy that all of you are here today. We are expecting about 300 people today, total, and we expect to be the largest gathering of people with Usher Syndrome -- Usher Syndrome community in history.

( APPLAUSE )

Okay. I have a long list of housekeeping items to go through quickly here.

We have child care. I don't see any children in here, but if you do have a child who is under the age of nine, I believe, we have child care. It is on the second floor. Best way to get to it is to go to the end of the hall and take the elevator up to the second floor. The stairs you see here that look like they go to the second floor go to the mezzanine. The second floor is above the second floor here. So you have to go up two flights of stairs to get to the second floor, and the child care room is all the way back down the hall right next to the auditorium on the second floor. So the elevator at the end of the hall is your best way to get there.

We have great people up there that we are very excited about, and we have lots of toys, so I'm sure the kids will be fine. But they will come back down if they need to.

We also have, for kids who are older than, I think, the age of nine or ten, I don't remember what the cutoff was. We have a field trip to the Museum of Science and they are gathering by the doors out here, the far doors. We have some great chaperones going with them. They are all from the Decibels Foundation. And I can vouch for them because I hired them all. And they are all great. And so they are going to have a great time. But they will be heading out in about five to ten minutes or so to the

Museum of Science. They will be back before the end of the day. They are going to play it by ear and see how well things go, but my guess is that they will probably come back around 4-4:30 or so.

Also upstairs next to the child care we have genetic counseling available all day long. So if you have any questions about your genetic diagnosis, or you have not gotten a genetic diagnosis, we have some of the leading experts in the world in Usher Syndrome diagnoses upstairs. They are right next to the child care room. You can just go up at anytime. I know a lot of people are going to want to go on the breaks, but if you think about it, everybody goes on the breaks, it is going to be hard to get much time with the counselors. So I suggest that if you do want to speak with them, you want to try to sneak out of various sessions, that would probably be the best way to do it. But I strongly recommend you do that. They can answer any and all questions that you have about the genetic diagnosis.

I know a lot of you have already visited the booths that we have outside. But on breaks, again, I recommend you go by and see all the sponsors of the booths that are out there. There is a lot of great information out there. There are Usher Syndrome bracelets, so hopefully everyone walks out with an Usher Syndrome bracelet like this.

We also have posters on the mezzanine level. That is one level up. That the scientists have put together. There is a lot of great science there, so you can go up and check out that stuff on the breaks.

The most important thing of the day, the bathrooms, they are right out this door; or if you are upstairs you just go down the ramp next to the auditorium and the bathrooms are right there.

This afternoon we'll have several breakout sessions. The breakout sessions will be in the, uhm, in the cafe upstairs or in here depending upon the breakout session. And so we'll give better directions about that. But we will be having breakout sessions this afternoon.

We are going to try and stay on schedule as much as possible. We are already late.

( Laughter )

And this being a gathering of deafblind people, ah, we expect to be running late the entire time. But we are going to do our best to stay on schedule. We actually have something that we hope to make a bit of a schedule change, we hope to have lunch at noon instead of 12:30 so that we can have more time for the family panel. The family panel is usually one of the most popular things that we do. So we'll try to give more time for that. But we'll play with the schedule all day.

Our speakers throughout the course of the day, the scientific speakers, we are asking that you hold your questions. We are going to have a Q&A session at the end of the morning. So all of the, ah, experts will be up here to take all of your questions at that time. So we won't be doing questions after each talk. We'll do them at the end.

We, ah, as many of you know, the Usher Syndrome Coalition runs a Registry for Usher Syndrome families. We strongly recommend that you join our Registry. That is the best way to stay in touch with the researchers and research going on, and for us to be in touch for you. For researchers, wanted to

make sure that you know this is your best way to get in touch with Usher's families as you go forward. So as we move towards clinical trials, this is how people are going to find you and inform you about clinical trials and about treatments. So you are going to want to be part of this Registry. You can register online, but you can also register today, just outside on the table right outside the door.

I want to make sure that I say "thank you" to all of our interpreters and our CART workers here today.

( APPLAUSE )

You don't know how much they need that applause. They have been here for -- many of them have been here for three days and spent the last two days signing deeply scientific information for -- over and over again for several hours. So we are very proud of them and thank them for all of that.

And as I mentioned earlier, and I will mention it again, if you have hearing aids or cochlear implants that have a telephone position, we, ah, we strongly urge you to use one of the Assistive Listening Devices that we have. They will help. And you will be surprised how much they help. And Marilyn Neault in the back, who is waving her arms right now, has a whole bunch of them. Marilyn, on Wednesday, drove all around town picking up every one she could find. We have lots of them so please take advantage of them.

At this time I would like to introduce Elise Faucheaux who is a mom from New Orleans. And she, ah, she also, ah, has done a lot of work for the Usher Syndrome Coalition; particularly helping us out in Washington D.C., and she is also a wonderful lady. So I ask Elise to come up here and do the welcome today.

( APPLAUSE )

ELISE FAUCHEAUX: Good morning to you all and welcome to the 6th Annual Usher Syndrome Family Conference. My name is Elise Faucheaux and I'm a member of the Board of Directors for the Usher Syndrome Coalition, as well as a member of their Governmental Relations Committee. I'm here with my husband Blair and my in constant motion three-year-old son Hunter who was diagnosed with Usher type 1C a little over two years ago. I want to start off today by thanking each and every one of you for being here. Everyone is part of a special community that values each individual member. Most of you are here to help yourselves or help family members as individuals, but you have no idea how being here helps the person sitting next to you and others sitting across from you. As a parent of a child with Usher Syndrome, within the hour of getting the diagnosis, I called a fellow mother of a child with Usher Syndrome because I felt like no one could relate to me like her. I started a blog after my son Hunter was born. Before I even considered Usher Syndrome to be the contributing factor to his deafness, I blogged about the road to getting bilateral implants. I blogged about his balance issues. I blogged about his very delayed motor skills. And the day we got the diagnosis I blogged about Usher Syndrome. I wrote about how one day we were going to give Usher Syndrome a new definition. The Usher Syndrome Coalition is making leaps and bounds to do just that. In the past year we have been represented on Capitol Hill at conferences and fund-raising efforts. Through joint efforts by the Governmental Relations Committee, as well as pro bono work from various professionals, our court language was included in the 2014

omnibus spending bill by the House of Representatives to try and obtain funding from the National Institute of Health. The Coalition's refusal to give up on efforts have been recognized by various individuals and organizations which means that we are making a real impact. I also have the pleasure of announcing the location of the 7th Annual Usher Syndrome Family Conference. If you are ready for a bite of award winning cuisine, a glimpse of historical art, and warm southern comfort, look no further than New Orleans, Louisiana.

Once again, thank you for attending the 6th annual Usher Syndrome Family Conference.

As Mark recently posted on the blog, there is hope for people with Usher Syndrome. There is hope in the research. There is hope for treatments real soon. And if you take time to make friends, you will see that there is hope in a life lived with Usher Syndrome.

Now I'd like to introduce Catherine Blanchet and Susanne Morrow who will be today's moderators.

( APPLAUSE )

DR. CATHERINE BLANCHET: So good morning, everybody. Well, we are beginning the first talks. And I'm really pleased to introduce Dr. Margaret Kenna, but most of you already probably know her, she is a part of the Usher Coalition Board of Directors. She is an otolaryngologist here in Boston Children's Hospital; and she is the current Director of the Clinical Research Program for Otolaryngology and Communication. Her talk is about Usher Syndrome: "Why does a diagnosis matter?"

DR. MARGARET KENNA: Thank you very much. I know many of you. And I would say that, ah, that we have had some versions of this presentation over the years, and I'm very happy to say that things are changing. I also want to thank the interpreters, and the CART Reporters, and the people doing the child care, and the genetic counseling. The genetic counselors are people you may know because they are people who also work with us.

So I don't have anything to disclose.

So when patients -- and this is something that all you guys know. When the baby is born, and they are told that they have a hearing loss, you actually can't believe it because the baby looks perfect, I mean they are perfect, but you can't believe that there could be anything that is wrong, or is perceived as wrong. And it is overwhelming, you are tired, people tell you that you need to have all of these tests and then tell you what you need to do. It is very difficult. But of course as parents, you want to do the exact perfect thing for your child.

So what will happen is that people will start to talk to you about, oh, all of these different things that could be going on, and the multiple causes of hearing loss, and this is a pie chart that keeps changing, but the purple stuff is genetic. And, uhm, and two thirds or three quarters of the genetic causes are patients who are -- want to refer to as non-syndromic. So when we first meet them as newborns or young children, they have hearing loss, but there is nothing else apparently going on with them, and we think "ah-ha," it is just the hearing loss.

But as that -- as the piece of that pie, the purple part gets bigger and genetic testing becomes more available, and hopefully something to do about it becomes more available, uhm, we, the annoying clinicians will push you, the overwhelmed parents to start thinking harder about whether you want to get diagnosed or not.

The other problem is that 75% of hearing loss is recessive. So each biological parent is likely copying one abnormal copy of the Usher gene. But if only one parent, so they think it is not genetic, and it is absolutely not in my family. And then people say, until very recently, this was an excellent point, even if we figure it out, what are we going to be able to do about it? And an excellent point. I've certainly wondered that for many years myself.

Bill Kimberling who is not with us today, but one of our fathers of Usher Syndrome and discovered many of the genes, and many of you have probably met Dr. Kimberling, put these steps out to think about what to do with an inherited or genetic disease. The first thing to do is find the gene. And over the last couple of days there has been a lot of discussion about how we can find the gene. We have found many of them. We have not found them all. And then you try to figure out, match what the patient has, to the type of gene they have, or the mutation they have, and then figure out when patients look like that, what is this going to look like down the road.

On the basic science side, you develop animal models to try to study the gene, and then you try to figure out, once you have an animal model or something in a Petri dish, how the gene actually works. And if you can figure out how the gene works, maybe you can do something about it. So until very recently, we really were pretty good at finding the genes, we were beginning to make some in-roads and to correlating what the patient looked like with the gene they had. But in terms of the animal models and figuring out how these genes worked, we really didn't have much information. But over the last few years, this actually has gotten to be quite different and very exciting.

And then what you want to do is you want to screen the human population. Our goal is to find everybody in the world with Usher, and then, ah, and then figure out what they had and then introduce them to therapies as the therapies emerge.

So some syndromes are really easy to figure out. When you meet the patient you know they have it. One of the common things we see is Pendred's Syndrome, and those patients have an enlarged vestibular aqueduct. And I'm sure many of you have heard this term and had cat scans and MRIs looking for it. And there is one particular gene for that. But patients who have Usher Syndrome have normal cat scans and MRIs, by-and-large.

There is a really rare thing called Jervell and Lange-Nielsen where you have an EKG, and those patients will present with fainting episodes, and occasionally what looks like sudden death episodes. So a really rare thing, but something you like to know you don't have, or if you do have it there is an invention for it.

There are some syndromes where it is very obvious looking at the patient that this is probably what they have. Ah, the Stickler patients have small mandibles, cleft palates. The Waardenburg children have different colored eyes and grey hair. So this is something we can figure out when we meet the patient.

However, when we meet patients with Usher Syndrome, they look fine, we don't see anything going on.

So why does Usher Syndrome seem so rare and why is this categorized as a rare disease?

Well, the diagnosis is still made in many cases very late. Ironically the children with Ush 1 may get diagnosed earlier because they are Deaf and they come to medical attention early on. But the Ush 2 patients, and the Ush 3 patients, you know, they may have hearing loss, but their balance isn't that bad, and so the truth is nobody knows. Uhm, there is really limited availability, genetic testing, and that is something that we can talk about later if you would like to, but there are very few labs still doing this testing, insurance does not always pay for the testing, which makes me crazy, uhm, many physicians and audiologists are not aware there is even testing available for something that seems to be so rare. The presentation is very heterogeneous, the hearing, ah, loss and the manifestations are all over the map. As we have said, the vision loss usually is later onset than the hearing loss. And when you go to see the ophthalmologists, they don't see it, especially in very young children, there is nothing to see. So it is not that they are bad ophthalmologists, there is really nothing to see on physical exams, so it doesn't get picked up.

So why figure out if it is genetic? Well, the non-syndromic patients look the same. We would like to know what gene it is because we may manage them differently, maybe family planning implications, or just want to know and meet other parents with the same thing. Here we all are. There are no distinguishing facial features, audiograms all look the same, we may manage them differently, and the outcome may vary with the gene. So this is a patient who has Usher 1B caused by the MYO7A gene and this is a bilateral to profound hearing loss. This is a patient who has Connexin 26 mutations, it is the same exact audiogram. I know both of these patients, and they look exactly the same, really, at the age of one or two, there was no distinguishing characteristic to tell one from the other. If we had not done genetic testing we wouldn't.

This is Usher 2 patient where they have mild to moderate, often initially in the higher frequencies, and this is a Connexin 26 patient with the same hearing loss. So again, just by looking at the audiogram, all you can do is be suspicious, you can't actually figure out what is going on.

So how common is Usher Syndrome? Well, I think the answer is that it is a lot more common than we know. These numbers keep going up as we are able to test people more effectively, there is such a wide range of presentations, something that everybody in this room had probably figured out. Uhm, we think that it is somewhere between 3 and 6, probably closer to 6 per 100,000 people. That is here in the U.S., and all over the world, that means that there is 3 to 6% of all children with hearing loss. Which is a big number. And of the kids who are, ah, who are deaf and who are kind of, perhaps, for cochlear implants, five to ten percent of those kids probably have Usher Syndrome.

50% of the deafblind adults have Usher Syndrome. And that comes out to numbers that you can see are very imprecise. Somewhere between 0.6 and 28% of the population. So that means that we really don't have a clue. And as I mentioned, still very late diagnosis.

So what does that really work out to in, like, real numbers? So a rare disease, as defined by the NIH, is considered to be less than 200,000 Americans. So if there are less than 200,000 Americans with the disease, you come under the rare disease classification. So in the United States, the estimated number is somewhere between 16,000 and 45,000. I think, probably, it is on the higher end of that. It is probably less than 200,000. But if you extrapolate those numbers worldwide, you can tell that most of the patients who have Usher Syndrome are not diagnosed with it, nobody knows they have it.

The carrier frequency, that is the chance that you are carrying it around, one abnormal copy of an Usher gene is one out of every 70 people. That varies with some populations, and sometimes it is more, sometimes it is less, but right after Connexin 26 that makes carrying an Usher gene the next most common genetic cause of hearing loss.

The next thing we need to do is rule out things that could be Usher, but they aren't. Like congenital CMV, it is an infection, a cold virus that people get, the baby gets it and they may present with hearing loss and vision impairment. Some of the other infectious diseases. Auditory dissynchrony, which is an unusual type of hearing loss that is not usually Usher Syndrome. And so forth. So you go through this list of things to try to rule out the things that are common or easily diagnosed to get a core group of patients to try to figure this out with.

Every now and then we find somebody who has more than one cause. We have at least one patient who has two mutations in Connexin 26. We also have two mutations in MYO7A, they are both recessive diseases, just luck of the draw.

So -- and there are other causes of both hearing and vision loss, and so occasionally we will see a patient who has a clinical diagnosis of Usher Syndrome, but they actually don't have Usher Syndrome. So that is important, too. Because the other diseases are as important to know about. So Alstrom Syndrome is progressive vision and hearing loss, it is genetic. Ah, Norri -- and Alstrom is rare, but not super rare. A Norrie Disease is super rare, it presents blindness in male infants and with progressive hearing loss. And then there are other things, mitochondrial disease. Congenital rubella, German measles, baby born with German measles, this is pretty rare, but we see kids with congenital rubella. So you want to rule these things out. Again, there could be two things going on.

And then causes that present with progressive hearing loss, and the Ush 2 and 3 as an older population with progressive hearing loss, and again you need to think about what other things might be causing progressive hearing loss because you want to make sure that you get the diagnosis right for the patient.

So how do we figure out that the patient has Usher Syndrome? Well, it is a clinical diagnosis initially in an older patient who presents with, ah, retinal degeneration and hearing loss, but we are seeing the kids as newborns, and as we just said, on physical examination, you can't see the retinal degeneration.

Now, older kids we may do electroretinography, which we can actually do on any age child. We know that the electroretinograms in most patients with two mutations, and Usher gene, will be abnormal as early as we can test them. So even if their vision appears normal we can see abnormalities in the ERG.

We look at their balance, although the balance is often widely variable, even the Ush 1 kids, some have terrible balance, some actually have normal balance or what looks like normal balance. And then we have to figure out what kind of gene we want to use to test them.

So why figure this out? Because until recently there was really nothing we could do about it. And so an excellent question: "Why figure this out?" Well, if it is recessive and there is very -- usually no family history, unless you come from a large family which is an isolated population, so perhaps, ah, cousins marry cousins, or you come from a culture where cousins marry cousins, that is how you find the recessive genes. People usually don't come from those populations so it is usually not in the family. If you find out what caused the hearing loss, we can sort of look at the other things; vision, balance, the other things that we are concerned about. We'll also find out what did not cause the hearing loss. People stay up at night worrying about what caused the hearing loss. If we can figure it out we can say "no. It is not this. Whatever this over here is." And that is really good. Just takes it off the plate, and at least if you are losing sleep, you are not losing sleep about that. You can plan for the future. You can plan for other children. If you have siblings who have not had their families yet, maybe they would like to know this. And as evidenced by this room full of people, you can talk to other people who have the same thing. And probably at the beginning, just as Elise said, at the beginning you want to talk to somebody else who has been in the same boat. The same boat diagnostically, the same boat emotionally, who do you call? I mean it is -- it is -- it is the thing you really need the most.

So why not look into having this testing? Well, an Usher diagnosis seems unlikely. People say "oh, that is so rare." Physicians say "oh, that is rare, you don't have t don't worry about it." It is rare, but it is not that rare. Here we all are. Uhm, or the patient seems to have good balance, or their vision, you know, seems pretty good. Uhm, say "we are not going to have any more children, why do we need to know?" Well, you need to know because the patient in front of you is who you are talking about. The results may be inconclusive and that is true, and we can certainly talk about that at the break, around the question and answer session, but it comes with the, uhm, testing of Usher Syndrome and actually all genetic things. Insurance won't cover it. I don't have enough time to tell you how crazy this makes me. Suffice it to say we spent a lot of time trying to figure this out for patients. It is very expensive. Hearing aids are expensive. Implants are expensive. Many young families have this much money and they have to decide where to spend it. This is a terrible thing that you have to think about. And very unfair.

Uhm, people say, well, there is no intervention that stops it or makes it better. Well, that is true, at the moment, there isn't much that we can do about it. But the last two days mean anything, that is coming. It is coming. And it is coming even in my lifetime and I'm old. So --

( Laughter )

-- I think for all of you who are not so old, I think things are going to happen in the lifetime for you and for your children and your family members, I really think this is going to happen.

There is a lot of anxiety. People say, well, "I'm afraid of the unknown." It is fear of the known. And it is fear of the unknown. So if you don't test you won't know. But if you test, and it is scary, and I think both of those things happen in the same person, during the same conversation. At 3 a.m., fear of the unknown is the worst possible thing. Which is why you should get up, walk around, have ginger ale and go back to sleep.

( Laughter )

Many parents think if I have testing I won't understand the results. We are fortunate to have genetic counselors. Everyone in this room, whether you have been tested or not, hopefully there is somebody, either upstairs today, the counselor that I work with and all of her colleagues are here all day, but hopefully in your neighborhood or where you live there is someone that you can talk to about this. Whether or not you had a diagnosis. Because it really helps.

So what if people don't want to get tested? Well, if they are adults, as my daughters remind me, "I'm over 18, you can't tell me what to do." Well, I can tell them what to do, but I can't be sure that they are going to do it. So that is the way that we have to approach our adult patients. If the parents say "I don't want to do this," I think that is a little trickier because, especially once we have intervention, I think it is really useful to know if this is the situation or not. But either way I think that it is useful, but that is my opinion.

So who do we test? Well, in the olden days we tested people because there was only research testing, so we waited until people had, you know, had a profound hearing loss, and they had a significant vision impairment, and then research testing was done, and that made a lot of sense because it enriched the pool of people to test. But then we started to test people who were profoundly impaired, who were late walkers, but half the patients have Ush 2, so we missed those people. So now I think we really try, if possible, to talk to people into getting tested when they are babies. That is hard. But as the testing has gotten better, it really provides you with information that can be difficult information at the beginning, but then you get to meet all of these cool people, Bella Dunning yesterday was talking about why it is good to have Usher. She said "you can travel all over the world." One day I heard her say to her dad "it is great to have Usher, next year we are going to Hawaii." And Mark said "we are? Really?"

( Laughter )

So I think that there are good reasons to figure this out.

So, uhm, we won't talk about this, the genetic testing, rapid evolution, right now we test mainly for single genes, single mutations, but at some point everyone is going to have their genome tested at a McDonald's probably. You get your coffee and get genome tested. And you think I'm kidding.

( Laughter )

I drink a lot of coffee so I'm looking forward to this.

But the other thing is you need someone who is going to explain this testing. So whoever does it, and wherever they do it, you need somebody who can explain what the results mean. So you will know what to do with those results.

And then there are lots of future directions which we have been talking about over the last two days that we will then talk about at the end of the meeting today. You know, what do we need to know about the hearing, and the balance, and why do patients, why are they deaf before they lose their vision? And is there something that we can learn about that?

Uhm, what other clinical findings are there?

People talk about their sense of smell and talk about the way their brain works. I mean there are some other things we don't know anything about.

What kind of responses to therapy are there?

What other great interventions are coming along?

I want to thank you all for coming. I want to thank the planning committee, especially Krista and my research assistant Julie Edwards who thought of everything that none of us thought of. Thank you very much.

( APPLAUSE )

( SWITCH OF CART PROVIDER )

## Session II: Psychological Aspects – Words from the Professionals Presented by: Ms. Ilene Miner – Family and Personal Responses to the Diagnosis of Usher Syndrome

>>: Good morning, everyone, my name is Susanne Morrow I'm from the New York deaf-blind project. We'll talk more about that later today. I have the great pleasure of introducing a friend and long time colleague of mine. In Dr. Bill Kimberling is the father, we have a mother in the nicest way possible. A mother in our field because, really the concept of post diagnosis and what to do next really came out of the work from Ilene Miner. She's a clinician had a started in 1980 that her direction in deafness and deaf-blindness. Without further ado, Ilene Miner.

ILENE MINER: Good morning, some of you are here on Wednesday when I went through this and I'm going to do it again but with a bit of a different emphasis. I'm a clinical social worker. Currently living in Los Angeles where I escape to be closer to my grandchildren. In the past I worked at Helen Keller and set up a Deaf Medical Program at Bellevue Hospital in Manhattan, but I've been working with Usher since I started learning sign language in 1980.

So, it is really important for professionals and also for the rest of us if we are with Usher adults, it is important to know about their experiences as children and if we are working with children, it is important to know about the lives of adults with Usher. I stole that phrase from a psychiatrist Sarah Gorner in Sweden, who I have never met.

I kind of made this flowchart showing stages that people go through. It is sort of a compilation of all of those families that well over 100 that I have had contact with over the years. Again, because you can't see Usher, the first thing you see happen is the diagnosis of deafness and their concerns about hearing loss and concerns about cochlear implant and different communication and educational decisions to be made. There's a lot of stuff that is going on when the children are little. When that starts to settle down, they get hit with a vision loss. It is extremely disorienting. Parents don't know what to do and don't know who to talk to. I'm going to talk about some of the things that has said in the survey. Since school intervention may need to be made. That's the role that is so important in the deaf-blind children's programs that exist in every state.

I'm going to come back later to more of this, but life goes on. People get married and they have children, they have jobs, there are big concerns about what kind of a job should I have? If I learn how to be a photographer, I will have to change my job. A wise person said to me "who stays in the same job for their entire life anyways" if you need a new job you will learn to do something else. There's grief and the importance of meeting others and other families with Usher remember to decrease isolation.

At the last conference, there was some informal discussion about what to tell parents and it seemed to me that out of that informal discussion, it would be a good idea to ask parents what they thought. I don't know if Mark is here, he allowed me to send out a survey through the Coalition and sent out a bunch more surveys to people I knew. We asked parents of people with Usher and we asked people with Usher.

I really want to thank everybody who answered. For the parents I want to give you a message from the mother of a 21 year-old with Usher. I open you encourage parents to realize that a child with Usher Syndrome has a world of possibilities ahead of them as long as they keep the bar high, learn the necessary skills and believe in their children.

Her son is now, in college and also working. She had a difficult time because her gene had not been identified when he was found to have a vision problem on top of his hearing loss. They thought he had a different syndrome and they went round and round for many years. Now he's doing well.

Then I sent a survey anonymous. Some people identified themselves in their responses, but I did not ask for any identification. Whether they had positive or negative things to say about their providers, I have no idea who those providers are.

I asked them about themselves, the diagnosis, their current age, the age of diagnosis, who gave them the diagnose? Res -- diagnosis? And how empathic that person was. I asked them if they had seen a geneticist and if they had any messages for people now. Who responded?

39 surveys were returned. 36 from the United States, one from the UK, one from Canada and one from Denmark. Go figure. I thought that was great. The states, people lived from New York to Alaska. There were quite the mix, parents of young children are Usher. There were parents of adult children with Usher. There were some families with two children are Usher in them. Three of those. In two cases, the parent and adult child filled out the survey together. That was really nice that they took the time to do that. It was not so easy to break down the data of experiences because the age range were huge. Adults diagnosed 30 years and some parents whose children were recently diagnosed within the year.

There was a consistency in what they reported. The reactions of parents as you all know was shock, devastation, confusion, despair, guilt, they felt that getting this diagnosis was traumatic, they were left feeling hopeless and helpless. The future was unknown. They felt they could not cope. Some people felt that they got too much information. Some people said that they did not get enough information. This caused depression and anxiety.

I want to say also that in the years that I worked with adults, many of them remember when their parents were told that they had Usher not because they themselves were told, but they have a clear memory of being at the doctor's office and the parents becoming visibly upset and crying and crying and not knowing what was happening.

Years later they say that's the day my parents found out. Even though, they, themselves, may not have found out for years and years. I have met adults who found out only as adults. They found out from their friends who noticed their peripheral vision loss. I've met people who were married and had children before they were diagnosed. All of that is happening less, I hope, then it used to happen, but that was a fairly common story.

To summarize what the parents told me that they said. They got too much information, too quickly to process. That was on one hand, but too little practical information. Who should I talk to? Where should I go? How do I do this? Several were told to take their kids home and teach them Braille. That still apparently goes on. One mom reported that her ophthalmologist was most excited about finding his first case of Usher and not the response of the family to what happened. Some reported that they were given reading material and some reported that they were given a list of websites that they had no contact information for real people, it was too clinical, too technical and the message was that there was no hope and nothing to do.

I think every parent virtually said that the Coalition and Mark had been their life saver. That was their connection to finding parents going through the same thing.

That was interesting because not long ago in the last 3 months I connected someone from California to got my name. I live in California and they got my name and phone number and sent me a request for information and itches able to connect them.

In terms of empathy questions, some reported that providers were empathic patient and others said that it was very clinical and did not acknowledge the devastation. Some reported that their doctor thought that the most important thing was to get their kid into a research study. Of the 37 respondents,

26 answer the question about empathy and seven, one was the worst score and 10 the best. 7 of the 26 answers rated their providers 1. That's really low. 9 of them rated 1, 2 or 3. On the other side, 3 people rated their doctors as a 10 when it came to empathy and there were some 8s, 9s and 10s. I think we have a little work to do. In terms of seeing a geneticists. I thought everybody would see one. 39 total responses representing, I wrote 50 children but it is really 45. Of the total, only 15 families were referred to a geneticists for evaluation. 17 families said that they were not referred at all, which I find stunning. 7 people did not answer the question. I assume that those are no. And it was not completely a situation of older folks not being referred and younger folks being referred. They were all mixed. Some families with younger children and in one case they had more than one child they had never been referred for evaluation. I did find that stunning.

The suggestions from the parents, prepare -- this is for the providers, prepare for the meeting, give us written material, we should not have to search. Don't give us a list of website. Connect us with families with Usher including the Coalition. Realize that we ask the questions over and over again because we cannot absorb everything in one meeting. Call us in a week and see how we are and remember that you may have given this information a million times but it is the first and only time for us.

I went online and I looked at Med-line for articles on parental reactions, there were none related to Usher Syndrome, but plenty on irritable bowel, diabetes, intellectual disabilities. I did find two models that I liked. One from a hospital in London, they have a community linkage team. These are people who are non-physicians but who are highly trained and one person is assigned to a family on the day of diagnosis and remains their advocate through the next years. They are always present at medical meetings they work with the school, and I just thought it was a really wonderful model. In Denmark they have deaf-blind consultants for children. Those families have somebody, again who performs a lot of those services, but also does a lot of counseling. In both of these cases they do a lot of counseling with the families.

Grief, this relates both to people with Usher and to parents. Grief is not linear. It is really cyclical, it is not once, it is a number of times. As I said this applies to both, there is often a resurgence of grief when there's a new loss in terms of vision loss, but it could be a complete unrelated loss. I'll give you one example of a woman I worked with way back at Helen Keller, who had Usher 2 and she became a grandparent and before I became one. Imagining it I thought it was the most wonderful thing. She became significantly depressed. I was surprised I'm a clinician but I should have figured this out. What she said was that she could not be the grandmother that her grandmother was, she could not be the grandmother that her mother was to her children because now she could not see and hear. She had quite a crushing depression.

So I think that a loss can trigger another loss. Parents and teens with Usher might get depressed that the doing things the things that their friends do. Getting a driver's license is one thing that comes to mind and parents are also upset because they see their child in pain. Sometimes when there are new accommodations that have to be made. Getting a first cane and being reminded that the vision loss is right there, for example, or learning Braille.

This picture is an elephant in the living room and two people talking around it. It was drawn by a young woman with Usher 1. That's an old phrase, you don't talk about the elephant in the living room. That was the situation in her family. Never talking about Usher. She had some artistic skills and drew this. I thought it was great.

So, what did the parents worry about? The parents wonder what they should tell their child with Usher and how and I'm going to use Mark's line. I use it over and over again. Parents should tell their kids a little a lot. Children really only hear things at their developmental stage. Everybody knows the old joke about where did I come from? The parent goes in a long description and the child says "Johnny came from Peoria where did I come from." You might tell a younger child that they have an eye problem or they have a problem in the dark and make accommodation for that and normalize that in your family situation.

Nobody should be telling their children that they will be going blind because nobody knows what is going to happen. We have a man in New York who recently passed away. He had Usher 1. For his whole working life he was a librarian at the School for the Deaf. He retired and became an Episcopal priest. He was around New York City taking care of business until he was so sick and passed away.

Parents are concerned what is going to happen as their child gets older? How fast will they lose vision? Parents blame themselves because it is a genetic disease. Parents worry about whether or not their child will be independent, drive, go to college, work, marry, have children, how can they do that? They worry about what is going to happen when they, themselves, die. They are concerned both from parent and child about whether or not their career choices should have limited.

I'll tell you a brief story. Years ago I took a kid from Usher from Minnesota visiting New York to Connecticut to visit another kid who had Usher. They were pen pals it re-dates e-mail. We went to visit and there was a third teenager with Usher there. As I went into the house the one mother who I did not meet before said "we don't use the B word" and I said I'm coming from Helen Keller, national center for deaf-blind youth and adults. That's okay. The kids got together. They happened to all use sign language. I'm fluent in sign language. So I sat there, while they were all talking. And the parent was somewhere else in the kitchen making coffee. The first thing that they said when they all met was "so, when do you think you are going to go blind" I don't know I'm hoping to get through college before I go blind "what about you"? These kids knew exactly what was going on and they needed to talk about it, but in that situation they did not have parents to talk to about it because parents were not allowing it because of their own short comings not because of malicious intent. We all need help with this.

Parents reported depression and anxiety and Mark has written so eloquently about this on his blog. Dealing with these requires time, some help, some action and some contact with other families with Usher and people with Usher. One professional with Usher sent me a note and I know who she is. She identified herself. She said I had a psychologist who did not know about Usher but he knew about loss and he really helped me with that.

In terms of coping strategies, the literature talks about problem focus coping and emotion focus coping. I'm going to throw that away and say that it is a combination that gets us through the day. For folks

with Usher and kids with Usher gets information is number one. Having access to tools, meeting other people and learns skills that they might not need right now, but they can call upon later and get retrained in. It offers mastery and competence. If you are always at the mercy of a situation that you cannot master. It eats at people's self-esteem. I told the story of a woman who never wanted -- did not want to ever deal with cane training. Finally she got caught in a movie theater when the lights went out. She was terrified she came and asked me for training and to set her up. To bring it back she went to her retina specialist and asked to be referred to the New York state Commission for the Blind. Her doctor refused because he did not know what the Commission on the Blind did and he did not know any Usher adults that live outside in the world and he did not understand the benefit of having a cane and represents independence. She trusted this man and she worked with him for 15 years. They had a fight and he finally signed the paper. Advocacy. I encourage families to be the askable parent. Answer kids with what they need to understand. Do it as Mark says, discuss it often a little bit a lot. Build in context with slightly older Usher kids. The same for the parents. You may want to find a parent who is slightly ahead of you in the game so you can see the successes that that parent has.

I did work for a month helping to put together a mentor program in London way back in the 90s for that exact purpose. To help older and younger people connect with each other both the families and the kids. In some cases, services are available. In some cases, rural areas they may not be. I think that teens need to feel good about themselves and will if they get some of those skills.

When counseling is necessary, people should take advantage of it, you know, having Usher does not cause emotional illness and it does not prevent it. Some people could be depressed. At that point they certainly should seek help. Everybody deserves the right. People in my business know what to do with depression and people deserve the right to feel better. People talk about denial. I once heard a counselor screaming at a person with Usher. "You have to learn this cane and you are in denial and you cannot continue." Denial can be a wonderful thing. We have people with diseases and say we are going to beat this. That's denial, they may beat it or may not. Support it. Make it a valuable thing to do instead of a badge of failure. If somebody says "I don't need these skills I'm not going to lose my vision" well I'll learn it anyway even though I don't need it. That's fine you don't need to say more than that. Usher Syndrome does not cause mental illness. It does not prevent mental illness. Some teens adults and families can benefit. In general people with disabilities don't get great mental health care. Advocacy becomes really important. In summary, Usher Syndrome about loss, change, adaptation, communication, normalization and fighting against that isolation and my role is help mitigate the impact on those we teach and treat and friends that we love. It is a good thing for providers to call a week or so after diagnosis and see how everybody is doing and send them to the Coalition I think that's very important. Thank you very much.

( SWITCH OF CART PROVIDER )

# Session II: Psychological Aspects - Words from the Professionals Continued
# Presentation by Dr. Claes Moller – Physical and Psychological Aspects of Usher Syndrome

DR. CATHERINE BLANCHET: Now it is a great pleasure for me to introduce Dr. Claes Moller from Sweden. He is one of the few clinicians, and maybe the one who assists in a number of Usher patients and is particularly concerned about the impact in everyday life. He is chief physician at the otology clinic and the research center in Sweden. Thank you.

DR. CLAES MOLLER: Good morning. What a wonderful pronunciation. I like that. Wonderful pronunciation of Orebro.

Thank you. I appreciate that.

This is a great opportunity, and I thank the Usher Coalition for inviting me, and also having me stay here for the family conference which is the most important thing. We have, during these two days, discussed a lot of technical things and treatments, but I will tell you now it might seem a little bit depressing, but this is actually to tell you how people in Sweden with Usher type 1, 2, and 3, how they have it on a daily basis. And these are people who are in the 30, 40, 50s, and 60s. So they have been -- they have had their youth a little time ago. So for those of you who have children, see that as an opportunity to say "this is not going to happen. And this is not going to happen." Because as Ilene said, we are the ones that can make it a change. And the only thing that differs a person with Usher Syndrome from someone who is normal sighted and has normal hearing is just the eye and the ear. Otherwise we are all alike. But we are also all unique.

The picture behind me is Bill Kimberling and Charles Usher. And Bill Kimberling got me going on this in 1987 when we flew in families from all over United States, to boys town in Omaha, Nebraska. To start to find a gene. We thought it was one gene. We hoped it would, at the most, be two genes. Well, it has turned out to be at least ten genes. And anyway, that was my first encounter with people with Usher Syndrome. And I went to Louisiana, to the bayous, I went to Texas, I went to Arizona, and you can imagine a Swede coming to these places, having hot potluck dinners, a lot of beer, and making fantastic friends with people with Usher type 1. At least we thought they had Usher type 1.

So the research we have done in Sweden have been on genetics, but also in trying to find out how is the vision, the hearing, the balance in different Usher types. But on the late year, the years now, the five last years, we have moved in to looking at how people live on psychological and physical health in people with Usher Syndrome. And a group that I have here is really, and truly, an interdisciplinary group. And I'm just starting to look for a pointer.

MARK DUNNING: It looks like a pen.

DR. CLAES MOLLER: It looks like a pen? This was a pen.

( Laughter )

Well, Mark.

DR. CLAES MOLLER: We'll do it without it.

Now, the people you see on this represent different professions. And I have the luck of having a group where the PhD students are not just out of college because they have a job. They have a clinical job. And then they have turned into being PhD students parallel with the job. So in this group we have a professor in sociology, a professor in psychology, we have me, a professor in otolaryngology, we have an ophthalmologist connected to the group, but not here. And then we also have PhD students who are clinical psychologists from training, and social workers from training. And one of them is here, Mattias, he is sitting over there, and he has a poster that you recommend that you can look at and I will present some data from that poster.

So it is truly an interdisciplinary group. It looks like a pen but it is a laser pointer.

It is truly an interdisciplinary group -- thank you -- which makes it so fun to do research because we, at the beginning, talk different languages, but we melt together, and we can find so much more knowledge when we are working together than separately.

And we have based our research on the Swedish database. And at the moment we have 460 families, and I have had the fortune to meet all of them, which is tremendous luck for 26 years. And you can never learn from records. You have to meet people. You have to talk to them. That will be the essence when you gather knowledge about Usher Syndrome.

And then I have two other families with other deafblind syndromes. Many of them actually who had a diagnosis of Usher Syndrome, but it turned out to be wrong.

So on this picture, we have a child who is playing. "Do I have a patient with a problem?" Can you see anything unusual with this child? No. But the child has Usher Syndrome.

"Does this child have a syndrome?" No.

Now I will show a picture of a girl in two different situations. On the left side she looks a little bit stressed, a little bit worried. She has wrinkles in her forehead and she can't really see very well. If you look at the right side, she has eyeglasses, she has a cap, and she is quite happy. Could be a normal childhood just looking into the sun. But this girl, we have now found out at this age, that she really has Usher Syndrome. You can't see her hearing aids or cochlear implants.

If we have a teenager, we have a severe problem with diagnosis because many teenagers, at least in Sweden, say I would like to belong to a group, as many young people, and so late diagnosis sometimes, ah, creates denial. And a severe consequence, as I will show you when we look at physical health later in life. And the problem is also that no one knows how other people see. That is so difficult for me to

answer "how do you see this color? Why don't I see in darkness?" Because I think I see in darkness. So the diagnosis of Usher Syndrome, up to now when we can do genetic testing quite accurately, have always been by parents, by teachers, and by relatives. Not by eye doctors. Eye doctors can't confirm, if they have knowledge to confirm, and not to deny it. But it is always parents this need to be aware that a child with a deafness or a hearing loss needs his vision. We hear with the eyes. And we listen with the ears -- we hear with the eyes. And we see with the ears. We use eyes and ears together without really knowing it. And if I have a deafness, or a hard of hearing, I need to see people's faces, which means that even a small vision loss can be very, very severe.

50% of children with hard of hearing or deafness have a vision problem. It might be minor. 50%. If you take the same age group, 7-year-old kids, who are normal hearing, it is 20%. So just the case that you have a child with a hearing loss, or profound deafness, means that there is a 50/50% chance that they also have a vision loss.

"Why is my child deaf?"

"Why is my child deaf?"

"Why is my child clumsy?"

"Why has my child problems at night?"

"Why don't I like gymnastics and sports?"

"Why can't I have a driver's license?"

"Why can't I hear? I think I have good hearing."

"Why can't I go on working this job I have?"

"What is deaf blindness?"

"I'm neither deaf nor blind."

We have a Nordic definition of deafblindness, sometimes people who don't want to say deafblindness because they would like to say dual sensory loss. And if you say that to a person outside of our world, they wouldn't know anything what that is.

Deafblindness is not a static diagnosis. It is a situational based diagnosis. I have so many patients, and many of you will recognize this, who will use a white cane, who has big problems going up on a train, or a bus, needs support. And then when they go up on the bus they pick out their book and start to read. And people get so angry. So it is a situational based condition. And we say that the individual needs of each person with deafblindness are immense. In some cases deafblindness is developed or acquired before language. In other cases it has emerged later in life. And specific skills, and experience, are required from healthcare services and governing bodies to meet the diverse needs of people with deafblindness and their families.

So how do I diagnose possible deafblindness and Usher? And this will be a quick thing to go through, not to stay on this. I use a pedigree. I need a family history. And as we heard before, it is usually negative. And that is also something that tells me that, hmm, this might be Usher Syndrome. I look for what we call dismorphology, which means that if I can see an extra finger, if the ear is malformed, or whatever it is, and usually it shouldn't be in Usher Syndrome. I look for neurology and ear, nose, and throat. I look for hearing. Vision. I do exams of balance function. I also do radiology, which means that I do a cat scan on the inner ears to see that they are normal and that the brain is normal, which it should be. We also test for the kidneys because there are some -- there are some other syndromes that might mimic Usher Syndrome, but could have other organs that doesn't work very well. And as we heard, the heart. And we also would like to test for some viral infections. And of course, today, the crucial diagnostic point is genetics.

But the medical diagnosis that we have now made is only the foundation, the basic, for the most important thing, the function of diagnosis. How does the hearing work? How does the vision work? The balance work? In what situations? What are the strengths in the person? The weaknesses in the person? How can we make a picture of that in order to make the best rehabilitation?

This slide shows the database I have for different types of Usher. The black is Usher type one. The red is Usher type two. And the yellow is Usher type three. And these are how many people in each decade are in the database. Most are between 30 and 60. And since this is a genetic disorder from birth, in the best of the worlds we would know as many who are younger as we have between 30 and 60. And then, of course, at age -- when age, you get older, people start to pass away. So this means that every person with Usher Syndrome has a wrong diagnosis until you find the vision problem. So many have had a wrong diagnosis for years. And many parents have strived, and strived, and tried to get ignorant physicians to find out that "yes, I am right, there is something else with the hearing loss with my child." And you have to realize Sweden is a small country. We are 10 million and the fifth largest country in Europe. And so it is vastly populated. But so is United States, actually. And you are spread out. So the likelihood of a small town eye doctor, or ear, nose, and throat doctor, the likelihood that this person will see a person with Usher Syndrome is 1:2 in a lifetime. This means that we need more specialized care for Usher Syndrome. We need, and you need, to see people who have seen more than one or two. And you -- and I bet that you all have different life stories of the time it took to get to a conclusive diagnosis.

Ilene talked about shock, denial, confusion, crisis intervention. And I would like to stress what Ilene said. Don't forget the child and relatives. I have so many of my patients who have come to me as adults and said "why didn't anyone tell me? Why was I left out? Why was I at the eye doctor as nine years of age, and afterwards my mom came out and cried and we went home and I didn't know anything? What a lot of misunderstandings I have had through my life because I didn't know."

So it is extremely important, and in Sweden, and especially Norway where I work, we had children groups where we gathered children from the age of 8, to 9 years of age, up to 20, and they are on the weekend, the parents are there also, but it is the children that sit in the front. The parents have to sit in the back and be quiet. And then we talk with the children. And as Ilene said, they know it all. They

know it much better. And in the schools for the deaf in Sweden, in the former times, the children knew who had Usher long before the teachers and the doctors knew. They had different signs. "Oh, he has Usher's." So don't underestimate your children. They are much more clever than you are.

( Laughter )

Than I am.

( Laughter )

And late diagnosis might cause some mistakes in career planning. And they can be devastating, or as Ilene said, also, why should you have one job during the lifetime. But it is the more you know, the earlier you know, the better you can plan. And for some people with Usher Syndrome, there is also a change of communication modes, which is very important to early on discuss. And I will come back to that.

I'll skip this.

And I'll skip this because I want to go into the studies.

Now, we have done studies on physical and psychological health among persons with deafblindness due to Usher Syndrome type 2. And this is one of my doctoral students, Wahlqvist who did an article on that, you can find it in Google. We have used an inquiry, a questionnaire, this is sent out to 5,000 Swedes every second year to find out about physical and psychological health. And we have also used what we call a hospital anxiety and depression scale, which assesses the likelihood of having anxiety and depression. And we wanted to send out this to people with Usher Syndrome type 2 to see how is their physical and psychological health compared to a large group of Swedes. So we sent out 110 questionnaires to people with Usher type 2 in the right age, between 18 and 84. And we got back 96. That's a really high number. Usually when you send out questionnaires, and you can remember yourself when you get a questionnaire, "hmm, yes, I'm going to answer it," and then you forget. So that was really good. And the mean age was 55. And the reference group you can see on your right side, ah, at that time it was 5,000 people. And a little bit more females who answered. There is always more females who answer.

At that time the genetic diagnosis of Usher type 2A was found in 60%. This has increased now since this was a few years ago. And the pure tone average, how bad they heard was 73 decibel. And their visual field was, in general, different of course, but most of them had a visual field around 10 degrees or less. So they had a severe visual field loss. But their visual acuity, and I know that this is not American figures, but that means that you are, from a visual acuity, 0.4, you are on the edge of being legally blind, but not really. So the visual acuity was quite good, actually. Now, this is very difficult for you to see, and I wonder if it is possible for me to have a hand microphone? Could someone lend me that? I need to stand a little bit closer so I can point.

Now, the Usher type 1 -- type 2, is blue.

Thank you.

The Usher type 2 is blue and have you to correct me if I'm standing in front of you. I think I'll stand here. Can I do that? Is it okay?

INTERPRETER: It is fine. Yes.

DR. CLAES MOLLER: The blue one is Usher type 2. And the red one is reference. And here we have some physical and psychological indicators of bad health. And the higher this is, the more bad health you have. And we just noted those that had, what we call, statistically significant difference between the reference group and the Usher group.

Headache. Nearly 50% of people with Usher Syndrome suffer from headache more than once-a-week.

Tinnitus, not so surprising.

Pain in shoulders and neck. Significantly higher. What surprised us was that eczema, skin rashes also is higher in the Usher group. Really don't know why.

Anxiety/worry.

Fatigue. It really caused a lot of cognitive effort when you are always having to think what you see and what you hear. And when you live in a world that is rapid, and you have to be online all the time, it takes so much drain from a person with a combined vision and hearing loss.

Sleeping problems.

Concentration.

How well can you accomplish things?

Unhappy and depressed.

Constantly under strain.

Feeling worthless.

But the most stressing thing we found was that in this group, over 20% have had suicidal thoughts more than once.

And suicidal attempts was also significantly higher. And especially we found this in men with Usher type 2.

Uhm, this sounds very depressing, and it is depressing when you look at the group base. On the other hand, of course there are big differences, and I will come back to what differences that was.

The study 2 on Usher type 3. The aim was to describe and analyze data on vision and hearing impairment among persons with Usher type 3. And for those of you who doesn't really know, Usher type 3 has a progressive hearing loss. And when you are over 30, at least in the Swedish material of 27 persons, the vast majority has a profound deafness that makes the hearing communication extremely difficult. And the other group -- and the other thing is that they also have a vision loss that progresses.

Now, what we could see when we took a material of 50 persons, they formed two groups. We didn't know that. But one group had quite good health. And one group had poor health. And when we did all of these statistical things to find out what could cause that group with good health, what were the factors, we found two important factors, and they are listed on this slide.

The group with good health had cochlear implants so they could hear better. But they also signed. So they had double communication. They signed, they knew visual signing from childhood, so in those cases where they couldn't see and they had bad vision, many of them were nearly totally blind, they could communicate by tactile signing. As a complement. So it is neither -- it is never neither/or. In my lifetime, cochlear implants are the biggest invention for some groups. But if you can have other communication modes when you have Usher Syndrome, like signing, could be supported signs, could be American Sign Language, Swedish sign language, it doesn't really matter as long as you use all the things to get into the brain, and that will add synergistically, one plus one is three.

I know that you are standing here, Mark. And I will only take two more minutes if I can do that.

( Laughter )

This slide is just a teaser, and I urge you to go up and look at Mattias' poster because what we have done is we have looked at this Usher group type 2, and we have looked how important is it to have a job. So we have two groups. They see the same. They hear the same. And one group has a job and the other has a disability pension. And in Sweden it is quite good Social Security system. You get a disability pension, not a good salary, but you get enough. And what Mattias and we have found is that a big difference in psychological and physical health is related to if you have a job or not. That is so important in this study. And I urge you to go up and look at this poster and discuss with Mattias because if you have children with Usher type 1, 2, or 3, please look into that they will know as much as possible, be independent, and get a job. Or two jobs. Or three. Or four jobs.

( Laughter )

But not be dependent and passive and with victim.

And the final thing. We have also looked, and I'm not going into detail with this, I can discuss this, we have compared Usher type 1, 2, and 3. We sent out a questionnaire to Usher type 1, as well. But these are difficult Swedish questions. So I made a DVD where we had interpreted all of the questions. So you could either look at the DVD and see an interpreter, and then you can stop, and then you can read the question, and then you can answer. So we got as many answers, 80% answers from Usher type 1 as we got from Usher type 2, and 3. And what we found is that there is no big difference between the physical

and psychological health between Usher type 1 or 2. And actually, some of these things people with Usher type 1 seems to have a better life than Usher type 2. But upper type 3 sticks out.

The problem of having to change communication mode when you are not prepared to, when both vision and hearing goes down.

So why is it important to know the cause early? Well, to get the correct diagnosis. And I mean medical and functional. To learn from other experiences in other countries. To determine the prognosis of the disorder. To get the best use of technical equipment. To get the best possible career planning for your life. To get the correct and continuous rehabilitation. And what we have talked to you in the last two days, that treatments are actually around the corner. I have said that for ten years now, and every time I meet one of my patients back they say "well, you said this ten years ago. Why is it going to happen?"

( Laughter )

"I don't want to wait another day."

Actually, these two days have lifted up, have given me so much hope, and you will probably hear more about it later today. That actually, as we heard, in our lifetime, and I want to be around at least 20 more years --

( Laughter )

-- so --

( APPLAUSE )

So patients and family often want and need a reason for the problem. And that might also be one of the more important things that we should all get to know as much as possible. And I urge you to go out and Google and look at other home pages that are American home pages. There are many of us who write in English.

( Laughter )

And French. And German. Spanish. But English. And there are a lot out there on the Internet now which can give you and your children hope.

So I'm more than glad to discuss this later during the day and coffee breaks. Thank you.

( APPLAUSE )

MARK DUNNING: Okay. We are going to take a break in just a second. But I want to make sure that I say two words about the presenters from the morning. Uhm, the most important takeaways that I can tell you guys is that, uhm, they, ah, the history of people with Usher Syndrome who do not get support, do not communicate, do not have community are not happy. People who get support, who have jobs, who communicate, and who have families that are supportive of them are happy. So Usher Syndrome

does not make you unhappy. It is the way that you live your life with Usher Syndrome that will make you happy or unhappy. So keep that in mind as you go out and you get some coffee and make yourself happy. We are going to start up again at -- I have no idea how long Claes ran.

( Laughter )

So we are going to start at 10:30, which means that we are going to start at quarter of. Which really means we are going to start at quarter of. So be here at 10:30.

( BREAK TAKEN )

(SWITCH CART PROVIDER)

## Session III: Gene Therapy 101
## Presentation by Dr. Luk Vandenberghe – Gene Therapy 101

MARK DUNNING: Hello everyone, we are going to try to start on time. If everybody could come back in and grab their seats, we are going to get started. Hi, everyone, if I can ask everyone to take their seats we are going to get started. One of the people who is late is the moderator for the next section. There she is. Okay so we are going to get started to try and stay on time. So, I know everyone is getting settled back in. I want to check with the interpreters to make sure we are good to go. And the interpreters look like they are good to go. I want to actually start with something that I forgot to mention yesterday to all of the researchers. I want you to hear this because I thought it was one of the best things that I've heard in quite a while.

My friend Monnie Ire who wrote the Usher Syndrome Registry. Monnie has very little vision at this point. He told me that he has bought a Lamborghini and he's going to drive it in 2020 whether or not you guys have found a cure. You have to get to work. I'm going to introduce Dr. Jennifer Phillips, it is all yours.

>>: Thanks, I'm sorry for holding up the show. I'm Jen Phillips and I contribute to the Usher blog and I do research at the University of Oregon. I'm happy to be part of these proceedings and I'm pleased to be able to moderate this session in which after hearing from experts around the world, we are going to hear from a number of our local experts on Usher Syndrome, who are researchers and clinicians who have done a great deal to change the landscape. The first presenter here today is Luk Vandenberghe.

DR. LUK VANDENBERGHE: Good morning everybody, my name is Luk Vandenberghe, I'm a scientists at the Mass Eye and Ear at Harvard. My laboratory focuses on developing gene therapies broadly, but specifically in the field of ophthalmology. We work on a variety of blindness disorders. Particularly retinal degeneration. Particularly of which you know the Usher disease is part of that. This particular session is an unusual one for me to present. Most of the time I talk to scientists and I have done this a few times where as this is challenging, it is extremely, like I said, yesterday, humbling and motivating and the reason why it is challenging is not only because I to some extent have to change my vocabulary to make this understandable to all of you, I think it is more challenging because particularly in the field of gene therapy there's a lot of hope, excitement and patients and as scientists we know the limitations of our technology as well as the prospects of that technology.

It is sometimes difficult to convey exactly that nuance balance between the two. I'm going to try and do that. I think most of the value for you will come out in the questions that you have for me and the many experts here in the audience. I think there's going to be a panel around noon and I'll be on there as well. For this session I want to keep it informal. Please raise your hands and go -- go to the microphone and ask questions. We'll try and get through the different segments that I have prepared for you, but please do not hesitate to interrupt me. I'm going to answer four questions for you. If I were in your shoes I would want to know and I would want to ask. Briefly without going into the specifics, I'll illustrate those four questions.

Even though I know you are a very informed audience I want everybody on the same page. The first question is a simple one to phrase but a difficult one to answer: What is gene therapies? How is this different than some of the other things that have been discussed over the past two days? What are the challenges in gene therapies? What is now creating this excitement in gene therapy? All of that is under what is gene therapy? The second one is the most pressing one is: What is gene therapies. I want to provide a nuanced response to that. The third one is a fairly practical one but relevant to start thinking of now, given the incredible activity in this field. How do I prepare for myself or how can I possibly participate in a future gene therapy trial? Some of the things that I think is wise to think about now and preparing yourself for.

The final question is once a gene therapy comes onboard and the other disease foundations, what do I consider on a personal level. It will be a personal choice to participate in these clinical trials for gene therapy.

Let's get started. I'll try to respect time here as much as possible. I'll put on a timer here. What is gene therapy? It is different from many of the ways we have done medicine over the past centuries. It really can be summarized in the concept of using the gene as a drug.

That has not been done before until very recently when we started doing this. Classically, one goes to a hospital and receives surgery, you can get a vaccine, most medicines that you are familiar with are small molecule drugs like aspirin and Tylenol. But the use of a gene for a drug is novel. It means that we have low experience with it and we need to invent the wheel. There's intrinsic differences using a gene rather than any of these other modalities.

I think the slide to build any kind of therapy but particularly for gene therapy you have different steps and you need different ingredients to make that drug. Ultimately we are making drugs. It requires that we have an understanding of the target that one needs to tackle. They can be seen as one is we need to know which tissue is diseased? What cell type is diseased? In terms of Usher which mean is involved in particular for that disease? The good news is that through the work of the people that have presented in the past two days, we know an incredible amount. I'm going to come back in one of the follow-up questions. You personally need to know through diagnosis where you fall and which targets is relevant to you? There's good news and hope. In terms of the target definition, we have it somewhat covered in Usher. That's not the case in many other diseases.

The second step is the molecular intervention. What do we do to change that target and work around the disease process and to bring therapy, to bring treatment? There's a lot of hope because to some extent Usher Syndrome diseases is simple. There's a single gene defect we need to either fix it or replace it or patch it or do something.

Again the simpler the problem, if you follow me, to some extent the simpler intervention is needed. One that makes the most progress is by taking the dysfunctional gene and putting a copy of that gene where it is needed. That's a simple concept. That's what many people in the field of gene therapy started rally around.

I think we are pretty good on that as well. Then the last aspect, again there's reason for hope. We have to find ways to deliver that gene. Genes are big. Genes are different than aspirin. So the challenges of delivering that to the right place are fairly large, people have worked for three and four decades to optimize the ways how we can develop genes. We've built a set of technologies that can now do this with relatively great efficiency and the great news those three aspects combined we've done before. Just in the past five years. People have packaged a molecular intervention a delivery mechanism and have brought it to the right targets. It has been validated by scientist colleagues it has been published in articles and people generally acknowledge that this is true.

This is very important when you consider moving forward and enrolling in therapies you want to have that backing of the scientific communities. You want to make sure that you are involved in something that is real. There are inherent risks and challenges. This is my answer to what is gene therapy? I hope this helped you out. In terms of molecular intervention you have heard through the foundation and the news, there are many different ways to intervene. I presented the most simple way of intervening. That's incorrect gene and you bring back the correct version of that gene. Sometimes that's actually not possible. That can be for a whole host of reasons. There's other mechanisms that people have uncovered where we can restore back some function through other methods of molecular intervening. One of those methods, for example, is to build a molecular prosthesis to bring back vision to adding a gene through a different way. This is the field of optogenetics. There's a third strategy. We have gene replacement or gene addition to work specifically on the broken gene, the second one is to build a patch, which is that field of optogenetics. And the third one is slow down the operate of degeneration. By delivering the drug to the retina through a gene that can slow down this. This is called neuro-protective strategies. Some of the challenges that there still are in this field of gene therapy, why we cannot do everything we want to do. It is particular relevant to Usher is that in all of these three targets, there are still hurdles. We have not defined all targets. In Usher Syndrome we done an incredible amount of work. There are certain aspects that we are at the early stages. The field of optogenetics. It is more in the stage of science fiction, before it really -- we can believe that this can bring therapies to patients. In terms of the delivery there are many challenges. We have a great set of tools but they cannot do everything we want them to. This is true for large genes. Many of the Usher genes fall into that category. The clinical trial that I mentioned before, one of the main reasons why there's so much

excitement and hope in this field is -- it cannot be directly used for large genes because the technology we have and some people call it a taxi cab. It is too small to bring some of these large Usher Syndrome genes into cells. Because if the cab would be big enough we could move faster. This is one of the reasons for Usher it is going at a slower pace than we all would want. The second question is: Where is my gene therapies? This goes back to the specific targets that I had mentioned. In general how to process word to build a therapy. Where we don't have decades of experience to build a gene therapy, not unlike many other drugs one has to go through four phases. The first phase we've heard most about in the last couple of days is the preclinical phase or the laboratory phase. That phase really tries to go towards one thing. That's what we call "a proof of concepts" something that can convince the scientific community and the patients that the combination of target, marker intervention and delivery, that they can come together in the right way and show that they can actually have a treatment effect. And have a treatment effect in a safe environment, in a safe setting.

That is a great challenge. Many of us are working on that. Many of the approaches that have been discussed. That on its own is a great challenge. In certain cases where all of the tools on the table this can go pretty quick. In a ballpark this would take in the range of two years if everything, all of the funding is in place and if everything goes as planned. For some of the other more challenging targets, it is unknown. The two years could be five years, ten years or with what we have right now, an undefined period of time. That's that first phase, the preclinical phase the lab phase, that's the phase where we use animals. The second phase is called the translational phase. This is where we have to do generic stage. We have to produce things up to pharmaceutical grade qualities. This is extremely expensive research. Not the most exciting research, but it is something that regulatory agencies here in the United States, FDA and Europe EMA, require us to do it before we even touch the patients. This is done for the right reasons, but it is a major hurdle in terms of slowing down that path that we are all waiting for.

This is a hurdle because it is expensive and when I say expensive, it is often millions of dollars. It is more expensive than the exciting research phase. Since this is a novel field, we can't just walk up to an existing organization that knows how to do all aspects of that. Most of the time we have to reinvent the wheel for this particular approach. This is a challenging phase for those reasons. Sometimes it does not work out. We prove that something is not as safe as it should be. Some things may drop off at that stage. Most of the time we've done our work in the lab well, they can make that stage.

The third phase is the clinical trial phase. This is the set of regulated stages where we test things in humans. It is very important to realize that this is still an experiment and it sounds harsh because for us to test in humans where it really matters, if these drugs that we developed are safe and efficacious. They are looking at safety. We want to provide this drug to the patient and see that it can be safe. And we look at: How much do we need to give to show treatment effect? And so forth. The second phase is looking at that. The third phase is often the largest phase with as many patients that we can find where we have -- where we basically define the parameters of how to have this drug on the market where you have the leaflet that you get with your drugs from the pharmacists that stipulates the side effects and dosages and so forth. This is the process for drug development. If one is successful of reaching phase III and show it is safe and efficacious. Then the drug is on the market and that's the final phase. Once it is on the market individual physicians can deliver it either according to the set parameters and they can use it sometimes off label.

Sometimes things that are involved in the retina which may at some point be tested out in that final stage. Let's see how I'm doing on time here.

I'll wrap up with two final questions: How do I participate in future clinical trials? One step back: Where are we in terms of development? Many of the Usher genes that are in the preclinical phase. Some of them are entering the translation phase. One in clinical trials the Oxford Biomedica studies and in terms of giving you perspective of a similar disease called LCA which is early onset blindness which does not have a cochlear phenotype or cochlear disease. We have a phase III clinical trial now. That will help us chart that roadmap that is useful in moving things quickly. If is one that is charted, we can move forward with the subsequent ones.

That's the state where we are at in terms of usher gene therapies. Two final questions: How do I participate in future clinical trials? There's pretty easy things that one can do now. I think that's diagnose, diagnose, and diagnose. We need to define for you what that target is. That's essential to consider any of these trials. Sometimes alongside that is natural history studies. They are not clinical trials they are not treatment clinical trials but they are helpful for us to later on develop. It is a benchmark, we first want to see how the disease developed without being treated to later treat it to see if there's a difference. Especially with smaller diseases like the individual Usher types, this is very relevant we notice specifically for USH2A this is something that you could participate in.

The third one is information. Try to gather as much information as possible. Disease foundations come in, physicians come in. Things you have heard picked up from the Internet or two phase whatnot. You just want to be informed. And you could put yourself as well in registry, the Foundation Fighting Blindness is starting a registry where people can individually put their medical files in. You still need to be found for these clinical trials. It is not like you will receive an e-mail unless you are somehow on a registry. Those are the things that I think will make you more attractive for a clinical trial so that they can actually find you. Last point but an important one is: What to consider? This will come down to you personally. What to consider when you want to embark on possibly enrolling in a clinical trial? The aspects there that you have to look at is like I said, this clinical trial stage which is hopefully going to be the next stage for many of these Usher genes is there's still an inherent risk. There's a risk because it is a new therapy the chart for the path is not fully charted. It is going to consider. Gene therapy is still something that we are learning our way. That's ultimately that there's many hurdles for researchers and physicians to move towards a clinical trial. People take risk into account. Ultimately it is a personal decision.

The second aspect of risk is that enrolling in a clinical trial may make you ineligible for a subsequent trial. Sometimes having participated in previous clinical trials not always but sometimes, yes. It can make that interpretation of what really happens with this particular drug, difficult.

What to consider as well from our perspective the people that do participate in the clinical trials. Obviously there's something that you are looking. It is an extremely courageous and noble endeavor. The goal is helping more future generations than necessarily yourself. There's always a chance that it can work. It is an experiment and things may not work out the way we were hoping for. In that sense this is an extremely courageous endeavor to participate in these trials. One also wants to inform yourself as much as possible about the technology, about what is really being done. Not everything that gets to that clinical trial stage has the same validity or chances of success and often people in touch with through the foundations and physicians may give you a bit of a balance. If there's two clinical trials, hopefully we get to a stage where we have a choice. One may be desired over another. That's again something that you have to inform yourself personally about.

The last aspect and you cannot stress this hard enough. There are thoughts out there not so much in gene therapy but stem cell. We've heard the incredible potential of stem cells worldwide and including the United States including Europe, there are people selling stem cell therapies that have not been vetted. You have to make sure that whatever you are participating in. I know we are looking for treatments and cures but it is important to stay on the safe side. There are real risks. You don't want to enroll in a trial that really is just not rigorous and may expose you. I want to end on a bright note. I think there's an incredible excitement. We cannot do everything we want to do. There's an impatience on your side as well as the researchers. There's a frustration when things don't work or the tools are not ready. Five years ago I would not be standing here and smiling to you. There's something happening in this field that will make this work. It could take time but overall it is a very good position to be in. A lot has happened in a short amount of time. Maybe because of the work of basically the scientists that are sitting next to you.

I'm not sure if there's still time for questions, otherwise I'll be happy to take them. Thank you.

>>: I would like invite everybody at the upcoming panel. We are doing fabulously on speaker time here. Without further ado I want to introduce another local researcher who will give us an update on the Usher research here that's Gwenaelle Geleoc.

## Session IV – Update to Families
## Presenters: Dr. Gwenaelle Geleoc – Usher Syndrome Research
## Dr. Margaret Kenna – Translational Research and the Usher Syndrome Registry

DR. GWENAELLE GELEOC: So I would like to first thank you all for being here. The families, patients, clinicians, scientists and geneticists. Your participation and contribution to this meeting have been essential and I feel very humbled being here today. During the past two days we have all been learning a lot. And for me, being a researcher, being in a lab, to see all of you is really an inspiration. And all the people from my lab have been saying over and over how it has been really important for them to be here, and now they just want to go back to the lab and do the work that they are here to do.

So indeed I work next door. I have a research lab where I work with Jeff Holt who gave a talk yesterday. We do research on hearing and deafness. And we have studied the development of the

sensory system in the inner ear and what we have learned has allowed us to understand better how the auditory system functions as well as the balance system. And we are slowly moving on towards looking at why mutations in certain genes cause deafness and balance disorders including the genes involved in Usher Syndrome. We are looking at those now and going towards gene therapy approaches.

So I have a difficult task to summarize two days of research presentation in 20-25 minutes. So obviously I won't be able to talk to you about all that was said, but I just hope to present some of the highlights.

I will introduce briefly, I know there are some families who are fairly new to Usher Syndrome, so I want to give you a brief introduction on that. I want to talk about the advances in understanding the patho-physiology of Usher Syndrome, which is what we are doing in the labs. And also advances in terms of the treatment some of it which was covered this morning by Luk.

So Usher Syndrome was actually described by Charles Howard Usher in a publication that came out in 1914 where he was looking at a group of patients who demonstrated inheritance of retinitis pigmentosa, RP.

Usher Syndrome, as you know, causes hearing loss, RP: retinitis pigmentosa, which is responsible for night-blindness and progressive loss of peripheral vision.

Many people with Usher also suffer from balance deficits.

Usher Syndrome is actually the most common condition that affects hearing and vision.

And there is a large number of, ah, patients who suffer from Usher Syndrome in the U.S., estimated between 16 and 40,000 patients. A lot of them probably haven't been diagnosed yet.

It is clinically and -- and genetically heterogeneous disease and those who have been here for the past two days, you have heard that even with similar mutations the rendition of the diseases can really vary from one patient to another.

There are three clinical sub-types. Type one, two, and three. Which are distinguished by the severity and age when the signs and symptoms appear.

So there are many genes that have been linked to Usher Syndrome. Fifteen genetic loci and eleven genes so far that have been linked to Usher Syndrome. And Usher Syndrome is typically looked at as an inherited disease. However, uhm, we have seen, ah, different mutations in, ah, in Usher Syndrome, that causes Usher Syndrome.

The Usher protein function, ah, of mutant functions, they work as transmembrane adhesion molecules. They are important for signaling. Scaffolding, which is sort of, like, building up a network together, Transport. And also they have been shown to be important for the development of the sensory cells of the ear and the eye.

So indeed, these Usher proteins are expressed in the two sensory systems; the eye and the ear. And, uhm, and deficiencies in the proteins or misfunction leads to the degeneration of the sensory cells of the ear, as well as, photoreceptor cells in the eye. In my lab we study the auditory system, so I can focus on that a little bit more. Uhm, this is the inner ear organ. And it contains different sensory organs; the cochlea, which is here, which is responsible for the sense of hearing. Also there are five vestibular organs that are responsible for the sense of balance. And they all contain the hair cells, you remember that term from before. These cells are really the receptor of your inner ear. And they contain little villi on the top, on the apical surface, they look like hair, but it is really not hair, they are really micro villi, and these are interconnected by links here. And what happens is when the sound propagates through the organ of corti, I'm sorry, through the cochlea, uhm, these stereocilia bundle are displaced in this direction towards, uhm, my side, this side of the room. And this stretches the links that we call the tip links, and it basically opens a gate and it lets ions come through. This is going to be the beginning of the electric signal that will allow the sense of hearing and also the sense of balance. So when you move your head, "yes" or "no" similar receptors are present in the balance organs here, and sense these movements.

I don't know if this will work. Yeah. In the lab we were able to displace these bundles and look at, ah, the functional apparatus there in the apex of the sensory cells. So Usher proteins play structural and developmental roles in stereocilia, and also in the synapse, at the base of the cell. Once that signal is, uhm, that electric signal is activating your hair cells, there is a neurotransmitter, a chemical system that is, uhm, secreted at the base of the cell and this will induce the creation of action potential and the information will be sent to the central nervous system.

So interestingly, a lot and most of Usher proteins are present in this structure here. So we have the tip link, which is highlighted in pink here, that contains protocadherin 15 and cadherin 23 Usher proteins. So there is a complex firing of molecules here, that are a lot of them are Usher proteins. So when those Usher proteins are malfunctioning, this system falls apart, the cell cannot really receive the signal, and eventually the cell will die.

In the retina, the Usher proteins are associated with the connecting cilium. And outer limiting membrane, as well as ribbon synapse. So they are also very important. And they are important for the development, and, uhm, and the transmission of the signal from the photoreceptor cell to the, ah, sensory, uhm, to the neural network.

So, uhm, so you may have heard the word interactome. The Usher proteins are all interacting, and we have heard a lot about that over the past two days. You can look at it as a mesh, you know, a network of elements that are interconnected, and if one falls apart the others eventually fall apart. That is pretty much what is happening. And this diagram here shows you some of the interconnection between the Usher one proteins and the Usher two. And there is a connection between Usher one and Usher two and Usher three.

What do we do in a lab? We take things part. That is pretty much it. We really take things apart. We look how the different proteins interact, how, you know, proteins fall apart, if you take one out, or if you

mutate, ah, a part of the gene that encodes for that protein. Similarly to what some of, uhm, the patients have.

And we have had a lot of talks over the past two days, and I'll highlight a little bit of work from Christine Petit and from Uwe Wolfrum on the next slides.

So in the lab, we often use mouse models. Some of them are mice that are naturally deaf that we looked at. And others we added Usher mutations present in Usher patients. One of the good examples is the work from Jennifer Lentz where they reproduce a Ush1c mutation found in Acadian populations. They use this mouse now to look at potential therapies including ASO for the treatment of Usher 1C.

In the lab we do auditory and balance test in those mice. Uhm, we use imaging and we look at the stereocilia bundles. We use physiology. We take the tissue, bring it to the microscope and we record currents. And we also use cellular and molecular work to look at interaction and expression of the different molecules.

So Christine Petit has been, a big part of, uhm, of -- has been very involved and has told us a lot about the different Usher proteins, what they do, where they are, and how they interact. And I just will highlight some of the work here. This is here looking at the Organ of Corti of a wild type mouse, it is not a mutant mouse, it is just a wild type mouse. And here we are looking at the cochlea. The cochlea contains three rows of outer hair cells. So if you look here, it is sort of like looking at -- looking down, sorry, at the sensory epithelium. So each of these are individual sensory cells, okay, and we can sort of see, uhm, at the inner cell, you can see those microvilli here. And this is here, uhm, the blown up picture here of the outer cell, and now you can see pretty clearly the stereocilia, and see in some cases links between those which are the tip-links that I was mentioning about.

And so, when we look at hair cells of mutant mice, and here are some examples: Sans, MYO7A, which are all Usher syndrome proteins we can see that the bundles are abnormal. Either the bundles are splayed, or they are shorter, or the tip links are absent. And so this is already, you know, very informative for us. And as I said, because a lot of these molecules are expressed in the stereocilia, uhm, often we do see stereocilia defects.

Uhm, and interestingly, uhm, there is work from Guy Richardson and others that have shown that during development the cells undergo a lot of changes in terms of the interconnecting links between each stereocilia. And what you will see in this table down below is that underlined in red are all the molecules that are Usher proteins. So it is really amazing to see how much of the Usher proteins are there, essential for the development of the sensory cell and its function. And now you understand why the cell falls apart and eventually you lose your hearing. And in some cases your balance. A lot of those molecules are also expressed in the sensory cells of the vestibular system. There are some differences, which is why, uhm, in some cases for Usher two, Usher three, there are no vestibular deficits. Uhm, but in a case of Usher one they are also present.

Okay. So basically what we do is we take things apart and we look at what happened when we take the wheel out: you know, is the bicycle still running? And then we can learn about the role played by

these different molecules. And Christine is really a good example of what has been done in the labs all around the world to understand what is really going on.

I will just highlight briefly some work from Uwe. Uhm, his talk was on the decoding of Usher Syndrome protein networks reveals insights in the molecular basis of the disease. Large contributions to our understanding of Usher one and Usher two interactome in the eye and in the ear. For example, a couple of years ago he demonstrated the role of, ah, interaction between Sans and Usher 2A, and I think there is a poster on that topic in the upstairs mezzanine.

And he also recently demonstrated that Usher 1G, which is encoded Sans, contributes to the periciliary protein network in the retina.

And now recently part of the work that he showed us, uhm, during these past two days; They have identified new binding partners for the Sans molecule. And this is really important because as we understand more and more what is going on and what are the other partners that bind to those Usher proteins, we can better understand their role and also, as we don't know all the genes that encode, uhm, Usher proteins, it is possible that we will find new Usher genes this way. And again, understanding how those different molecules interact we can understand better, uhm, how to intervene, eventually, to either repair or replace this missing link by another player that could really take over the role of that non-functional protein.

Okay. Uhm, in the lab of Monte Westerfield, they don't use mice, they use zebrafish, and there is a poster upstairs. The zebrafish is a wonderful model because it can be produced very quickly and a lot of work can be done in the lab, right under the microscope where one can see the sensory cells right there. It is a very useful model. And, uhm, Monte has done work that is, uhm, sort of changing the way we think about things. And in particular he demonstrated that Usher 1 proteins, ah, seem to pre-assemble in a portion of the cell that is called the endoplasmic reticulum. And what he showed is that disruption in some of those Usher 1 proteins, that form this complex, uhm, result in disruption of the traffic. So that the molecules are not brought where they should be going. And the cell is under what we call ER stress, which is just a cell stress, and eventually they undergo apoptosis. We don't think that this explains everything that is going on in Usher Syndrome, but we think that it is probably, you know, part of the picture that we haven't been thinking about until now. And possibly if we could slow down this apoptotic process, we could allow the cells to survive, and while waiting for treatment, this might be a way to go. Okay.

So in terms of, uhm, treatment, and strategies for, ah, for restoring function. Uhm, I won't highlight all of them, but I would like to talk about a few that were discussed this week. And, uhm, and so there is, you know, possibility of reinserting the missing link. And, ah, you heard from Luk Vandenberghe who is generating AAV vectors for this purpose.

We have a lot of progress using gene therapy and, uhm, and Jeff Holt has, uhm, done some exciting work on, ah, on using AAV viruses to restore function in a deaf -- in a mouse model of deafness. And I'll talk a little bit about that.

And, uhm, and also there are possibilities of correcting translation. And again, that depends upon what mutation that, uhm, that we are looking at. Uhm, but if the, uhm, if the issue in, you know, in the particular limitation results in a misreading of the gene, and, you know, and truncated protein, there are ways to restore function and restore expression.

And there is, uhm, amazing recent work from, ah, from Jennifer Lentz using antisense oligonucleotides. And I'll talk about that.

And Kerstin Nagel Wolfrum has work on translation read-through, and correction of expression and function of harmonin in nonsense mutation, mutation that result in the absence, complete absence of the protein.

So just a quick word on, ah, on Luk's work, even though he just presented pretty much everything so I don't have much to say. But I think Luk is doing really amazing work right now to try to develop the best viruses that we can get to target photoreceptor cells. We are also working together to target sensory cells of the ear. The main goal is to obtain a virus that does not induce an immune response from the receiving host. Uhm, and he is really making some great progress there. And I'm very encouraged.

Uhm, so the way that the work would be done, ah, eventually, would be to, uhm, to reinsert, uhm, ah -- well, insert the AAV construct by sub-retinal injection, and, uhm, and what he has shown is that there are different type of AAVs that would target different type of cells. So depending upon what your goal is, you can use a different vector to insert a gene into a different cell type.

In terms of the work that has been done on the cochlea, ah, there has been -- I would say that the past two or three years have been really exciting, and we are really seeing things happening. This is all, you know, mouse model. So we are still far, far, far from being able to give -- give something for the patients. But I think every step of the way is, you know, extremely encouraging. And, uhm, and we are trying to target, again, the outer cells and inner hair cells of the cochlea. And, uhm, and in our lab we are doing round window injections of AAV vectors, and we have been able to demonstrate that, ah, that some AAV vectors are really targeting the sensory cells. We don't get 100% of the cells targeted in vivo but we do get 100% percent in the dish, but our goal is to get 100% in vivo and we are really working towards that. And I know it is going to happen.

So Jeff actually used this approach, ah, to rescue function in the model of, ah, of a mouse model of deafness, that is called the Beethoven one mouse. And you can see here, ah, this is the Organ of Corti, now really stepping back. Each of these little red, uhm, dots here is a sensory cell. And in green, this is a vector that expressed, ah, the green fluorescent protein, so you can tell which cells have received this vector. So we did the injection, ah, at one day after birth in the mice, and then we dissected out the tissue to see, you know, how many cells are infected.

And you can see that there are, ah, most of the inner hair cells, which would be the rogue ear. And our goal right now is to get a lot more hair cells because the hair cells are important for the amplification of the sound. And are essential for the sense of hearing.

So what Jeff did, uhm, he was able using those vectors to, uhm, to restore function at the cellular level. In the organ with some response, uhm, at the, ah, at the, uhm, deeper level. At the system level we got some rescue of auditory, uhm, brainstem responses. And also behaviorally, the mice did respond to -- did -- we called it a startle reflex. So you made a quick click sound, the mouse then jumps. If the mouse doesn't hear, the mouse doesn't jump. That is how we do this.

Okay. Uhm, one of the, uhm, really exciting, uhm, works was presented, uhm, yesterday, I think it was. It was from Jennifer Lentz where she showed the work she has done using antisense oligonucleotides, and these are just really shortcutting sequences that go, and will effect, uhm, specific region of the gene that you are interested in. And, uhm, and allow for, uhm, for, if you wish, uhm, blinding those parts this we don't want, uhm, the, uhm, the transcription system to see. Uhm, so in this case she is looking at a Usher 1C, uhm, mouse model that I was just mentioning about. Which has the mutation. In this particular case, in the mutation, induces a cryptic splicing, and what is expressed is truncating and non-functional. This is what you want to have and this is what you get so. What she did is she worked with Isis Pharmaceutical and looked at a different compound that can allow a rescue of the reading of that gene. Uhm, with that, ah, treatment, the, uhm, the outer hair cells and the white type mice, you know, this is looking, again, at the stereocilia, that is what you would see in the white mice, but this is what you see at one months of age as you see these mutations. So you can see the cells are going away, they are dying.

So using this translation correction -- oops, sorry. Okay.

Uhm, she was able to restore function. And this is just one, uhm, picture of, you know, of many that she showed yesterday. Uhm, but we -- but we can see, uhm, so this is, uhm, here the mouse that was, ah, injected with the control, so the mutant mice were injected with a control. Here the mouse is injected with the ASO-29, so that the, ah, the construct that she demonstrated worked. In the triangles, those are the later stages. And then here the control mass in, uhm, in black.

Uhm, so what we can see here is that this is where you want to be. Right? Okay. And in red is, uhm, is where -- sorry. Maybe I should just go for the blue right away. In blue is where she had the most success. So it was injecting this ASO vector at early stages. And it was just one injection and we just believed at that stage those vectors can reach the auditory organ. She also demonstrated some success with rescue at the retinal level.

Ah, finally, I will, uhm, just tell you briefly about work from Kerstin. Which is really unique. Uhm, she is using, uhm, TRIDS, which are drugs that target in-frame nonsense mutation. This is in the absence of -- total absence of the protein. And TRIDS are where, uhm, initially identified as, uhm, as from antibodies -- amynoglycosides. There are different ones that have been produced because they are toxic for the liver. So there are now ones produced that can be used. And what it does is again, sort of, you know, allows a read-through of the gene. And, uhm, and she has worked on various mutation, in particular, one that has got a pR155X and what she was able to demonstrate is that those drugs allowed, uhm, recovery of the protein expression. And not only is the expression recovered, but she also demonstrated that she was getting a functional harmonin and she was -- and the harmonin was allowed

to fund the complexities that it was supposed to do. That is really, really encouraging. And I know they are doing more work in that sense and finding different ways to use these drugs for -- in particular, for the retina. And she has also recently demonstrated that this works on many other Usher's, and she has done that on Usher 1F, 2A, 2C, and 3A. And any nonsense mutation in Usher's that she has tried seems to be responding really well to this treatment.

Okay. So finally I will highlight a review of what was just published, Jeff Holt and I. It is called "Sound Strategies for Hearing Restoration." We published that in Science recently. You can ask for that. It is easily accessible. An there is a shorter version of the review that may be easier for you to read, for those -- for all of the sign terms I've been using. But I think it is really an exciting era, and I feel very fortunate to be able to do this work here.

And finally, I will conclude with the many faces of Usher Syndrome research, and this is only some of us. Uhm, these are the speakers that we have had over the past two days, uhm, we have many other folks who are, uhm, who are there to work for you. And so what I would say is that we do have the workforce. And we have the will to make progress. We are a little bit short on funding. We are trying really hard, but it is a hard time. And I think for not just the U.S., but I think in Europe it is the same thing. So, you know, it is where we are. But we are doing everything that we can, and we are really excited to be doing what we are doing in the lab. So thank you.

( APPLAUSE )

JENNIFER PHILLIPS: Thank you very much, Gwen. We are going to hear once again from the wonderful Margaret Kenna.

DR. MARGARET KENNA: Registries are for people who have Porsche addicts. They are for people who like purple eyeglasses. There is a registry for everything. And most of the registries that people think about are based on their hobbies. We like to make lists for people who know what is -- their laboratory studies, and in this case it would be their vision, their hearing, their balance. But also -- so those patients can figure out what all of the research is up to, and so there can be a connection going both ways.

So when you have a history, as everybody said, for natural history studies. Well, natural history studies are basically just taking the patients who have something, and in this case Usher Syndrome, and following them going forward. And in that way we actually have some idea about what this particular genotype, the vision -- the genetic cause, and the different mutations in the genotype, what they are going to look like. I mean patients will often say, okay, now we have this. What are the other patients who have this look like? And what is going on with them? And how has that gone? And those are called natural history studies. So they are not dangerous, but they are time consuming, and we need a lot of information. But in order to get the right medication, or intervention to the right patient, we have to know who that right patient, uhm, is.

We also want people for registries who want notification of important Usher notification, whether that was about studies, whether it is just about meetings coming up, there is, ah, presented research or

clinical news, anything that you might want to know about what is going on, that is why we should do this.

I think this room full of people really shows networking, and if you have a new diagnosis, or coming to a new country or state, and you want to hang out with the other folks who have Usher Syndrome, this is the way to find them. And I think that is extremely important, and of course we always tell the parents of children with newly diagnosed hearing loss, a vision impairment is actually the people who know the most about this, and they are the other parents. I mean we know some stuff, but the people who really know, and who can feel it in their brain, and in their stomach, which is where I think people feel things, and in their heart, are the other parents. So it is good networking. And a terrific resource for people who have a new diagnosis or a better defined diagnosis. So say you know that you have Usher Syndrome type 2 clinically, but now you've known that for 30 years, but now you know what the gene is, so you might want to go back and do additional research on that particular gene.

So there are some really famous registries that have nothing to do with Usher Syndrome. But when we think about crafting registries, this is a good place to start because some of these have been really successful. There is a study run here in Boston called the Nurses' Health Study where they began to get information from nurses 30 years ago. And this -- now there are about 40,000 nurses worth of data in the studies, and they have been really turning out, ah, studies based on the information that has been entered initially and then kept updated over the last decades. And a huge amount of extremely important work has come out of the Nurses' Health Study.

NHANES -- and the Nurses' Health Study has been funded by the NIH basically -- and the NHANES stands for National Health and Nutrition Examination Survey. I think they called it that so they could say NHANES. It is I mouthful of words. They collect basic health data on 5,000 people across a spectrum of, ah, of representation in the country, and then they can use that on a really big population basis to talk about different things. So for example, there is some very important studies that have come out in the last few years based on NHANES data that looks at the incidence or prevalence of hearing loss. And one of the slides I used the other day, the NHANES data says by the time you are 19 years old, 19% of the population has some degree of hearing loss. So a study of that size, with a wide representation can be very useful for really big population based data.

The SEER is a huge, famous cancer registry that covers the entire United States and some other parts of the world. And they look at all kinds of things, and they started small, and then they had the collecting data from the different, ah, cancer registries, really all across the world.

And then a new one that I think might be applicable to the Usher Syndrome community is iCARE, the International Collaboration for Autism Registry. And I think they just came up with the acronym after naming it. And what they have done is established a registry that connects to all of the other autism registries. And so their goal is to have a place where they are sort of the helm and they have reached out to all the other registries. And I think of the Coalition as the home perhaps reaching out to other registries.

So there are some registries that exist already, besides the one we know about for the coalition. The Foundation Fighting Blindness actually started their initial registry for retinal disease in 1992. It is entirely on paper. And that has 11,300 patients in it, but it is not readily available because it is on paper.

The new one, which they actually discussed yesterday at this meeting is called the Retina Tracker. It will be entirely electronically based. The information will be collected from this point going forward so that is prospective collection, and it is updatable. So they will actually want updates on vision and other medical issues and so forth going forward. And, uhm, they are going to collect information in a uniform way, which is very important because then you at least have a chance of getting the same type of information from everybody, which when you want to enter a clinical trial, or you want the outcome from a clinical trial, is really important. Because if you take a random assortment of patients and treat them all with, say, aspirin, the outcome that you are going to get is also going to be close to random because everybody is a little bit different. So you want to have some matching on some basic stuff.

The National Eye Institute, at the National Institute of Health, also started a natural history study for patients with Usher Syndrome in 2005. Uhm, they also offered, through this registry, ah, genetic testing. I'm not sure about what has happened with that, but it is there and has a couple hundred patients in it.

The Usher Syndrome Coalition, this is this meeting. I'm going to talk about this in a minute.

And then there are some individual collections of patients around the world. Dr. Moller said earlier, he's had, along with his team, it sounds like they have seen every Usher patient and family in Sweden, which is a really big gift. And they have been able to interact with these people on all kinds of levels. So this is one kind of individual collection of patients.

There is something else called a Leiden Open Variation Database that is collecting genetic data and that is based in Europe. And there is a huge amount of genetic information in there about Usher and a lot of other things.

And then locally a lot of patients in this room may have had their genetic testing done through the Laboratory for Molecular Medicine. And that is the lab with Dr. Neimrod. So there are lots of these places where the data -- it is not exactly in a silo, but if you don't know it is there you won't know to look for it.

So the Usher Syndrome Coalition Registry began enrolling in 2011. And this was created by Mani Iyer who has Usher Syndrome. And it has been a really true labor of love, and very, very important to categorize and collect the patients. Many of whom are in this room with Usher Syndrome, so we can begin to figure out these things that we are talking about. What is the diagnosis? How is it going to look going down the road? What are the options in terms of therapy?

And so far what it contains so far is the name of the person, the type of Usher they have, where that particular person lives, would they like to be notified about upcoming clinical trials, and would they be willing to participate in trials.

It is HIPAA compliant. That is the federal set of guidelines that protects a patient's privacy.

And there is some governance. So if someone wants to utilize the data within this particular framework, there is a governing board, they can look at the request, and then give access to the data in a anonymized and very secure fashion.

All of these other databases I mentioned are also HIPAA compliant.

These are some very nice, ah, three very nice pictures that, uhm, that Julie Edwards who is my research assistant, currently upstairs doing child care, and she keeps me sane and honest. This is a global distribution of Usher patients based on the registry data, and I'm trying to see if this is the pen or the pointer. But as you can see, each of these individual points represent a patient or group of patients, uhm, in these different, ah, locations. So you can see that there is a very wide representation of patients in the registry already, but you can also see that there is some places that are really missing. So when -- so there has to be more people in Russia than this little clump here. There must be people, uhm, obviously in Africa. And all of these places where they haven't had an opportunity, perhaps, to have any kind of experience that we are having here today, even though there is a registry.

Ah, this is a more detailed look at the countries in Europe. And as we have been discussing, many European countries seem, at least from my view to be very excellent in identifying and, uhm, and really collecting these patients together on many different levels.

And then finally, uhm, these are where the registrants from the United States came from, including at least one family in Alaska. So, uhm, what is great is that a lot of these people represented here are actually at this conference over the last couple of days. So obviously the word is getting out. But totally this is about 540 different individuals, and obviously as we have talked about, we think there are 40,000 patients, perhaps, in the U.S. alone, and they multiplied that times the rest of the world and they are obviously missing an opportunity.

There are some issues with registries. Uhm, some people establish a registry for a very specific reason. And so they collect information based only on that particular reason. And there is nothing wrong with that, of course, but it tends to keep the information kind of in one little place. Do we need more than one registry? We don't really have enough time to talk about this, but maybe. And maybe we need a connecting person, or a group to get information about all of them. Who should manage it, or what group should manage it. Who should have access to the data, which is a very important question. We want people to have access to this data. We just want to make sure that it is secure, and that people's privacy and safety are guaranteed.

Should the registry be connected to each other? I obviously think they should be. It doesn't mean whole place data from place A to place B, but if you have a question and know they have it over there, it shouldn't be a big deal to get it.

And then how do you protect the data.

There are lots of different kinds of registries. There are Excel spreadsheets that go on forever, like this. And so for a 20-person registry, where you ask five questions, you know, Excel works pretty well. If it gets bigger than that, then there is no hope.

Usually things in Excel spreadsheets are a one-time collection of information. Uhm, it is very straightforward to the person to put in the data. It is actually straightforward to understand the data. But it is really tricky to maintain.

Everyone in this room has Excel or probably some version on their laptop, on their phone, whatever electronic device you have, you still need to make it safe, and you still have to make it HIPAA compliant.

The things that you can't really do well with Excel is that you can't collect a lot of information because then, you know, it gets to be 400 different columns, and then the next -- and the column you want is over in the next town some place. It is, uhm, it is not, for that reason, it is not the best way to do natural history studies because as you start to collect data over a period of time, it gets to be too big.

Uhm, eventually if you only do it once, and collect the data once, the registrants will move, and you will not be able to locate them. And as I said, you can't really grow it beyond a certain point.

Uhm, there are some registries that are updatable, and the one that the FFB is going to roll out, that is their plan. Uhm, you can ask for as much data, theoretically, as you want. You can ask for complex data like family history, medical history, audiometric data, and can I speak directly to how complicated putting audiometric data into a database is. Uhm, of course genetics.

The pro's are that you get natural history data. But natural history means you are following them over time. So somebody needs to be in charge of this over time.

You can update the contact information. In general this way you know the families will continue to be available, both for information coming in, and for, of course, information going out.

And if you build it correctly, you can apply statistics to it. So, ah, for example, that we are building all of our clinical databases is something called RedCap which is a clinical database software that was developed at Vanderbilt, specifically for this sort of thing. Uhm, the downside of the updatable database, unless you have more than -- if you only have one or two patients in it, it is very expensive. It is expensive in time. It is expensive, therefore, in money. And you need dedicated people who actually understand, uhm, how to enter the data and what you are really looking for. And of course you might still -- it may not be complete, but you can only do what you can do.

And in any registry, patients who enter their data need to know their data is safe and secure. Some people are out there, and they don't care who knows what they are up to, and that is fine. But some people are very private and they are likely to hand their private information over only if it can be certain that information won't be widely disseminated, and I think that is entirely fair and very appropriate.

Uhm, for example, we have been talking about how to let your children know that they have a diagnosis of Usher Syndrome. So theoretically, depending upon what you put into the registry, the child

can get access to the registry. I don't know about you, but my kids are savvy with computers. Two-year-olds can do stuff with computers. So they might get access that they don't know the full extent about yet. So we need to be cautious making sure this was carefully kept information.

Uhm, and then, you know, who do you want to know? Who do you want to be able to share your information with? Who should be able to contact you? Are you willing to update your information? And, uhm, and what is interesting about the one at FFB is that they are hoping that the ophthalmologists and the otolaryngologists and the other physicians involved with these patients will be willing to enter their data on an on-going basis. I think that is an excellent idea, speaking as a physician. I would say that's a challenge. At least it would be a challenge for me. Maybe not for anybody else.

So what would be the ideal registry? What would it look like? Well, it would have all possible data. So if that is the case, what we do is hire a medical student who is really enthusiastic and they collect all possible data. So when you are starting a new study with a medical student or somebody who has not done this kind of research before, they want to collect everything on everybody I know because I've tried to do that. And you can do it for one patient. Once. But you can't keep it up.

Information goes in both directions. You can update it. And that there is a parent registry given that there is going to be, always, more than one registry, that somehow connects to all of the other registries.

And that if you start a new registry for people who are, you know, who -- I don't know, who only live in the western part of Canada, that is going to be your registry, that when you do it you know you have to build a connection through a parent registry.

And so, as I said, I think the coalition is kind of like this. They are the parent organization. Working with all of the other Usher-related organizations.

So, you know, if it turned out that the Coalition was the guiding force here, we would have to figure out how to pay for it, who is going to do it and all that stuff we just talked about.

So I think at some point we will need to talk about what we want. We should definitely see what else is out there. Obviously, I think, this is going to require some funding if, in fact, this is what people decide to do. Figure out who is going to do it. And then we can present the results in two years.

Thank you very much.

( APPLAUSE )

I hesitate to say what is happening.

MARK DUNNING: Okay. Can you give me a thumbs up that you are good? Okay. That is the sort of dedication we have to the CART.

# Questions and Answers:
# Dr. Margaret Kenna
# Mr. Mark Dunning
# Dr. Claes Moller
# Ilene Miner
# Dr. Luk Vandenberghe

So we are going to do a, uhm, a panel Q&A session right now. Uhm, so I have, uhm, Luk and Gwen and Marley and Ilene and is Claes still around here some place? Excellent.

So if you guys want to come up front, this is an opportunity for you guys to ask any questions you have about anything. From the registry, to the coalition, to, ah, to the psychosocial stuff that we heard this morning, to gene therapy, to hearing, vision, balance, anything you want.

We also have other very, very smart people here in the room who -- feel free to stand up if you have anything to contribute.

We also have microphones so you can ask your questions. Don't be shy.

>>: The microphone needs to be straightened out. It is reverberating, making it hard to hear.

>>: Hello? Yes?

>>: There is an echo.

>>: Hi, there. My name is Cathy. CK name sign. I work for the Helen Keller center. This is my first Usher Syndrome Coalition, although I've been involved in the field since 1987. And when we were talking about registry, we have nine regional office, plus our training center in New York. And I, personally in the southwest region, I'm from San Diego and I work in Nevada, Arizona, Hawaii, and California. I always say that I touched over 200 people with hearing loss and vision. And we always say half of the people we touch or work with have Usher Syndrome, or at least half. So I know for me, from this point forward, I will refer people to that Usher Syndrome Registry, or that Usher Syndrome Coalition Registry, but when you gave the numbers -- and I used to be the regional rep in the Northwest region, and Hawaii, Alaska, Idaho. We know so many people with Usher Syndrome and we are not working together. And also yesterday when the researchers were talking about wanting to know about unusual cases, we each have them. There are four other regional reps here right now at this conference in different regions. So I encourage all of you to meet your regional rep, get some resources. There is a great technology program going on right now. If you have combined hearing/vision loss and earn under $45,000 a year, free technology. So that even increased our numbers of people with Usher Syndrome and working with them these last two years. So there is a booth out there for iCanConnect. Go find that. And from this point forward I vow to refer. And we also have a Helen Keller registry. So somehow we have to work together. So yay.

( APPLAUSE )

MARK DUNNING: So I have just a comment on that. I spent, ah, quite a bit of time talking with, ah, Nancy and Chris from, ah, from Helen Keller last night. Just about that. And, uhm, and we are -- and we have been working closely to try and collaborate and to get all of those folks that Helen Keller knows, ah, into the Usher Syndrome Registry and finding ways that we can work together.

>>: My name is Moira Shea and I just wanted to make a comment on the psychological -- on the psychological impact of Usher Syndrome. And in my life, what I found was very, very helpful was to always be one step ahead of the game. For instance, get that cane, or get that dog before you really need it, learn the Jaws software before you can no longer use a computer. But if you are one step ahead, it really makes your life easier.

And I have a question for Luk and gene therapy, and I know you alluded to risk factors for gene therapy. Would you be more specific about what the risk factors are? I heard it could be tumors or other biological, ah, reactions, but could you delve a little bit deeper into the risk factors of gene therapy? Thank you

DR. LUK VANDENBERGHE: Is this on? Can you hear me? Thank you for the question. To some extent the risk factors will be very specific to each specific therapy. But I think that there is a couple of things that are general that can be said. Overall I would argue that both on the eyesight, and that is where we have the most experience, but I think that can be extended, to some extent, to the ear sites. We are in a pretty good spot because these are small organs. The dose that is required is small and can be delivered locally. And all of these are very important for addressing safety and risk. Small doses mean less risk, but with any drugs, also with gene therapy. Local. Keeping it local is something that is also very important for safety. The experience we have on the ophthalmologist side, on the eyesight, has been overall, extremely, extremely positive. There are no major, what is called adverse events. So I think all in all that is one of the reasons why this field has been, ah, receiving so much excitement and enthusiasm. There are risks, and risks -- or there are at least conceivable risks. The risks can be related to the surgery, so that local delivery. One of the appealing things is that we want to keep it local, so therefore we need a surgeon to deliver it. And like any surgery there is a risk, there is an anesthesia risk because these things, for now at least, are delivered under anesthesia. The drug, itself, as I mentioned, often, up until now, has been a virus which can cause inflammation. Again, we haven't seen that, or we haven't seen that to extents that it causes damage. But these are some is of the risks.

And you mentioned a possible tumor, or oncogenic risk. Certain technologies have that potential risk. In the eye or the ear, as far as I know, we haven't seen that. But that is something that, for example, we have to very carefully look at, ah, what that risk is. So I -- so I would say in some way we are in a very position in terms of safety. But I think that it needs to be highlighted. Again, that these are still experiments, and that safety is still something that we actually -- the goal of the experiment is to establish the safety. So it can be 100%.

>>: Hi. How are you? My name is Carly Fredericks, I'm the mother of an 8-year-old little girl named Ava who has Usher Syndrome type 1B. I want to thank the panel for the hard work and dedication. We

were so looking forward to this event and we really do appreciate it. My question is I know that we have come so far with genetics on being able to identify exactly what type and sub-type, ah, each person with Usher Syndrome has. Uhm, I find I get most confused, especially when explaining to family or meeting another person with this specific type is has there been any research done, uhm, as to once they are identified why there is such a drastic difference amongst how everyone progresses? You know, that is something that I'm really interested in ands had there been research done, so if you have a specific type, why everyone is progressing at different rates?

DR. CLAES MOLLER: That is a very interesting question. If you take a large sample, as we have a large sample of people, if you actually look at Usher type 1B, they are more alike than unlike. But then you always have people who stick out, and what we are looking into now is what other factors can do this. We have been talking about sunlight for the eyes. We have been talking about active and passive smoking. We have been talking about sound exposure, noise exposure. We have been talking about different diets; what are you eating? So there is a lot of things. And we are trying to gather these data now to see could there be. And then we also have -- do people have other genes that interact? So there are probably a lot of different things that can add to that some persons can see fairly well up until they are 60 or 70. In my studies, people with Usher's type 1 and 2, when I say most, 70% have a central vision when they are 65 to 75 years of age. They can still see pretty -- quite well.

So I heard this over and over here that you get "blind." We don't use that word in Sweden because "blind" to me is "blind." You have a severe visual impairment in Usher Syndrome, but very few, in my terminology, get blind.

DR. MARGARET KENNA: I think as Dr. Moller said. In Ush 1B, which is MYO7A, they may have two, ah, mutations that are very clearly pathogenic, or they may have a mutation that has never been described before, so we don't really know how it is going to go. Some of our patients, people travel the world and, you know, you have children with people from other parts of the world. We have some patients with four, five, or six different mutations in several other genes. So that all of those pictures of the interactome that Dr. Geleoc up here, and there is that main gene and then another gene over here. So I've got quite a lot of that. And even within the same family, even though the patients look quite similar, very often the hearing will be a little worse in one patient or progress a little more rapidly, the same with the vision. And that is probably because there is some difference as Dr. Moller said in what is called epigenetics. If you drink too much coffee, in my case this would be a problem. So if you listen to too much noise. But there are a lot of things we don't know.

>>: In response to your answer. One thing that always pops up in my mind and something we have done a little research on in our family. Uhm, have you found any common factors with the diet? We had met an ophthalmologist that was really big on, you know, nutritional ophthalmology, and he had mentioned that there seemed to be a combination between people who can't I do jest phytanic acid, and they found also that people with Usher Syndrome can't breakdown phytanic acid. So when we are sitting there, and I hope I'm explaining this correctly, but we had our daughter's phytanic level tested, and 0.5 and 3.5, and her results were that she was storing at 8.2, which was extremely high. And we

started, you know, cutting those things out of her diet in hopes to slow down the progression. Or is that something you've ever heard of? Is there any research on that?

DR. CLAES MOLLER: I think your physician has misunderstanding there. If you have a problem with phytanic acid, you have a different disorder called Refsum Disorder, which is not Usher Syndrome. It has resemblances with Usher, but the cause is totally different. So it is not that people, as far as we know now, people with Usher Syndrome have some other general common problem with some food or something like that.

>>: Right.

DR. CLAES MOLLER: That is not what we know today. Do you agree?

DR. MARGARET KENNA: Yeah. I think so. There is some discussion about vitamin A, which we can certainly talk about that. The data for vitamin A is mainly in adults, and it is from decades ago. But, uhm, but we will talk to the families about vitamin A and you don't take too much because it can kill your liver. Maybe it will be good for your eyes. On the converse, vitamin E, but there is some research to shows vitamin E might be bad for you. This hasn't been studied in large populations and definitely not children. So it is one of the things, these are the kinds of things in the long-run that we love to know.

>>: Great. Thank you for your answers.

>>: My name is Eric, and my daughter Megan has Usher 1B.

DR. CLAES MOLLER: Can you speak up a little bit?

>>: I'm sorry. My daughter has Usher 1B. And my question was about the restoring the function of cilia, ah, you mentioned the study by Jeff Holt and that offers a lot of promise. My daughter has a cochlear implant. It has been a miracle for her. And, uhm, and, you know, she is who she is today because it has been so beneficial. But my question is, if she were to get second implant, would that damage the pathway in the cochlea, destroying the cilia that are there, or is there any other potential that can be generated after a cochlear implant is implanted, or even after a first one?

DR. GWENAELLE GELEOC: That is a very good question. You know, Mark sort of asked me that question not long ago, and he said, you know, did we make the right decision in having Bella receive the cochlear implant? And I would say "absolutely yes." Uhm, I -- I don't have a clear answer if a cochlear implant will absolutely limit the usage of, you know, versus for gene therapy. If it is gene therapy to restore hair cell function it may. But I would say that at this point we still are a long way before being able to deliver it up and use it in patients. So I think that is something that you probably would -- you should discuss with your physician. I'm not a physician. So I can't really advise you too much on that. But I would just, you know, be clear on, you know, even though we have had successions in the lab, we are still a long, long way to getting a treatment.

The work from Jeff Holt was not on the Usher Syndrome gene. But as some of us have talked about over the past two days, anything we have in restoring vision or hearing in, you know, in other models, that are not necessarily having the dual sensory loss I think is a big way forward. So we are extremely encouraged, but we are very cautious in terms of how long is it going to take to really validate it, uhm, using it for, you know, Usher Syndrome genes, and then, you know, eventually move onto clinical trials. It is going to take a while. For the auditory organ, which has a little bit more difficult access. But I am hopeful that it will happen.

>>: So I guess --

DR. CLAES MOLLER: If you were in Sweden, we would probably, or I would, recommend bilateral cochlear implants. We give it to every child and we give it to every person who wants it who is deafblind. If you have Usher Syndrome you have such a hard time localizing who is talking and where. And once you've found it, the person who is talking, and you can see the lips, the problem is that the person has stopped talking and someone else has started talking. You can't localize with one ear. So that is why we -- that is why we now give everyone. And I would say, uhm, time flies. And the things you can achieve if you have a bilateral cochlear implant during these fourth coming, ten, or twenty years. Which it might take. If it ever comes to stem cell therapy, it -- I wouldn't recommend to wait for that reason. But that is in Sweden.

( Laughter )

>>: Okay. And of course my daughter is a teenager, and --

( Laughter )

-- and if anybody else here has a teenager, I don't mean to insult you, but they can be very hard-headed. And for her to take on the challenge of potential benefits of having a second cochlear implant, can't get that through her thick skull. So it ultimately, I guess, comes down to the parent's decision about the costs and benefits of getting a second.

DR. MARGARET KENNA: Yeah. For very young children, you know, there is a relatively small language window for children -- language acquisition for children who are born deaf. So obviously for people who have some degree of hearing loss, and they have hearing aids, that is a very different conversation. But for children who are born deaf, and really not benefitting from their hearing aids, those first two or three years are really crucial in terms of learning spoken languages if that is what the family decides to pursue. So I think that we say, like what Dr. Geleoc says, at least one implant now, if that is what your goal is, and there is quite a lot of data, for better or worse, that says that if you let the other ear go a long time it is just not clear what a long time is, although you may get some benefit from the implant, it might not be as much if you did it sooner rather than later. Very variable, though.

>>: Thank you.

DR. MARGARET KENNA: Teenagers, on the other hand, we don't have enough time for today.

( Laughter )

DR. CLAES MOLLER: Can I say one thing that is important, we are starting in England, in the UK, we are starting to get people, adults, with Usher type 1 who have congenital deafness and signing. And they want a cochlear implant. Not to be able to hear speech because they don't need it. They sign. But they need to hear their baby crying. Calling. They need to hear some traffic. They need to have some other when the vision goes down. So that is a new group. Totally different perspectives. But this will come. And it has started in the Deaf community in Sweden, I believe.

DR. LUK VANDENBERGHE: I think my presentation, which I hope exuded hope and excitement. This is, to me, clearly a situation where one bird in the hand versus a potential of many more. At this stage, gene therapy has no drugs on the market. We know too little of it. There is a great prospect. And that is probably largest in the vision space. But I would not delay any of these decisions based on a potential at this stage. And I'm an advocate of gene therapy. So I would say that these are still dreams for the most.

MARK DUNNING: Can I comment on that, as well? Uhm, I was once advised by a very wise, ah, person when we were trying to determine whether or not to get the cochlear implant for my daughter, uhm, that you should take advantage of whatever technology is available today and not worry about what you -- about what is available in the future. Uhm, there are a bunch of people up here in the front who have lived their entire lives using sign language, and that was the technology available today and they have done great with it. And there are kids like my daughter who had the cochlear implant available and they are doing wonderful with it. There will be a generation in the future that has gene therapy available to them, and they will do great with it. Uhm, but I think to hold onto something that may be coming in the future and to think about something that may be coming in the future, uhm, is to deny yourself and enjoying yourself in the present.

( APPLAUSE )

Megan, did you have a question?

>>: Yes. I have a question.

>>: My name is Megan Kennedy. I have Usher 2A, and I've seen several doctors with different opinions. And I really value all of your opinions and I wanted to know -- I don't know how much research there is on environmental factors that may, uhm, increase how rapid vision loss happens. Do you guys have an opinion on the environmental factors? I had one doctor tell me he was doing research on lab rats who never went completely blind because they were always indoors and were never exposed to sunlight and the sunlight affects that. And I know that, uhm, there is different opinions on it. I've had other doctors tell me that in some ways it doesn't affect it. So I'm just interested in hearing what your perspectives are on that. And if you are not sure what to give your opinion on that, I'd like to know what resources you trust to inform my own opinion and what environmental factors might be.

DR. MARGARET KENNA: So I think, as we just mentioned, uhm, there is certainly not enough research on this. But the three or four things that I think we do know something about, uhm, actually Dr. Cosgrove from Boys Town actually talked about exposure to light. And he is raising his mice in the dark, or pretty much in the dark. So I guess the good news about that might be that their vision is prolonged, but it is hard to live in the dark. I'm sure it is very boring to live in the dark. And we make a recommendation to all of our patients, as do many ophthalmologists, not just for Usher, but for everybody, to, uhm, to wear certain types of sunglasses, which are more recommended in others, but to protect your eyes, in general, and then perhaps with, ah, with the retina, in particular. And then even inside, like here where it is really bright up here, many people wear sort of the types of lenses that will darken with light. And there isn't -- I mean this is information based on mice, but it is non-invasive, and it is a relatively straightforward thing to do. And I think it is probably good for your eyes anyway. And that is an easy recommendation to make. I think vitamin A is trickier, like we just discussed, which were and have remained state-of-the-art, but they were done 20 years ago on adults with a clinical diagnosis primarily of Usher 2. Again, vitamin A is good for you up to a certain point, but it is toxic to the liver. And, uhm, and let's just say if you've ever seen anyone with a liver transplant, you might not sign up for that today. And I think we tell people to be smart, but cautious. And then there is some evidence that vitamin E, too much vitamin E might be toxic. So that we tell people to stay away from. And I think those are the main things that people talked about. Oh, smoking. And salmon. You can ask Dr. -- you can ask Mark about salmon.

MARK DUNNING: As much as you want to stay away from salmon, the opposite is what you are supposed to be doing. You are supposed to eat salmon.

DR. CLAES MOLLER: Actually, there has been a test on animals, ah, mouse who have been smoking.

( Laughter )

And one group was actively smoking, and one was passively smoking.

( Laughter )

And it really affects the retina as came out in an art can about hearing, that smokers, that they took away alcohol, et cetera, as risk factors, and just looked at smoking, also damage your hearing, increases your hearing loss. I think nicotine and smoking is one of the other things we should stay away from.

DR. MARGARET KENNA: It is interesting. There is a lot of information on the hearing loss side about environmental factors, smoking is one of them. Uhm, obesity is another one that has been shown in some early studies to possibly effect hearing. Now, whether it affects vision I don't know, but obviously it would be good to maintain as much as you can get. I feel bad for the mice, though.

MARK DUNNING: Okay. Actually, if I can jump in front of you, I've got a question over here. And I'm in the interest of staying on time, too. So let me just run this over.

>>: Okay. Yes. Hi. My name is Dana and I have Usher type 3 and I have two cochlear implants which I received in my 40's and they were miracles to me. I was able to hear with a hearing aid, but never did

as well as I would do with a cochlear implant. I'm interested in knowing whether they are coming close to medical treatment. And how do we keep track of these therapies, by the timeline on that. Is there any place online other than clinicaltrials.gov where they post, you know, where these therapies are, or when they might possibly be developed? Because I have to run from conference-to-conference, doctor-to-doctor, all around the world just to find out what is going on. So shouldn't there be something online that we can keep track of these things?

DR. LUK VANDENBERGHE: That is a very good question. And clinicaltrials.gov is the one site where you know a clinical trial is either venire, or is on-going. So I think this is a very relevant resource. Uhm, so in terms of a specific, ah, Usher type 3 clinical trial, I think there is something in the works, uhm, that -- that is not very public. And that is exactly towards your question, ah, why these things aren't always as public as they could be. I think there is a variety of reasons for those, but I think often foundations do try to get that data together. And do try to get at least what's publicly available together. So I think refer to the various foundations as much as possible to find that information. Uhm, ah, I'm afraid there is no -- there is no very good answer to your question. Ah, it is even hard for somebody in the field, like myself, to continuously keep track. Sometimes there are companies involved. And they have all kinds of strategic reasons to, ah, to reveal information at certain time points. Uhm, that being said, from the moment a company wants to have patients enroll, it is in their best interests to come out and to be public. And again, clinicaltrials.gov is probably the best resource to find out about that.

MARK DUNNING: I can give you another, ah, follow-up to that. That's one of the goals of the Usher Syndrome Coalition and the Usher Syndrome Registry is to ensure that people who are in the Registry are informed about, ah, all of the research that is going on for Usher Syndrome. And, ah, and we are in touch with all of the lead researchers now, and you can see them all sitting up here at the front. So we find out, as soon as they have something that they can share. So stay in touch with the Usher Syndrome Coalition and we'll be sure to keep you informed on that.

I do want to just mention, and I see a line of people for questions, which is great, but I think that is going to have to be the end of the line and I know Randall has a question over here, as well. I'm not sure that we can take anymore than that. So that is just a warning.

DR. MARGARET KENNA: So with regard to Usher type 3, Kumar presented the day before yesterday, I believe. And I know he works with the, uhm, with the Usher 3 foundation and also Foundation Fighting Blindness, and they are in development of something specifically for Usher 3. Right now I know he is not at liberty to say what it is, and I don't know what it is, but I know they will be looking shortly for patients. So I would probably contact one of those two organizations if you think you might be interested. Or you can talk to Kumar, yourself.

>>: Thanks. My name is David. I'm a father of a fifteen-year-old son with Usher 1F who two years ago wanted to be an astronaut and now wants to be a microbiologist. He is sitting here taking notes.

My question is the following: We had my son's sub-type identified in 2009, I believe, here at Harvard. And there was a lot of fascinating information presented over the last couple days about the next generation sequencing, about better sequencing, better technologies and capabilities. And then

presented information about the Registry and the importance of getting the most accurate data into the Registry. Do we need to get, ah, his gene resequenced? Should we get his genes resequenced? That is the specific question.

And I guess the more broad question is what should we, as a community do, with regard to sequencing and getting the genetic sequencing of the entire family, grandparents, siblings done onto you guys for the benefit of the whole community in this Registry?

DR. MARGARET KENNA: I think there is more job security in microbiology than being an astronaut.

( Laughter )

So I think he has made an excellent choice.

With regard to whether he should be re-sequenced. If his, uhm, DNA was sequenced at the, ah, Laboratory for Molecular Medicine here at partners, and you have a firm diagnosis of Usher 1F, two different mutations, I don't think it needs to be -- if this is the situation, you don't need -- it does not need to be re-sequenced. That is the state-of-the-art lab. You can certainly ask them. The one thing about that lab that is cool is that they update the mutation database on a fairly frequent basis. So if you have one mutation that you are sure is pathogenic, disease causing, and the other one they are not too sure about they will update it. But if they were sure the first time it is unlikely they will do it now.

MARK DUNNING: Anyone want to touch on the question about whether or not the other members of the family should be tested?

DR. MARGARET KENNA: Oh, sorry. So I think, uhm, people always -- we always recommend that the parents get tested, certainly. Either to look for the particular mutation, or in the family, if one of the parents has something that looks like a, perhaps, minor version of what we are seeing in the child, then we actually recommend sequencing the whole gene. Every now and then we see a less severe version of the exact same thing in the parent, and this is a recessive mutation, but stranger things have happened. Uhm, and then if you are interested in having, say, siblings, either your child's siblings or your siblings who may go onto have their own children, very often people are interested in doing that, as well. That is obviously up to you and what information you want to share. But very often people are interested in doing that.

>>: That is a personal, ah, benefit.

DR. MARGARET KENNA: Yes.

>>: But for the greater community, is there benefit in having -- is there significant benefit, I guess, in having more of this data available?

DR. MARGARET KENNA: So I think the research question, which is what this sort of is -- from a research standpoint, many of these mutations they are discovering are what are called private, they are in that family alone, or they are the first patient, or family to ever have described it. So it is important to

have as many people with that information as possible so when the next one comes you will have something to say. But I think for therapies, although right now we are talking about treating patients with Usher Syndrome, there is some discussion about treating people who have one mutation, for example, who still have a lot of -- they are heterozygotes, the parents, basically, who still have a lot of function in the eye. And if we are doing therapies, not intra retinal, but systemic, there are things to measure. So there are a lot of research opportunities, as well.

DR. CLAES MOLLER: I think you should beware that there are a lot of companies out there, or some companies out there who offer genetic testing in some sort of old-fashioned way, which means one-year-old. And --

( Laughter )

And we have physicians, at least in Europe, who send directly, without contacting a geneticist, or a specialist, and then you get an answer. "Yes. Two pathologic, probably pathologic mutations." And you settle with that. We don't settle with that. We always want the parents so that we can really be sure. And we want to have the latest technique. Because I've had a couple of patients who have had the wrong diagnosis. For Connexin 26, but they really had Usher Syndrome. So beware of a quick fix and go to a specialized hospital like here in Boston.

MARK DUNNING: So we are getting short on time here. So, uhm, so -- I know we have four more questions, uhm, but if we can try to keep the questions brief.

DR. CLAES MOLLER: The answers brief.

DR. MARGARET KENNA: You mean the answers brief.

( Laughter )

MARK DUNNING: If we can try to keep Marley away from the microphone.

( Laughter )

This next up is our Lamborghini driver Manny.

>>: Hi. My name is Manny, and I didn't have a question. I just want to say something about all the state of computer software these days. I'm a software engineer, I worked as a software engineer for the last 30 years, and I'm glad I went into that field because it served me very well. Uhm, I just want to tell you that some companies are doing a lot for access of living. Companies are spending millions of dollars, and they have a whole group dedicated to activities of living. So for the blind, or for the visually-impaired, to use software and think of it as a career path, actually.

Uhm, but that -- and there are -- and there is a whole lot for the blind using software, and blind programmers, and all kinds of things. It is amazing what is out there. So maybe young adults and, ah, and teenagers, if you are looking at a career path, you might look into all of that. That is all I wanted to say.

MARK DUNNING: Thank you.

( APPLAUSE )

MARK DUNNING: I know -- thank you, Manny. So microbiology and computer programming for kids. No astronauts.

( Laughter )

I know Randall had a question. Do you want to bring a microphone down?

>>: I am Randall DeWitt's aunt Charlotte, and Randall is down here because he has vision problems and hearing problems. He is the President of the Deafblind Contact Center, and I'm going to hand the mic this way to his interpreter.

>>: Hi. I'm Randall DeWitt and I do have a major concern I would like to explain. All of the information we have gotten in the past two days has been wonderful, but now that the families are here, I wanted to talk about an issue that I've experienced and seen. We can kind of see Usher Syndrome people being in different groups. There are some who have cochlear implants. Some have who used sign language. Some who use spoken English. And we know that there are treatments coming along in the future. But my concern is how are we people with Usher Syndrome able to communicate with each other when we use different communication modes? There are some people with Usher Syndrome, and I'd like to give you an example, actually, of what happened yesterday. I was having a meal with people that I already knew who communicate tactilely, and I felt comfortable with those people, but I saw other young folks with Usher's and I wanted to be able to communicate with them, but these are people with implants, and I wasn't sure how to approach them and how we could actually communicate with each other.

ILENE MINER: Hi, Randy, this is Ilene Miner. I, uhm, don't have an easy answer. I think that is an on-going issue in the field of Usher. That even before the advent of -- of implants, there were folks who had Usher 2 and Usher 3 early on who weren't communicating with people with Usher 1 who used sign language. And I think that it brings it back to the need for better services, which governments aren't providing, but as I said, in Denmark they have something called Deafblind Contact Persons, and that is a really nice example of a system that is nationwide providing what we call SSPs. So if you had an SSP with you, when you wanted, you would be able to communicate with people and they would be able to communicate with you. There are also technologies -- you know, technology, and I'm not the person here, there are people here who speak to that, that you can type back-and-forth. It is a real problem. And I think the advent of the Internet, and Usher Syndrome groups online, Facebook pages, blogs, allows a way for people to connect with each other. But it is an issue that people who use spoken English and people who use American Sign Language, or Swedish sign language, or any other sign language, uhm, are going to have difficulty communicating if there is not a method; whether it is technology or a person. And people with Usher 1 and across lines and who use sign language can communicate more easily. I can make do in another sign language, but I can't make do in another

spoken language. So you've brought up an important issue, and, ah, and there is not an easy solution for it at this time.

>>: Swedish sign language and American Sign Language folks can communicate just fine.

>>: We always find a way.

ILENE MINER: Yeah. I know that. I've been in that situation. And it amazes me. You can let me loose in Sweden and I'll figure it out. Laugh will have

MARK DUNNING: I would like to dress this, as well. Uhm, first of all, Randy, thank you for bringing that up. I know that it is a, uhm, an uncomfortable question for a lot of the people in the room; both for those who are signing and for those, ah, who don't sign. Uhm, and I think that it is very important that be right there on the table and be something that we openly address, and openly try to find ways to bridge. Uhm, the Usher Syndrome community is not just, uhm, people with cochlear implants, or people who sign, or people who use canes, or people who use dogs, or people who use tactile sign, or ASL. We are talking about doing this conference in a couple of years in Europe. Well, wait until we get to Europe and we are trying to get all different spoken languages and all the different tactile languages and all the different, ah, uhm, manual languages together. It will be an incredible challenge to try and overcome. Uhm, I think Ilene, though, mentioned one of the best ways to do this. Unfortunately it doesn't help us in this type of an environment, but, ah, but e-mail and the technology that allows us to be online today really does allow us to connect a lot better than we have been able to in the past. What I would say, though, for those of us who are here in this room today, ah, take advantage of, uhm, of talking to people like Randall and to Rene and vice versa. I know Randy, you said you were uncomfortable approaching people with cochlear implants. Do it. Uhm, that is the best way to overcome it. Uhm, that -- you've all heard -- those who were here yesterday heard Rene talk, and laughed right along with everything that he had to say, uhm, and I hope you notice at the end that he and I tried to communicate tactilely. I don't know tactile sign language. But I know Rene. And I know that between Rene and I we will find a way to make it happen. It is less about the communication method.

( APPLAUSE )

So we have time for two more questions, as long as Marley doesn't answer.

( Laughter )

>>: Just to follow-up on the last question, uhm, I think just being in the conference, in general. And being around people, I'm very new to the Usher Syndrome game. I know my wife Megan was up here asking a question. We were both inspired to go home and learn sign language. Just as a way to be more involved in the community. So just him asking that question, or posing that issue to the community is one method and one way to, ah, to --

( APPLAUSE )

-- to get people to do that.

I do have a question. Uhm, and it may -- and it may also be another follow-up on some of the other stuff, but it will be quick. I promise.

Uhm, I'm wondering, ah, in Claes's presentation, talked a lot about health, physical health and emotional health, which I think are huge for any person. I deal with nutrition in all aspects. I think it is a big circle. You can't just look at genetics. You can't just look at exercise. You can't just look at diet. Have you to manage every aspect of your life holistically to some degree, as goofy as that sounds. And you have to kind of take responsibility for yourself. And I'm just wondering what, uhm, kind if there is any consistent markers, uhm, I know for -- I don't know if she wants me to tell everybody, but what I find, or found in her, especially when we first met was, uhm, some pretty systematic -- some chronic inflammation. Uhm, and so I'm wondering across the board, across every time of Usher Syndrome you see, whether you see, uhm, any consistencies with inflammation, whether you attribute those to more diet, I know stress causes 70 to 80% of diseases and other things like that, and what you might find across the board?

DR. CLAES MOLLER: The thing we have -- we have found in our research, across the border is two words that have been, uhm, sort of specific for dual sensory loss and deafblind and that is spelled out by the W-H-O, and that is activity and participation. We people communicate. Communicare means in Latin to do things together. And the problem that we will probably see in bad physical and psychological health is exactly what was talked about previously that if you can't communicate with other people you get -- you tend to be lonely. And those that lose their communication skills, and us who don't have the new communication skills, they -- those people will be very lonely. And that is what we see. Those are the ones that really get physical, other illnesses, and psychological bad health. And if you want to talk during the lunch with Mattias -- raise your hand? He is a clinical psychologist who works with people with Usher on that aspect.

>>: So there is no -- that is great. Thank you. That is a great answer. So there is no, I guess, genetic, biological, like, implications to cause -- like Usher 2 genes, ah, in the mutations cause a higher level of inflammation in people, that is not necessarily --

DR. CLAES MOLLER: Ah, we had a Swede who in the 50's, ah, went to people with Usher type 1 and then claimed that 25% had psychological, developmental, and psychiatric illnesses. We can't find that.

ILENE MINER: Right.

DR. CLAES MOLLER: We can't find that. And we have seen the same population as he did. That is probably because they didn't learn sign language at that time. They were oral. And they couldn't communicate even with their parents. And that makes you psychologically ill or psychiatric ill. So we see it as mostly sensory deprivation. When two senses are not working properly, and you don't have alternative communication skills. Like tactile or whatever it is.

>>: Yeah. I just want to follow-up, the vitamin A side of things. I'm not against it. Not for it. Whatever. But, uhm, like if you just look at, like, it just poses the idea to me, because we have had some success with some stuff, and I will share it real briefly, real briefly, uhm, that, ah, yeah, I've asked

Megan, what have your doctors told but that stuff? Yeah, vitamin A. And you might say overdosing on that is dangerous and toxic to the liver, uhm, supplementing with that might be very dangerous in that regard, but, uhm, like, ah, fresh raised, I should say wild caught salmon with omega three has great levels of vitamin A. Carrots. Juicing carrots. You can't, to me in some of the things we have done, she had really bad macular edema, really bad, highly inflamed state of it, we were able to pretty much eliminate it in about 30 days, 30 to 45 days by supplementing with fish oil, but sourced from the natural, not the processed source of fish oil. And also juicing vegetables and fruits like that. And she is overdosing on nutrition in a moderate way. Uhm, but natural -- in my studies with diet and nutrition, uhm, natural sources of those vitamins and minerals are really something your body can't, ah, can't not handle, or -- or that I think is the levels that are dangerous if it is -- like I said, uhm, a little bit of on the overdose side of nutrition, to the point where she doesn't have to get steroid injections anymore for dealing with, ah, fluid on the, ah, on the back of the eye. Uhm, so it is just -- I just want to point out that there are things out there like that, it is not to steer away from saying don't use vitamin A because it is toxic to the liver. Go eat salmon, go eat that stuff, and go try to incorporate those lifestyle changes. That dealt with the inflammation, but a huge part of it was stress. She fell in love. Got married. Cool shit like that. And it -- and more my point being -- more my point being that it is a huge circle, it is a huge circle, and you are saying that the psychologically she isn't stressed, you also have to look at the diet, you also have to deal with all your environmental factors and pay attention to what is going on, and tinker, and work with what might work for you, what worked for her in her edema may not work for another person, but inflammation was the problem, and we tackled that through diet and nutrition, and those injections are nasty, and I believe she doesn't have to get them anymore, and there is just cool stuff like that out there. I wanted to share that a little bit. Thank you very much. This is a great symposium. Thank you.

( APPLAUSE )

MARK DUNNING: We have time for one more quick question.

>>: My name is Andrea. I've got three children. Two with Usher. They are 18 months and five and have been diagnosed. I have children's sunglasses, would you recommend anything better than that? And then as parents of young children, if we take really detailed notes on diet, when puberty started. I was just -- maybe correlations between hormonal changes, pregnancy, and maybe a precipitous eye drop, would that help you guys if we start taking this natural history, it seems like there is nothing out there, kind of like the long-term nurses study -- as vision wanes, is it true with that visual tissue, is it pretty hardwired, so if there is something like a visual prosthetic, would that be able to have visual memory and come back? That's it.

DR. LUK VANDENBERGHE: I'll comment on the second part. I don't think we have the full answers on that. Mainly because we don't have those treatments. And we haven't done that, ah, we haven't -- we haven't begun to evaluate that. The data out there from the therapy trials, which is a form of visual prosthetics, has been promising, has been, ah, ah, indicating that, ah, that this is hardwired and this isn't lost over time. I think that the earlier the vision loss, the higher the risk that hard wiring may not be that solid. I think that is all I -- all we know at this point.

DR. MARGARET KENNA: I think in terms of keeping track of all of those things you mentioned, nutrition, and what's going on, I think we all -- I think it is pretty clear we don't know the answer of that. Keeping track can't hurt because very often things, you know, that if you -- you might notice something, and say, gosh, you know, and then you start to look at another patient. So I think there is no harm, and if we had enough people we might be able to see patterns. So without making you too crazy, I think it is probably a good idea.

Oh, you know what? I can't speak to the sun glass brand. Not because I -- I think it is a conflict of interest. I don't know. I think you would have to actually find a good ophthalmologist and ask them that. And I know that Dominic actually had a slide yesterday, and I can't remember what it said. He actually had a particular type of light that he recommended or a filter. Do you remember?

DR. CLAES MOLLER: I work with another patient who -- I have 20 patients with, uhm, which I have seen with Alstrom Syndrome, and that is a very rapid retinal degeneration. They are all virtually blind when they are twelve to thirteen years of age. So it is different from Usher. But many parents have now started to have contact lenses with Polaroid, uhm, instead of sunglasses because it is very difficult to have small children to have sunglasses. But actually contact lenses. And one, ah, two of them, just case anecdotes, two of them who have had contact lenses for the longest time have still not good, but at least a little bit of vision, and they are 20 years of age. So that is just anecdotal. But that is what we learned from that natural history when a parent comes and tells us, and they are often very smart, you know. And I haven't seen that in Usher Syndrome because I just haven't seen it. But we have two parents who have started with contact lenses in their children with Usher Syndrome. So talk to your ophthalmologist about that.

DR. MARGARET KENNA: Good idea.

>>: Is there a science behind the contact lenses or just anecdote?

MARK DUNNING: There is a, ah, uhm, Dominic's -- I don't know if Dominic is still here. But, uhm, but I --

DR. MARGARET KENNA: I don't know what you were going to say.

MARK DUNNING: University of Iowa. Her name was on the tip of my tongue.

DR. MARGARET KENNA: Arlene Drack.

MARK DUNNING: Arlene Drack has been doing studies on this, she is working on the science of it.

>>: Can you spell her last name?

DR. MARGARET KENNA: D-r-a-c-k.

MARK DUNNING: D-r-a-c-k. We can get you in touch with her. Don't tell her I forgot her name. She would kill me.

This is all the time we have for this. Of course we are late.

We are going to be back here at 1:45, no later, and we'll start exactly on time. Thank you.

(Lunch Break )

## Session V – Patient Care and Rehabilitation
## Dr. Nadja Högner – Stress in Individuals with Usher Syndrome Type 2
## Dr. Catherine Blanchet – Usher Type 2 Syndrome: Hearing, Educational, Socio-Economics and Vocational Impacts
## Ms. Susanne Morrow – Focusing on Now for Tomorrow: A well-rounded curriculum to strengthen students with Usher Syndrome

MARK DUNNING: We are going to take our seats. We can get started. So we are going to start our next session and so I'm going to introduce our moderator for the session. She's a good friend of mine. She's on the board of directors for the Usher Syndrome Coalition. She has Usher Syndrome herself and it is Martha Steele.

MARTHA STEELE: Yes, I'm not Mark. Nobody can be Mark. Thank you very much my name is Martha Steele. I have Usher Syndrome 2A. I live in the Boston area and I work at the Massachusetts Department of Public Health, helping to direct one of their bureaus in environmental health where I spent most of my professional career of about 30-35 years.

So, this panel right now is patient care and rehabilitation. We have three speakers. Our first presenter is Nadja Högner. Her topic area is stress in individuals with Usher Syndrome. Nadja.

DR. NADJA HÖGNER: First, I want to thank you for the possibility to speak here in this great area. I want to thank the organization team for organizing this really fantastic meeting to Mark and Krista and to all of the others.

My name is Nadja Högner and I'm working as a research assistant and the temporary leader of the Department of Education and Rehabilitation of blind and low vision individuals for the institute of institute which is part of a University in Berlin, Germany. You can see the institute here in this picture. The Institute is part of the main building of the University which are situated in the center of Berlin. It can be seen in this big picture.

Last year I finished my PhD about stress in people with Usher Syndrome type 2. First I want to talk about the theoretical background and the objects of the study. Following I will present the methods and some main results which will be discussed. Concluding I talk about some possible implications for the practitioners in Germany. The sensory impairment in Usher Syndrome leads to difficulties in many

different areas, such as recreation and work and communication and orientation and mobility. That can be seen as risk factors for stress.

*(Högner's presentation transcript removed due to publication rights. See abstract.)*

Due to their dual sensory impairment people with Usher syndrome are assumed to have a high risk of stress experience. The purpose of this study was the development and evaluation of a questionnaire (SQ) to assess frequency and intensity of stress by external stressors in people with usher syndrome type II (USH2).

The construction of the questionnaire is based on the domains of the component "Activities and Participation" of the WHO's ICF concept, which have been modified. These modifications lead to the domains "Communication", "Orientation and Mobility", "Activities of Daily Living", "Interpersonal Interactions and Relationships", "Recreation and Leisure" and "Work and Employment", which were used to postulate external stress factors. The questionnaire was administered to 262 adults with USH2 (ages 17-79, mean age = 51; 53 % female; 32 % employed) and evaluated through item and factor analyses. The evaluation shows good indices in terms of item and factor analysis. The a priori postulated structure was well reflected in five factors (after exclusion of the items belonging to the domain "Work and Employment" since most adults were unemployed).

In addition to the SQ, the standardized stress questionnaire "Trierer Inventory of Chronic Stress (TICS)" was administered to compare stress frequency between the USH2-sample group and a German reference group (n = 604). The investigation concluded that people with USH2 experience stress more often in the TICS scales, which indicate a lack of social-emotional need fulfillment ("Chronic Worry", "Social Isolation", "Being Overwhelmed with Work" and "Social Tensions"). Less stress was experienced in scales which include high expectations ("Work Overload", "Social Overload" and "Success Pressure").

As a result of the examination of differences between the single factors' and the TICS scales' mean values, it turned out that the biggest stress in SQ (related to frequency and intensity) was seen in the factor "Orientation and Mobility" and in TICS (with regard to frequency) in the scales "Chronic Worry" and "Social Isolation"; these obviously are the central problem areas of the participants of the study. In the SQ as well as in TICS stress frequency and stress burden were dependent on person specific variables (age, gender, partner and work).

The results give indications for rehabilitation arrangements to avoid and reduce stress in people with USH2 especially in the areas of Orientation and Mobility, Chronic Worry and Social Isolation.

MARTHA STEELE: A recurring theme helping each other, communicating with each other. Our next speaker is Catherine Blanchet and her topic area is hearing educational socioeconomic and vocational impacts of Usher Syndrome, Dr. Catherine Blanchet.

DR. CATHERINE BLANCHET:

Thanks to the organizing committee for giving me the opportunity to make this presentation today about Usher Syndrome type 2. I'm a French clinician and an audiologist working in Montpellier, a small town in the south of France. I work in the National Center. This is a particular unit which was created in 2004, thanks to a national government for studies rare diseases. It is an interdisciplinary department dealing with rare diseases both affecting hearing and vision.

First, I want to emphasize the importance of sensory inputs for the development of spoken language. Let's keep in mind what Claes Möller said this morning, we hear with our eyes and we see with our ear. Hearing is of course essential for developmental language. The baby can hear and recognize words and give them meaning and finally access to grammar. But hearing is not the only input required. The vision is the second most important sense involved. Take the example of referential communication, which is a primary step of nonverbal communication in infants, all of the parents know that their baby look to the parents to have eye contact and they can point to things and after getting attention. The babies can also quickly recognize faces and emotions and later they learn to use even unconsciously lip-reading to improve their speech perception. In case of bilaterally congenital profound hearing loss without any hearing rehabilitation children can hear human voices and sometimes neither surrounding noise. So they have to other choice but to use their vision to develop a communication logically based on sign language. In case of congenital blindness, the visual inputs are absent. And despite normal hearing, some delays are known to occur in spoken development, spoken language development in particular, in referential communication and in the constitution of the lexicon. Thus in case of isolated sensory impairment the remaining sense is used to complete the perception of the missing one.

Usher Syndrome is characterized by both hearing and visual impairment. And a key feature is that the visual loss is delayed compared to the hearing loss. The hearing loss is congenital, that means it is present from birth while the visual loss begins during -- later during adulthood.

In Usher Syndrome type 2 is usually moderate for severe hearing loss with a down sloping configuration. That means that the children can hear low frequencies, can hear human voice, they can recognize male and female voices and know when they are being called thus their natural inclination is to use spoken language in hearing rehabilitation.

However they don't properly perceive high frequencies which include some things that is important to understand the meaning of the language. The children will compensate the lack of hearing with lip reading or cued speech. When they grow up the loss of vision eventually occurs and what that is used so far as an alternative. So the aim of the study is to analyze the impacts of this dual sensory impairment and hearing aid acceptance and communication mode and educational and vocational and socioeconomic status and last but not least daily life autonomy. The patients studied were selected from the patient who attended the national Genetic Sensory center. 73 patients with Usher Syndrome type 2 syndrome characterized with the molecular level were selected. They underwent a face to face interview a visual assessment and cochleo-vestibular assessment..the median age at the first consultation was 41 years old.

Since this study started before the introduction of the nation neonatal program we did not know the onset of hearing loss. But it was diagnosed in childhood with a median age of 5.5 years old. We can notice that a few patients the hearing loss was diagnosed later when their vision began to decline and impacted their communication through the loss of lip-reading capacity.

As expected the visual loss occurred during night vision. For night blindness it was 18 and 26 for the visual field reduction and the 32 years old for the diagnosis of retinitis pigmentosa are but for some patients, we can notice that the visual loss can occur as early as the first decade of life.

Overall the mean age of Usher Syndrome diagnosis was 35 years old. Now, let's consider the hearing loss and its rehabilitation and its impact on communication. As expected symmetric sensory neural hearing loss was found usually moderate with a severe or down sloping configuration. At the time of consultation, 22% of the patients did not use any rehabilitation device and half of them refused to consider it.

21% of the patients use optimal hearing aid. It was unilateral hearing aids where as the bilateral hearing loss. It may be explained because it is expensive. In France we are lucky because we have a national Social Security and the patient if they have both impairments the system will cover the hearing aids costs, but if he's an adult he has only his related hearing loss, the system will only cover the third of the price.

The second problem was the 10% of the patient produced not powerful hearing aids to not restore the high frequency loss. These patients were usually young adults, who wanted to hide the disability and have some relationship with other like-normal people.

Finally, 58% of the patients had bilateral external behind the ear hearing aids and at the time of the consultation the patient needed a cochlear implant.

An assessment of speech perception evaluation was carried out to evaluate the usefulness of hearing aids and the residual use of lip reading.

The tests were performed with a speech therapists and the first task was for the first patient to repeat monosyllabic words word afterward with two experimental conditions first with hearing aid only and then with lip reading.

The median score was 83% with hearing aid only. And with the in addition of lip reading the median score increased to 93%. That means there were much us of lip reading in the majority of the patients.

8% of the patients could not improve their because of more advanced stage of loss of vision. The second task was connecting this discourse tracking. The patients had to repeat meaningful sensitive fragments for five minutes to measure the number of words they could repeat per minute. This task is more difficult. It is not only dealing with single words but also with flow of speech. It is closer to more real communication conditions. Among normal hearing adult, the connective condition is about 120 words per minute. In Usher Syndrome patients with hearing aid, the median score was 78 words per minute which is decreased compared to normal hearing. With the in addition of lip reading even if some

patients could increase their sore the CDT score was decreased for 28% of the patients. That means that for this patient the residual lip reading capacity was not sufficiently efficient to increase the perception of fluent speech. Intelligibility was normal for the patient and the patient could use oral language. One patient can also use sign language.

Now, let's see the social impacts. Concerning -- many of the patients have mainstreaming education. 54% needed part time inclusion and 8% attended a school for the deaf. We compare the highest final academic degree with the French general population using the data of national demographic institute. In both populations, 53% did not achieve high school graduate level, but in Usher patients more achieved a training vocational certificate which was better than the general population. It may be explained by the parental concern and educational supports. Among the patients who receive higher education levels, they chose short rather than long studies.

>>: Considering social and occupational status there was a similar distribution between layer force and economically inactive population. In both populations, workers were 53% with the majority of employed compared to say unemployed. In Usher cohorts, 6 patients benefited from work arrangements like adapted working hours. 12 patients, that means 30% of the workers still have to drive even at night to commute.

The difference between the two populations concern -- in Usher patients cohort the retired people were underrepresented because they have not reached the age of retirement yet.

The most important difference is the important part in which the cohort of disability pension recipients, 15%, versus 1 in .5% in the general population. In fact for those patients they used to have a job but had to quit it early with a median age of 45 years old.

The dependency can be marked by five patients who live with their relatives and 12 patients who need caregivers to go outside their home. At the time of the first consultation, no patient had attended a low vision rehabilitation program yesterday. Whereas -- so Usher Syndrome type 2 disability which changing their life. Concerning hearing, when the visual loss increased it is usual to the patient to consider the hearing not any more as a disability but as a valuable help for low vision rehabilitation. It is not easy because the patient has to live in the world between hearing and vision. Concerning hearing, -- they are necessary between audiologist, speech specialists and low vision therapists. The objects of hearing aids might be sought out. Of course it is important to understand speech in environments or even in noisy or quiet environments, it is also essential to preserve the perception surrounding those and to localize them to increase the safety in the streets. In particular, in France, because French drivers are not always so well educated as a Boston driver, so be careful if you come to France.

More seriously, we should avoid the use of assistant and we should use orientation and mobility training in each new area to help the patient to adapt his new perception. Presenting France national program has been implemented to increase the medical access and the rehabilitation program early in life for all of the patients with a rare disability. In 2005 we have created a network which includes all of the hearing loss services and the low vision rehabilitation resources and this program can provide more personal support program all along the life in an Usher Syndrome patient. I thank you for your

attention. Thank you very much, our final presenter in this particular session is Susanne Morrow. Her topic is focusing on now, for tomorrow.

SUSANNE MORROW: Good afternoon, my name is Susanne Morrow I'm the project coordinator for the New York Deaf-Blind Collaborative. Go Susie! I have my Peeps here in the crowd. My other peeps are in the crowd. I'm also a sign language interpreter. Thank you for your work because I'll be in your shoes another day. I'm here with my colleague Kathleen LaBeck who will introduce herself shortly. I'm here to talk about specifically post-diagnosis. We have a diagnosis and what do we do next? In schools in terms of support for the kids and support for the families? I'm the coordinator of a grant. How many of you know that you have a state grant that is specific for kids who are deaf/blind? This is the first problem. So, we are a federally funded grant that is funded by the office of special education programs. We are what is called a technical assistance grant. We provide resources, support, training to families, to service providers, educators, all specifically around students between the ages of 0-21 who have combined hearing and vision loss. Of course, a huge part of this is for kids and young adults who have Usher. Our website is here. It is NYDBC.org. What I want to point out is that you can go to the national website which is nationaldb.org and find your state representative. We've been talking about this for the past three days. How important it is that we are connected and the fact that you are not aware that you have free state services is a concern.

If you go to nationaldb.org and look up your state deafblind representative. For anyone from here in Boston or the local area the booth is out here and you have New England Center for Deaf blind services. Every state has someone you can turn to.

I want to emphasize other colleagues from Helen Keller National Center. You each have a Helen Keller National representative for you. We work closely together.

For today's discussion there are three points that we want to share with you. The first is specifically around a curriculum that I designed for a support group for young adults who have Usher. The second point is Usher Syndrome family socials that we've hosted and thirdly about the concept of interdisciplinary teaming and best practices in service delivery.

About this curriculum, well what we know is that we have diagnosis and obviously we are getting closer. We have made a lot of strides in the field about accurate diagnosis but the concern is the lack of follow up in terms of educational support. Supports for those doing the education and providing mental health support to students out in the schools. For students and for you as families.

I'm going to talk specifically about students who attend the School for the Deaf. A lot of that information can be extrapolated for kids who are mainstreamed. Particularly for those who attend the school for the deaf, they have expertise in deafness and hearing loss and they know how to make language choices, but they don't know about vision, different eye disease or appropriate modifications. That in and of itself is of concern.

There was a big push about, ten years ago or so, particularly with the state deafblind projects to get out there and help state schools for the Deaf to do more screening and make those observational

identifications to then make appropriate referrals for students. Because given the statistics we've been talking about a good deal of students are at risk for Usher Syndrome especially for those attending the school for the deaf. There's no standardized curriculum available to those individuals to provide the appropriate supports within the classroom. Again, particularly around the psychosocial aspects.

The counselors, transition counselors and social workers and school psychologists have their best interests. There are therapists available but without the appropriate training or resources, they are left scrambling. Looking for isolated resources to try and grasp their hands on. I just mentioned to you the National Center's website. How many of you knew that there was a national website?

Again, even for this group that is really in the know, a highly educated group of individuals, still not knowing what resources are available. Right, again, constantly trying to get the word out.

So what happens? I live in New York and we have seven state schools for the Deaf. It is a lot, we are a large state. The largest state school is located in Queens. Just given the number of the students there. This looks at 0-21 for us. They are at the highest risk for a significant number of kids with Usher Syndrome. As what we call ourselves the TA project the technical assistance project we are responsible for outreach, training and raising awareness and over the course of time staff become more aware, but then not exactly sure what to do next.

So we look at the number of students and this is a large school, so they have approximately 320 kids which is pretty big in this day and age because we all know that the population for the schools for the Deaf are shifting significantly because the numbers are smaller. Given the location where we are the numbers are pretty high. They are at risk of having a good number of students.

Their requirement for hearing loss into state schools in New York state are pretty high. They have severe to profound hearing loss. Of course they could also be kids who have Usher type 1 and Usher type 2 depending on where they fall on their audiogram. During a specific period of time in 2011 they had a good bubble of kids. 7 students between the ages of 15-20. Think about it: in one school that's a significant number.

A significant number that left counselors saying "what do we do" we want to make sure we support these kids the best way possible and that leads to supporting families.

Also just to make clear, too, the language use is sign language at Lexington School for the Deaf. Some with auditory amplification, some students with hearing aids and cochlear implants, there is a mix. The primary mode of communication is visual. They very much identify with their Deaf sighted peers. They identify with their peers who are sighted and who are Deaf, embrace Deaf culture in a high degree and would grow up and be part of the broader Deaf community. This draws the picture of who we are talking about.

They were scrambling so I said let’s pull together some resources. I had some specific experience working with this particular population. I was fortunate, I started my career at Helen Keller National

Center 20 years ago, I must have been 12 at the time. Given that role, Chris knows me well. There was a chuckle there.

If you don't know Helen Keller National Center it is the only rehabilitation Center in the country for those who are deafblind. About 50% of the folks who come there have Usher Syndrome. Having engaged with countless young adults, both at the Center and also at different teen events. Which are weekend events where I've been asked to coordinate interpreting and support services and have the good fortunte to spend countless hours with young adults with Usher Syndrome who have become my teachers over the years. Out of this grew this idea, instead of relying on scattered resources let's put things together. Let's make it easier. There should be an easier way to do this. Ilene Miner was one of the first to publish on this and how to put it together in a package on a regular basis. We designed a multiyear curriculum. To get through content and the real comprehensive pieces we knew it would take time. Looking at this as a pilot.

I should say, too, each of these students because they each have an IEP individualized educational program. It was noted that they would receive ongoing mental help support both in a one to one and a group setting. Because they have the good fortune of being in a large environment with multiple students. We wanted to identify outcomes asking, when we do this what do we expect? As a federal grant we are looking for outcomes. We have to measure and report back to our supporters. Looking at some pre/post measurements. There are many that we were lucky to impact over the course of a couple of years. Some of the main key components are: We wanted the students to have a better understanding of their own vision and hearing. To better understand. I think we've talked quite well over the past couple of days about more information is good. Now we have to think about these are adolescents. We have to be cognizant. Understanding their own hearing and vision status and the etiology. They have no concept of deaf-blind culture. Let them store that away. We had to focus on of course self-advocacy skills in terms of communication and access. Being at a school for the Deaf where everyone signs if you know about Usher it is difficult to watch a fast moving object. Sign language is a fast moving object from one person to another.

How can the student self advocate to make that experience easier? To educate their peers and their teachers about what will work for them. We wanted them to understand or start to understand the service delivery system. What is available to them? They are not experts or expected to be at that age they are experts about what they need. Starting to learn a bit about services and things that can be provided.

Also wanted to design it in a way that basically kept their interest. They are teenagers after all. The idea was not to go in and talk to them. That's not going to work. I have a budding 14 year old, I know that very well.

We wanted to look at articles that were age appropriate. Some are great for parents but not okay for young adults. Being extremely cognizant of that. Bring guest presenters in with expertise in deafblindness that means a lot of different types of people and connecting with people that they can understand. People from their own community. Have the session focus on group activities. Doing more

and talking less. Talk a little, let's do a fun game. That game happens to have an educational component behind it. Really critical is the community connection. Having that understanding of someone else is out there like me. You know, I think for the parents in the room, I have spoken with a lot of parents over the years. Envisioning what your child will look like in the future is difficult if you have not had an opportunity to meet them. Allow the community members to come in and interact. We did that through uses technology, most likely. (shows the curriculum on the screen) This is a little complicated. This is how the curriculum fell out. Several components here. The left column talks about what outcomes did we intend? We didn't want to do something just to do it. We wanted something that has a purpose. We were able to identify outcomes. The next one talks about: How many lessons did this take? Content is heavy. We talk about give a little, step back, give a little step back and review. Some sessions took multiple times. Each one would have a particular topic. The first one: What is Usher Syndrome? That's complicated, difficult to understand and then the design was always about a discussion and a group activity. Discussion and group activity. These are resources. We wanted to be able to provide a tool with resources we didn't want the counselors or therapists to find their own tools to support these activities.

Being in the field where we are outcome driven and data driven in the field of deaf blindness we have designed a series of outcomes. Outcome and performance indicators. If we go in to provide training what are you looking to achieve? To be cognizant of those asking for support. The category of social engagement, the category of orientation and mobility et cetera. The nice part is that they are also broken down into service provider outcomes. For example, the list I have up here. I randomly chose one. The critical one for the service providers in the classrooms, what do they understand about deaf blindness? And break it down. All the while we're supporting this curriculum and we are educating the professionals at the same time.

There's a series of outcomes for young adults around self determination. Those pieces are tied into it and family outcomes. What were the pieces that families need to know? That is a separate document we can get to at another time.

We also had some unanticipated outcomes as anything that you host, other things happen that you don't predict. A lot of the content sections took double or triple the amount of time. That's always a good learning lesson. Because they are young adults. You say to yourself, didn't we talk about this last week and the week before? That's okay, let’s review it. Be cognizant of where people are in the given movement of development. Ilene Miner's book spoke about how this is cyclical. To be able to be responsive to that.

Next is to capture outcomes, such as self-reported change of knowledge. Across all content areas. We did pre-post questions and they could self-identify change of knowledge across all of these different content areas.

Then it was interesting, definitely unanticipated was that this group that we hosted for two years then faded out and this went into one on one counseling. They really felt, they themselves and the parents because you all drive the IEPs, really felt that their young adult had gained so much knowledge and

affected their perspective in such a way that they did not feel the need for the larger group and went to one on one support counseling where it was needed. From there led into another outcome the Usher Syndrome supports for both children and young adults and their families. The last one, which is critical, is partnerships across state schools. We have a good system where the state schools for the deaf talk to each other. This was a specific one where they partnered together. Specifically around the Usher Syndrome family socials. Some things that came out of the curriculum, we know it has to be flexible, the resources are there, but to think about it in a broader comprehensive fashion will be very helpful. Think about where the young adults are developmentally, specifically. I think we have a lot of good possibility to take this curriculum and adapt it for the folks who are out in the mainstream setting. The concepts are the same it just has to be tweaked. Of course parent engagement is critical throughout the process and follow up support and education for families is critical.

The next piece that fell out of it, we started hosting family socials. We felt that the students were starting to get a lot of content in the classroom, but the parents were falling behind. We don't want to leave anybody behind to take this in a comprehensive fashion. We did what Claus did before. We bring the families together in a casual environment on a Saturday, come together and this is where the state schools partnered together and we'll open the doors and let other schools come to us. Not just about having those people in one building. There are holistic ideas, students meeting other students. We did not care if it was Usher type 1 or 2. Then have the students have a safe place where they could speak and a safe place for the parents. Maybe we were not as nice as Claes Möller because we didn't allow the parents to stay in the room. They left and had the opportunity to have their educational component. We picked a topic that was educational but fun based around it. Activities and a light way to support that. We've seen some nice things that have grown out of it. When you hear the students say "when are you meeting next" the idea of partnering and meeting with others with similar life experiences and the families getting registered with us. I'm going to throw that in there too. That partnership is critical. We need you too. The last piece which is a critical component that covers this whole entire concept is this interdisciplinary team approach. Thinking about collaboration, collaboration and what does it look like for these young adults? Kathleen is going to speak a bit about that in terms of best practices in the role of the teacher for the visually impaired based in the state schools for the Deaf in New York.

(Switch of CART Provider)

>>: Hello. Hello. Hello. Boston. How are you? My name is Kathleen. And I will be speaking to you today about my experience with families and as well as the trans-disciplinary approach.

I would like to start by thanking the Coalition for everything that you are doing for all of us in the field. And I would like to thank the kids and families who came here because I understand that many of you practically moved mountains to come here. I was speaking to a few women from Australia, and they were discussing their 28 hour trek here. And I promise not to complain about my 7 hour drive home

( Laughter )

after I heard that.

I am a teacher of children with vision impairments. And I've been doing it for five years now. Several members of my family are also TVIs. I have an older brother and younger sister. So it is a family business. And we've also been able to recruit some family friends and cousins and what not. So it is nice to have our own "coalition," if you will. And it is very nice to bounce ideas off of fellow TVIs.

My role working with families is truly an honor. Uhm, it is really, probably the best part of my job is working with the families and working with the kids. Being a teacher is great, too, but having that personal one on one connection with people is really paramount to my success, and to my children's success. And I've had very varied experiences. Uhm, my very first student was thirteen years old, she did not have Usher, but she had a progressive, very quickly moving vision impairment, and I didn't know what to expect when I first met her. She was being home schooled. And you know I'm walking into a situation where a kid is being home schooled, very large family, you never know what to expect, and as soon as she met me she said "Hi! My name is Kinsasha, are you going to teach me Braille?" And I literally almost fell over because she was so empowered. This 13 year old young woman was "take no prisoners." She had an attitude of, "yeah, I have this thing, I need Braille because I want to be able to read to my brothers and sisters." I couldn't even believe it because when you mention the "B" word, "Braille," people are just not feeling it. But this young girl was just like "okay, what do I need to do? What do I need to do in order to live a happy and better life?"

And now, five or six years later I'm currently working at a School for the Deaf, and that hasn't necessarily been the case. I've gotten a lot of, uhm, resistance from kids who have not been nice to me in the hallway, or who refuse to come see me. And also from families who are ignoring e mails and don't want to talk to me. I understand because I represent the issue.

I think what the major difference has been with my experience with the families is knowledge. And I really applaud the families for coming here today, and for being brave enough to say, "you know what? I need to learn more about this. What is this about?" Because when you have the knowledge, you are, therefore, empowered. So that young girl I first spoke about, who wanted to learn Braille, she was fully in the know. She knew everything that was happening to her. Everything that was going on with her health. She did her own research. She actually taught me quite a bit about the field of blindness and vision impairment because she was my first student. It is really remarkable.

And then you have the other families, and the other kids, and what the overriding factor tends to be is, uhm, fear, and denial. And as professionals in the field, many people have spoken about it, we need to meet people where they are. And so it has been challenging, but providing information to the families, and to the kids; particularly during these Usher teen socials, has really been extremely beneficial to everyone involved. Because again, if you demystify it then things don't seem quite so scary. And in keeping up with that, uhm, the trans the trans-disciplinary approach, what that is, specifically, has to do with the educational team of which the parents should be involved. And are encouraged to be involved. Even if the administration at the school is telling you "not" to be involved. I highly encourage you "to be" involved because the squeaky wheel gets the oil. Because I can do what I

can do as an advocate for your kid. And believe me, I've definitely ruffled a few feathers here and there, and I'm okay with that. But if a parent makes a phone call, or if a parent writes a letter, or if a parent shows up on the doorstep, things tend to happen. So just keep that in mind.

But what the trans-disciplinary approach really is, it is the whole team getting together, hopefully on a regular basis, to really discuss the student. It is very student specific, and they are there to discuss what they are doing with their particular student, as well as sharing skills and information that is specific to their field. So in the room could be the P.E. teacher, the physical therapist, the teacher of the children with vision impairments, the orientation and mobility specialist, and the psychologist, et cetera, et cetera, and of course, the parent, which would be the most beneficial. And then the idea is to design what would truly be best practice for this child as an individual because as we have all learned, just because you all have the same type of Usher doesn't mean that from a psychological aspect you are handling it the same way. Or even your vision, where is your vision? My vision is not your vision. My hearing is not your hearing. So it definitely needs to be individualized.

And accountability is most assuredly necessary when you are taking this approach. Uhm, it is highly encouraged that there is a note taker. And oh, "so the PT had this idea. What is the follow up on that? Who is going to follow up with that person?" If I say I'm going to do something, then there should be somebody else in two weeks who says "hey, Kathleen, did you get that done?" Or "where are we in that regard?" It is best, if you are meeting on a regular basis, sometimes the logistics of that aren't necessarily the easiest, but if admin really is into it, then it will happen. You are hoping that it can be at least once or twice a month. And one of the things that I would most assuredly have to share with the parents is that for you all, you are the greatest advocates for your kids. And I thank you all very, very much for coming here today. It has been really, truly, a great honor to speak with you. And keep up and do your best. And poke administration. Thank you very much.

( APPLAUSE )

( APPLAUSE )

>>: Speaking of poking. How many of you know that there is a National Family Association of the Deafblind? Right. National Family. Get connected with them. See the Helen Keller booth. They have brochures out there. For your young adults there is a consumer driven organization called the American Association of the DeafBlind. Get them connected there. Connect with us at the State DeafBlind Projects.

I have a few samples of the curriculum with us. I'm happy to share those resources with you. Any other questions, let us know.

Again, thank you very much for your attention.

( APPLAUSE )

MARK DUNNING: Yes?

>>: Can I say something about the New England Consortium?

MARK DUNNING: Sure. Do you want to risk the wrath of being late.

>>: The wrath of Mark. I just wanted to speak for Tracy Evans who is not -- she is not here right now. Uhm, but who let people know we are in Massachusetts. We do not have a state School for the Deaf. The services are not, uhm, centralized in the same way that they are in New York. But we do have a New England Consortium for Deafblind that is located at the Perkins School and which provides educational teams, or individuals at the request of parents, or schools, or programs. It is federally funded. It is at no cost to parents or school districts. And individuals, professionals, vision specialists, hearing specialists, are available in response to any inquiry. So I just wanted to be clear that New England Consortium does offer services, uhm, and you can collect information or check online.

MARK DUNNING: Thank, Eleanor.

Okay. Thank you, everybody.

## Panel: Psychological Aspects – Patient Journeys
## Family Panel:
## Ms. Elaine Ducharme
## Mr. Ryan Thomason
## Ms. Molly Watt
## Ms. Chloe Joyner
## Mr. Mike Walsh

MARK DUNNING: So our next session is our -- probably the most popular thing we do at these conferences. It is our Family Panel. So I would like to ask Molly and Chloe and Mike and Ryan to come down. And I'm going to check with Elaine and see how she would like to play this. So if you guys want

to come on down. And I know that David Alexander wanted to say a word about a project that his daughter is doing. So while I figure out what is going on with Elaine I'll have you say your two minutes.

>>: Hi. My name is David Alexander, and I want to thank Mark and everybody else for giving me this two minutes. Uhm, I've spoken to many of you about what I'm about to talk about, and I've been given two minutes, so I'm going to go fast. Put on your seat belts and we'll do that.

Uhm, I have a daughter, 35 years old named Rebecca Alexander who, uhm, has Ushers 3, that is associated with Azeshanic Jews. And Rebecca is a psychotherapist living in New York City with a very thriving practice. She also has been doing, for many years, ah, teaching spinning classes, and she also, crazy as it may be, ah, does these civilian military combines where you are crawling under barbed wire, and crawling over fences, and all I will say about that is exercise is key, Usher Syndrome or not.

Rebecca has written a book titled: "Not Fade Away" which will be released on September 10th of this year. Uhm, it is about to get national attention. I, uhm, cannot tell you what it is because it is not public yet, but you'll be able to, ah, read about that.

She will also be on the Today Show on September 15th, I believe it is, and some of you may know, but a number of years ago Meredith Viera and along with Rebecca's brother, her older brother Peter, did a piece on the Today Show. And Peter recently did a piece on a young woman, she is actually a young girl still, uhm, in Manchester, Michigan, which is near Ann Arbor about Usher Syndrome, so he is doing his damnedest to bring the awareness of Usher Syndrome and RP and these other diseases.

The purpose for her writing the book is several fold. One is she wanted to do it for a long time. She wants to do it to help people who are similarly situated to herself. Or have other, ah, RP diseases, or frankly any other type of disability. Ah, as importantly she is doing it to raise the visibility of retinal degenerative diseases, including, especially, Usher Syndrome, throughout not only the United States, but throughout the world.

Uhm, the book is very personal. It is, ah, very positive. It is not pie in the sky or naive. And it is not religious in any sense. Uhm, traditional religions, I guess, other than ones just having faith. And it is very powerful and very positive.

And so I, uhm, ah, I recommend it when it comes out. Not just because I'm entirely biased.

( Laughter )

Ah, which is obvious. But, ah, but other people who have read it, and who have commented on it, including Meredith Viera, and Rebecca will be on her show when it starts. And the woman who wrote Brain on Fire. And others have said that. Those are not just my words.

So I've been handing out these cards, and if you don't have one and you would like one, they are out by the table. And I'm done.

( APPLAUSE )

MARK DUNNING: We always have time for a proud Usher dad up here.

Okay. So, uhm, so, ah, as usual, we are running behind. So we are just going to keep going. Uhm, because this usually livens everybody up as soon as we have the family panel here.

So we have, ah, tried to get a broad mix of, ah, of families. For those of you who don't know about the family panel, we do this every year. It is our most popular thing that we do. We ask, uhm -- try to get a cross-section of the Usher Syndrome community. And have them come and basically tell their stories and answer a few questions. And then we open it up to the audience for questions, as well.

So I'm going to just ask that if each person could introduce themselves, I'll let you guys introduce yourselves, and then I'll ask you a few questions. So if you can just tell us your name, where you are from, and your relationship to Usher Syndrome that would be great.

And Elaine, I guess we'll start with you.

ELAINE DUCHARME: Hello, everyone. My name is Elaine Ducharme. I am from Waltham, Massachusetts. I grew up in Connecticut, though. I became deafblind -- I was deafblind at birth. I have Usher Syndrome type 1. I don't know if I'm 1A, B, or C. I know I'm type 1. I had Coates disease and I lost my vision at some point. And I've been fully deafblind -- born deaf, became fully blind by 31.

RYAN THOMASON: Hi. My name is Ryan Thomason, I am 32 years old. I have Usher Syndrome type 2.

MARK DUNNING: Sorry.

RYAN THOMASON: There we go. Hello. Not used to hearing my voice.

I have Usher Syndrome type 2. I am from Seattle, Washington. I'm currently living in Utah. I have, ah, a wife and two kids. I am an ordering product manager for a corporation, and on the side I run a website called Watch My Read. And when I'm not doing that I'm training and competing in races.

MOLLY WATT: Hello. I'm Molly and I'm from England and near London. I have Usher Syndrome type 2A. I'm severely deaf. And at the age of twelve I was diagnosed with retinitis pigmentosa. You guys obviously know how it works. And I was also diagnosed with macular edema, and that affects everything else. So that has been really my downfall. And as a result was having a really strong support system at home, we created, uhm, a charity, the Molly Watt Trust where we try to raise awareness for Usher Syndrome because we need it. There is so much ignorance out there, and it, you know, it stops people getting jobs, and, you know, and you've all probably experienced it. I've experienced quite a lot of it.

I'm 19. I will be 20 next month. So counting the days.

And, yeah, that's it, really. That is the basics.

CHLOE JOYNER: . Hi. I'm Chloe Joyner. I'm the mum of two children. One is seven, a boy, with no vision or hearing issues. And my daughter is four and she was diagnosed with she was 18 months with type 1b. And I'm from England if I didn't say that.

MARK DUNNING: We kind of guessed that.

MIKE WALSH: My name is Mike Walsh. My accent is not as cool. I'm from Wisconsin so I'll try.

Let's see. I have Usher Syndrome type 2C. Uhm, I was diagnosed when I was 19. After my brother was falling -- falling around and he fell into a pond and so because of him I was diagnosed at 19. I started getting symptoms about five years ago, and recently, uhm, I started going around the world raising awareness with a campaign called Flight For Sight. So that is what brings me here. And thank you.

MARK DUNNING: Excellent.

So I'm going to get started with this question. But I'd like to ask you: When did you first find out you had Usher Syndrome?

What was your first reaction to it?

Would you have liked to have gotten the diagnosis sooner?

Again, I'll start with Elaine.

ELAINE DUCHARME: So I was born deaf and I grew up using sign language. Obviously I'm older, you can tell. I'm 57. So 57 means the 60's when I was growing up. Uhm, I didn't know. People didn't know that I had Usher Syndrome until I was about 18, I believe. My left eye started to lose sight and I started to struggle with my right eye. And so I knew I had problems, and my parents said eye problems, don't worry about it, but your balance, I have pretty bad balance. So the balance became a problem. I didn't have great night vision. So I went to -- I did go to a Deaf School growing up, and of course I got made fun of because kids make fun of people for stumbling and things like that. I did start to take, uhm, family workshops, that was the only thing that was really, ah, around and available for me. But I didn't understand, uhm, what it meant. And my parents really said "oh, don't worry about it. Don't talk about it." And so eventually I went to Gallaudet University and that is where, really, I started to learn about Usher Syndrome.

My brother is deafblind, as well. And my brother and I my parents went to Gallaudet University and they offered a family workshop, and that is really where they learned to understand this is, what Usher Syndrome is. I was 24 when I really understood. And I was able to talk with somebody, a man who had Usher Syndrome, himself, and started to tell me about it. You are going to have to be prepared for tactile sign language. You are going to need to be prepared for a cane. And with Braille. And I was very resistant in the beginning. I did not want to be deafblind. I did not want to be -- I didn't want to enter that world. And, uhm, you know, I started saying "well, I'll wait. I'll probably be blind when I'm 80. So I'm not going to be ready for that. I'm sure. I'm 24 now." So I was obviously in denial. So I started to

really, you know, look within myself, and realize, okay, you know, I'm in denial, I need to learn the skills that these people who have Usher Syndrome are telling me, and, uhm, and by 27, uhm, I had really started to not being able to rely on my sight at all. And I'm happy that I was able to have that kind of self-learning at 24 and able to really start to say, "okay, I need to be prepared." I did -- I went to the Helen Keller Center, and I learned about myself. I learned about my identity. And I was able to -- once I accepted who I was, I was really able to, you know, I was really able to take off at that point. But I know that I was very late in understanding that. And in accepting that. So once I finally did, though, in my 20's, I just took off and life's been great.

MARK DUNNING: Can I just follow-up really quickly. Would you have liked to have known the diagnosis sooner?

ELAINE DUCHARME: (Shaking head no.) Hmm, I -- boy, I honestly don't know. I really don't have a good answer for you. I don't know because I can't look back. I mean that idea that I was, like, "oh, I have until 80 until I'm blind." That denial was -- that was hard. So maybe knowing sooner would have made me be able to accept sooner. Once I accepted, that is really when I was able to learn the skills I needed. So I don't know if that would have impacted when the acceptance happened.

MARK DUNNING: Great. Thank you.

Ryan?

RYAN THOMASON: I was diagnosed when I was 27 years old. And we were sitting in a room and it got all dark, and they had just done an eye test and my wife was sitting behind me and the gentleman just said "you have Usher Syndrome type 2. There is not really much we can do about it. Find yourself a doctor." And just kind of left it at that. I had hearing aids since I was two years old. And we just never really connected the dots up to that point. I did play sports in high school, and I was always very athletic, and doing sports in college, and everything like that. But apparently a couple car accidents didn't come into my parents head that maybe I shouldn't be driving.

( Laughter )

But only one of them was really bad.

( Laughter )

But, yeah, that is how I was diagnosed.

MARK DUNNING: So would you have liked to have known sooner, maybe, like, before that car accident?

RYAN THOMASON: Uhm, it is a difficult question to answer because I don't know if I were to make changes in my life. I'm very happy with what I have now. With my wife, my kids, my job, and who I am. So I don't know if I had done things differently if things would have changed. So I'm very happy with, you know -- even though it has been difficult, you know, it is my life, and it is what I have.

ELAINE DUCHARME: Sorry. I just want to add since you said that. I have to so strongly agree with you. I think, you know, as I'm thinking about the question, I think maybe it was best how it happened, you know, because I accepted when I accepted. And maybe if I had known earlier I would have just worried for those 18 years before, you know. So I think that I agree. I'm happy with where I am. So maybe it was meant to be when I found out.

MARK DUNNING: Great. Thank you. Molly?

MOLLY WATT: 18 months old I was registered severely deaf and I was given hearing aids. I've relied on them -- I still rely on them, obviously. But I was just deaf, if you like. Until I was in year 6. You guys, your educational system really confuses me. So basically eleven years old, uhm, I started noticing I couldn't read the board, I was very clumsy, and I got lots of headaches. So soon after that I got registered with Usher Syndrome type two. And they said to me I would lose a lot of my vision until I was in my late 20's or early 30's. But they were kind of wrong about that because within two years I was registered -- well, you call it legally blind. Uhm, so I have virtually no vision in my left and I see through a tunnel in my right eye. Uhm, so, yeah.

The question regarding when I was diagnosed. I can't really imagine it being any different. Uhm, it has been a -- it has been a tough journey, and all I can say is that I am so thankful I have my family and the support system that we have found on Facebook. There is no way I would have coped at the age I was.

CHLOE JOYNER: And for us, it is a story shared with many young people here. My daughter's deafness was picked up in the newborn screening program in England. She was two weeks old when we were told she was profoundly deaf. She had her first hearing aids at six weeks old. And so the story moves on a bit, uhm, and she was late to sit, and late to walk, and the geneticist that we were seeing, just to explore the causes of the deafness mentioned Usher's at approximately 9 months, when she was 9 months, and referred us for an ERG. In England they have them without sedation, so they can happen on young children. We were there for -- and I guess from that point, as a parent, your heart plummets, as you perhaps remember. And we kind of would -- we didn't receive an official diagnosis until she was 18 months through the ERG. And, uhm, and I felt, at that time, that we had only gotten vertical after the deafness diagnosis. So it was a big blow. Uhm, and early stages of coming -- finding my peace with it, that is the way I phrase it, rather than "coming to terms" because it is a continual process. Finding my peace with it, the early stages were very similar to the deafness diagnosis, and we had to go through the same stages, but I think the nature of diagnosis is very different. Uhm, you know, with the deafness we could be working on it. We could be helping her. Supporting her communication through various sign, exploring possible, uhm, cochlear implants, which she now has. But you receive a diagnosis of Usher Syndrome, as we all know, and there is no immediate prospect of being able to do anything about it. And I've personally found that very hard as a parent, uhm, not having any control over something so precious. It is hard. So, uhm, I guess the question that I would perhaps answer is whether I would have liked to have found out later --

( Laughter )

Uhm, not earlier.

( Laughter )

And I think I probably would say, actually, I don't know -- I actually would have liked to have found out later. I understand that there are -- and I'm open to other ideas. I've heard different cases for this over the last three days, so I'm very much open to discussing it. But, uhm, I think absolutely to be able to consider any practical steps you can take, that's fantastic, and useful, and important. But in terms of being delivered this news, which is, you know, so difficult, and yet we are powerless to change it, the best description is, uhm, that dream you have when you are walking and you can't get anywhere. You are just heading towards something that you are powerless to change, and yet you are very frightened of it. And that is how I feel as a parent. I mean every step that we can take to empower ourselves we will take. But I still think it is very hard to live with a diagnosis like that from such a young age when you -- when you are not anywhere near even the treatment stage or anything that you can do.

MIKE WALSH: Uhm, yeah. Like I said before, I was diagnosed at nineteen. And my reaction at nineteen, I had no symptoms, uhm, everything was peaches and cream, you know. I could drive. I could play sports. Peripheral vision was excellent. I had -- and going further back I was diagnosed with having -- needing hearing aids around three. But when it comes to Usher Syndrome, life was good. And then all of a sudden my parents are dragging me down from Madison, Wisconsin to see a specialist, Dr. Fishman. And all of these crazy eye tests, you know, painful. We've all been through them. And, ah, you know, all of a sudden they are like "you have Usher Syndrome. " And as I said before, this all happened because my brother fell into a pond. Yeah.

( Laughter )

And, ah, so he has hearing aids, as well. So we both had hearing aids, and we are brothers. He is five years younger. And, uhm, and so they have connected the dots and they suspected him, so therefore me, as well. And, ah, so all I can think of, if not for his diagnosis -- for his early diagnosis, I can only imagine had I been driving along at night in the past few years, I stopped driving a couple years ago, but had I been driving along and not knowing what was happening, just assuming I was having a bad eye day, something serious could have happened. But to answer the question if I wish I had known about it earlier, uhm, I would actually say I wish that, you know, in a perfect world I would like to know about it later because at nineteen I had no symptoms, and so basically between 19 and the time that I gave up my driving at 35, uhm, I'm 37 now, so about two years ago. For sixteen years my parents were like "how's your vision? How's your vision? How's your vision? How's your driving? How's your driving? How's your driving? How's your driving?"

( Laughter )

They really asked me no other question in life.

"How's your eyesight? How's your driving at night?"

So, ah, so --

( Laughter )

-- thanks to my brother, I knew.

There is my dad over there if you want to bug him.

( Laughter )

He is taking a picture and doesn't know how to use that phone.

( Laughter )

He is a great support though. Thanks.

MARK DUNNING: Okay. Excellent.

( APPLAUSE )

So I think you guys have sort of touched on this, and again I'll start with Elaine and we'll work our way down. But how has Usher Syndrome impacted your daily life?

ELAINE DUCHARME: You mean my life now. So let me think. Today I don't even think about the word or, you know, Usher Syndrome. I mean I'm 50 -- I'm almost 58. I lost my sight 30 years ago. I've been deaf all my life. So I really think of myself as human. I mean I'm just Elaine. I think that is because it is so long. My daily life, I don't think about it anymore. I forget. I'm just very used to it. It has been decades that I've been a deafblind person. Yes, I have Usher Syndrome. Yes, my name is Elaine. But I don't really think about it day-to-day anymore. I am so used to, ah, to -- so used to that. I'm so used to who I am.

Uhm, and, uhm, you know, obviously everyone needs the support that they need. And they need their family and their friends. My wife and my family and friends are incredibly supportive and helpful. But at this point my life is great.

MARK DUNNING: Okay. Excellent. Thank you.

Ryan?

RYAN THOMASON: Uhm, my daily life starts at 6:15 in the morning with my six-year-old poking me.

( Laughter )

Telling me I need to get up and be dad.

So, uhm, and then I spend the morning with my kids, and my wife takes me to work. And she is pretty much the reason why I can get around and do stuff. My wife is Wonder Woman to me. She does a lot for our family. And I just work and I get home and I'm dad again. And kids go to bed and we have some adult time and then it starts all over. Uhm, you know, little things do happen here and there, but,

you know, at this point I've just kind of learned to brush it off and to keep going on. So my -- so my family is a major distraction for me.

( Laughter )

When it comes to Usher Syndrome and all of that kind of stuff.

MOLLY WATT: Sorry. Can you repeat what your question was?

MARK DUNNING: So how has Usher Syndrome impacted your daily life?

MOLLY WATT: Uhm, well, I think because my sight, ah, progressed much quicker than I thought it would, uhm, my life's changed quite a bit in the last few years. So what my daily passions were a year or more before, has changed. I have a guide dog and she couldn't come because she had a bad gut. So I thought it would be -- putting her on an airplane for seven hours, people wouldn't appreciate a dog with a bad gut. So she is home. So she is my other half, really. She is, uhm, I rely on her 100% now in the dark, during the day. Whereas before it was just in the dark. Uhm, in crowded places, I get really claustrophobic. I've just finished college where I received really, really good, ah, support that involved a note-taker. So, uhm, so I received all my notes through e-mail and I did a lot of my work on my Apple Macbook where the accessibility is brilliant. So because I was lucky enough to have the technology and support system at home, my daily routine at the moment is okay. I'm still able to live things -- do things like everyone else at the moment. So I think that is how it should be, really. So at the moment it is just, you know, you know what it is like, you just plug along until something else changes and you have to find new strategies, you have to find new ways around things. So, yeah, that would be my answer.

CHLOE JOYNER: Uhm, my daughter's vision hasn't yet deteriorated, apart from night vision. So our daily lives are not really affected by the reality of living with Usher. But they are affected by the prospects of living with Usher. Uhm, we have to spend our energy, apart from having fun and being a family and raising two young children, the energy that is left over from that, uhm, we split between trying to prepare ourselves as a family, and prepare our child, and her sibling for life with Usher, and prepare ourselves as parents. And trying to also do the things that we can do to change the reality that may face her later on. But we try and focus on the challenges now. The one, uhm, thing I was saying, my daily life that I'm affected by Usher is a small period, uhm, just before sleep, each day, uhm, I like to go to bed quite early and enjoy that when you get to read a book. Instead, since my daughter has been diagnosed, and this might sound really negative and I hope it doesn't, but perhaps other parents will relate to it. I find that period when you are not doing the usual things to your brain to stop it from thinking negative thoughts, when you are about to drift off to sleep, and you start inserting difficult thoughts you need to tackle, that is a challenging time for me. And I have found since my daughter is diagnosed, I wait until I'm completely exhausted to go to bed because I really dislike that period when I start to worry about the future, basically, and I don't have enough, uhm, enough to help me get through that. So that's one thing that my daily life is affected by Usher. Uhm, Usher Syndrome. And I think that it is a sign that, you know, it is a continual process to be able to come to learn to live with the syndrome and the prospect of it.

( APPLAUSE )

MIKE WALSH: So daily life. Uhm, I mean I'm often trying to figure out different ways to say "what?"

( Laughter )

"Pardon? Excuse me? Didn't hear you." By the third time you just nod.

( Laughter )

Anyway, uhm, so when it comes to vision, you know, it is -- in the last year or so it has been very interesting. I wear hats now. Seriously. Stop.

( Laughter )

Uhm, so that's been new, uhm, daily life. So it has been such a, ah, a big part of my family in terms of raising awareness and we help raise money. My brother is a stand-up comedian, most of his act is about being blind. So there is a lot of talking about it. More so recently since I started my campaign in January. And so I've -- I went from being extremely passive about my condition. And even when I stopped being able to drive at night, and then stopped being able to drive altogether, I was like "all right, I'll just get rides everywhere and be forced to talk to my parents more."

( Laughter )

And I even fooled with a plane. My friend, all right, go ahead. "Is this legal?" So I can still do a lot of stuff. And it has been an adventure. My daily life right now is learning as much as I can and being the opposite of passive about it. Like Molly said, it is about strategy. Tomorrow my vision will be a tad different, but more so like a couple years from now. I love technology, and everything that is happening, and I'm really excited about all the stuff. We all saw the stuff about the finger reader that the guy was developing here at MIT. That is cool stuff. And I hope to check that out soon. Yeah. Life's good.

MARK DUNNING: So let's start with Elaine for the -- for this next question. And you guys have all sort of alluded to this. And I think we already know a lot of the answer. But, uhm, what is your most significant support mechanism?

ELAINE DUCHARME: First, of course, is my family. As for most of you, I'm sure, my family has been a great support system for me. My siblings support me so much. The positive people around me, uhm, who share their energy with me, and share their support with me, and allow me to support them. I'm allowed to work with people who have Usher Syndrome and offer them support when they are going through grief and empower them through their journey has been incredibly helpful. Teamwork is really key and has been key for me. I want to make sure that I see happy people every day and work with happy people every day. Uhm, I love hanging out with people, people call me the Queen Social Butterfly. I'm always with people. You will see me always chatting with someone. And for me that is a really big support, too.

RYAN THOMASON: My wife is my biggest support system. We have been married for 6 years before I was diagnosed. We got married at 21. So, uhm, so diagnosed at 27. And my son was already one years old at the time. So, uhm, so she has definitely been my biggest support system. You know, through the highs and the lows of everything. Uhm, and my kids, obviously, uhm, my son is -- he is very, uhm, aware of what is going on. So he, you know, he helps, you know, a lot for a six-year-old, even though he probably shouldn't. But, uhm, and then, you know, just my family, you know, my aunt started a foundation to raise money for Usher Syndrome, and the rest of my family has been really active in trying to, you know, help support that every year. And, you know, and raise money. So, uhm, so definitely been having a great support system so far.

MOLLY WATT: Uhm, yeah. I have to agree. Definitely before anything, family. My family are all very positive, outgoing people. I always say in all of my talks just how grateful I am to have them. My grand dad always said, you know, life you are dealt -- you are dealt a hand of cards and it is just how you play them. Uhm, so that is something that has always stuck with me. And that just goes to show the kind of family I'm from. And also it would be the whole networking family. Uhm, I'm seriously overwhelmed by the amount of networking that we have done, and I mean where would we be without social media? It is just amazing to meet people from other countries that we have met through Facebook. And I mean the messages that I get online on a daily basis, they just mean so much to me. Uhm, so, yeah, definitely it has got to be family, friends, and of course -- I mean he will kill me if I don't call him out on this, but my boyfriend, as well. He is good, too.

( Laughter )

He always gets mad when I don't mention him in my talks. Yeah. So definitely my family. My friends. And of course my boyfriend. The best support system I could ever have. Yeah.

( Laughter )

CHLOE JOYNER: So thinking of support, I would say my partner. Although we have actually dealt with it in different ways, we have still provided support to each other. And continue to do so. But also my friends and friends that have become friends since the diagnosis have been really important. And they have sometimes come from unexpected places. And, uhm, and unexpected people, but they have just shown themselves to be really special people and I am now lucky to recognize how important that is from within this community and the strength that I take from those people and from daily life, as well. Uhm, so I would say that my friends and my partner.

MIKE WALSH: Yeah. I'm going to go with family, too, just because everyone else said that.

( Laughter )

Yeah. My family, my dad who is about ten feet from me, still trying to take pictures.

( Laughter )

Got it?

( Laughter )

I mean -- did you get it?

( Laughter )

All right.

Yes. So he is a great guy. He is on the board of the Foundation Fighting Blindness. So the minute we were diagnosed he was on the phone with whoever and, you know, he has done a lot of great work.

And then of course my brother, I mentioned him before, we sit around and have a lot of fun about it. As I said, he is a stand-up comedian, so we have -- we write jokes all the time about being blind.

( Laughter )

I'll tell you all about my blind dates.

( Laughter )

I am single.

( Laughter )

Molly mentioned, ah, about social media, and that's amazing. Uhm, I would like to, ah, I want to say Facebook groups are pretty amazing. I have found, just in the last couple of months, I've been playing around with them. Facebook groups, if you type in Usher Syndrome, there is a really big Usher Syndrome group. But even more so there is a big retinitis pigmentosa group, and you can ask a question on there, and you will get 20 responses in, like, a day. Just people with their experiences. Uhm, it is really, really wonderful. So I recommend you check them out. And you can be on them anonymously. There are closed groups. Public groups. Be careful with that, however you want to approach it.

And also the other support, of course, since I started my campaign on Facebook, Flight For Sight page, I -- in just a couple days I announced my condition to all my family and friends. A lot of my friends didn't know about it because I've always been passive about it. So I just exposed myself. And within a few days I had 15,000 views on one post and, uhm, and, you know, 600 likes by the weekend. Uhm, and so it was really amazing. People were asking me questions. And part of my journey was to figure out "how do I answer those questions? How do I explain it better?" They say "what was that about? I didn't know that about you." Because it is a hidden thing. So you just never know about people and the experiences they have. That has been an amazing support, all the online support, people, friends, and the people I haven't met. And I've met people here who are following me. That has been interesting. All right. Thank you.

MARK DUNNING: So, uhm, so you guys have all been very positive about everything. I'm going to, uhm, to -- I don't want to bum anybody out, but I do want to ask a question. Can you describe for us your most difficult experience you've had because of Usher Syndrome?

ELAINE DUCHARME: Can I answer last on this one?

( Laughter )

Can I take a pass and be the last person to answer? I need a little bit of time to think about that.

MARK DUNNING: Sure.

Ryan, are you ready to go?

( Laughter )

RYAN THOMASON: I'll take this. I'm not as funny as Mike.

( Laughter )

Probably the hardest stuff was from before I was diagnosed. As I mentioned, I got in my first car accident when I was 16. I didn't see that the stoplight had turned red and didn't notice it until the last second, hit my brakes and hit a police car going through the intersection.

( Laughter )

And then my second accident I accidentally pulled out in front of a car and got T-boned and a couple -- and went 40 feet into a ditch.

So, uhm, you know, just walking on college campus at night and walking into a tree and everyone asking how much I had to drink. And I was like oh, a lot. But I didn't have any.

( Laughter )

Just, ah, but those -- but the more recent stuff has been the more emotional for me, uhm, we just -- we took a family vacation with some really good friends of ours to Las Vegas, and as you know, Las Vegas on the strip is very busy. And walking with my six-year-old and my wife trying to, you know, keep my four-year-old and all of us from running into stuff, and my six-year-old devised this system to, you know, he would hold my hand, squeeze it two times and he told me that meant I needed to stop. And then if I squeeze your hand three times that means we can go. And if I pull your hand a little bit this way we are going left. And if I push your hand that way we are going right. I think it was more of a devised mechanism on how to control dad more.

( Laughter )

But he did that on his own because he knew I was having a hard time with all of the people. And that really impacted me emotionally, and I got him an extra nice present from a store for doing all that on his own. So that is really been the hardest thing, just emotionally, ah, with my kids and stuff like that.

MOLLY WATT: Uhm, well, I don't really necessity how to put this into simple terms, really. When I think -- I think the hardest thing for me was because I grew up as, uhm, many of you know as a deaf

child, very visual. So I relied on lip-reading. And I did get by in mainstream pretty well. And then it wasn't until my sight got pretty bad where I thought that I would need better support, maybe smaller classrooms, and I thought this would be better, and in a School for the Deaf. There is actually a boarding school in England. And I went there and ironically I -- at this point I was in denial about going blind. So I actually thought "oh, yeah, I will be just like everyone else." I wasn't. Uhm, I kind of -- I got bullied because I wasn't like them. Uhm, I couldn't sign. I couldn't understand what they were saying because of the lack of sight I had. Uhm, and it was kind of that realization that actually I'm not like them, and I needed my sight, and it was trying to convert from being such a visual person to using my residual hearing. And that was the biggest, like, hardest transition I've ever had to make. Uhm, yeah, I think that is definitely hard. And, uhm, and following up the whole experience at boarding school I was bullied pretty bad. And when I left I had pretty bad anxiety and depression. I had to go to counseling sessions. I refused to go to out of the house. I didn't want to be seen. I didn't want to be seen out or with my guide dog. And those three years of my life were really difficult. And I still go to counseling, but a lot of those issues I've overcome since I'm not in denial, I've accepted what is happening to me now. So things are getting better.

CHLOE JOYNER: I think, for me, the thing I find hardest is just sometimes it will strike you. You think you are doing really well and then suddenly you see something or you just random on a Tuesday afternoon and a thought comes into your head. You can just get that frozen sense of dread, uhm, as a parent. But yeah, I guess having something outside of our control for our daughter is something I find very difficult to accept and deal with.

MIKE WALSH: Uhm, yeah. Difficult points. I guess growing up when you have hearing aids and you are in a high school where no one else has hearing aids, uhm, it is very, ah, stagnant socially. You wonder why you don't have a girlfriend and stuff like that. Uhm, but then you grow up, I'm growing up, do we have a grown up? When you become, or nowadays, ah, when I meet people, especially with my campaign, I, ah, people ahead of time know about my situation. And when I meet them they are really excited to meet me. And, ah, and so forth. And so it is -- you become more, like, this is part of who you are, and it is interesting. Everybody's unique, and in different ways. So you just kind of own it. "Yeah, I have to wear hats all the time." I get to wear cool hats and cool shades. You just kind of own your life. And as far as other difficulties. And Ryan, Ryan would be happy to know I've crashed a few cars even with no symptoms.

( Laughter )

So, you know... difficulty -- well, like I said earlier, I'm always trying to hear better. For me the hearing is actually harder than the seeing. Seeing, I don't know, I can get through it. But you always miss things here and there, you can't -- you need to have people repeat them. But one instance I can remember, uhm, was, ah, just slicing my head open the night before a final and showing up with stitches in my head. My face. It was right there. And the teacher gave me a weird look. But just little things like that, bumps and bruises there, but you heal, it is amazing.

MARK DUNNING: Elaine, do you want to answer this question?

ELAINE DUCHARME: I am ready. Thank you for giving me time to think back. I've got a whole life to look back on. And I have similar bullying in schools. Similar stories about "are you drunk?" And I'm really just bad balance. I have people who would, you know, make fun of the fact that I bumped into tables, and all of that. All growing up I had that. Uhm, it was hard on my family. I would -- I would bump into them a lot. Or I wouldn't see something that was on the floor. Like I remember, you know, my mom had just cleaned the kitchen floor and I bumped into the cat's bowl and it knocked over everything and she had just cleaned it. That kind of thing. That you are not realizing why you are doing this. Or on the basketball team in high school, I passed to the wrong person because I couldn't see her and I got called out for that. I remember I went to Rochester institute for technology for a nine-week session, and I got an infection in my eye, it wasn't related, but it meant I couldn't see for a period of time. And I remember that, you know, I tried to take some sort of self-defense class or something, and I couldn't do it. I couldn't do anything that I was used to doing. And I went outside, and I realized that I couldn't see at all. And I bumped into someone who, you know, promptly yelled at me like "what are you doing?" And to me it was completely dark. I couldn't see anything. I didn't know where my dorm was. I just, ah, remember, you know, hoping, like, "I think it is this way." And I just decided that I -- I had to fly home. I quit college at that time because my vision just went for a very brief period of time, very quickly. And, you know, it was -- that was hard. It is always hard at night, you know, socializing with friends when it is dark. It is really hard. Uhm, and I'm not able to, you know, enjoy. So in college I would, uhm, I would just drink more so that --

( Laughter )

-- because I was bored and I couldn't see what anyone was saying. So that wasn't a great coping mechanism, but I did that for a while.

Once I was fully blind, that was a big challenge. Like I said before, I didn't want to learn Braille. I was in denial. I mean I accepted it once I was there, but I hated it. I still kind of hate Braille, you know, honestly. You know, I accepted it, and I have learned it, and I have moved along. I know who I am. But those were all challenging years. I would say, uhm, you know, through my teens and my twenties were the most challenging, uhm, times. And during my career I just have learned to work my way around many of those challenges, but I would say the early years were the hardest.

MARK DUNNING: Okay. Thank you very much. And I know those are difficult things to talk about, which is why, uhm, I want to ask you what has been your happiest experience related to Usher Syndrome? Elaine, do you want to go first or start at the other end of the table?

ELAINE DUCHARME: I'm good. I'll take this one.

( Laughter )

Happiness is good. All right. Let me see.

So I would say I lost my vision mostly at 27-28, as I told you. So I was -- it was a very hard time in my life. A sad time in my late 20's. Uhm, so, uhm, I hadn't really experienced social life with, uhm, with

Usher Syndrome or deafblind people. Mostly hung out with Deaf people. So I went and joined, there was an association for, uhm, deafblind people by Helen Keller. I went, uhm, in '84, I believe, it was in Seattle, Washington. And that was the first time where I was in a large group of people who have Usher Syndrome. Usher Syndrome one, two. That moment, for me, was -- it was lovely. It was really meaningful moment. I remember that, uhm, and I think that is the moment that I really started growing, as a person with Usher Syndrome. I really feel like since that moment I was able to find happiness. I was able to just say, "okay." I have a lovely wife. I have lovely friends. I love, uhm, I love my life. And I was able to, uhm, to -- I was able to do that. I actually love being a deafblind person. It is great.

MARK DUNNING: Thank you.

Ryan, do you have a happy moment?

RYAN THOMASON: I'm always happy.

( Laughter )

Because I've got two kids that don't make me -- they don't give me a choice. I have to be happy. They are always doing fun stuff. And keeping me smiling and entertained. And, uhm, I think one of my more recent experiences on Father's Day, we went to a place called Anna Island, it is a big ranch, and they have some fun stuff. And I always -- one of my first things when I was diagnosed was I -- I've always been into sports growing up. And something that always worried me was would I be able to play, you know, football with my son? Would I be able to play catch with my kids? And on Father's Day we had mitts, and gloves, and someone threw a baseball at me and I caught it just fine. And I felt really good about that. And we played catch for a very long time. Just as a family. We were just throwing the ball around. And, uhm, and, you know, I didn't really tell anybody about that. But it is -- but that was a really happy moment for me. Just being able to do some of the stuff that I never thought I was going to be able to be with my children. So my kids are always trying to find ways to keep me happy.

MOLLY WATT: Uhm, I think, uhm, actually just after the darkest part of my life, uhm, I was forced into a gap year. So I wasn't in education for a while. And like I said before, I didn't do a lot. Uhm, and we started searching for other colleges for me to go and complete, uhm, my two-year further education, ah, course. And a lot of the local colleges refused me because they had never had anyone like "me," and I don't know what that means. But as soon as they heard the word "deafblind." It is like "oh, no, we haven't had one of those." But we eventually found this college, which is about half-an-hour drive from where I live. I wouldn't go and see it because I was frightened at that point that I was going to get rejected again. I just thought no one was going to want me and I wasn't going to go very far in life. And my mum went and they said that the -- mum said -- she spoke to them. And they were -- they were very open to the idea. One of the first things they said is "look, we have never had anyone with Usher Syndrome, but we really want to learn and work with you." And that was the best attitude I could have ever asked for. I then went onto go to that college and I -- and I restored my faith in the community again. It was like "oh, there are actually some decent people out there now." And so it felt really good to actually be accepted for who I was, to be able to walk around the college, with my guide dog, not

being bullied, and just generally feel comfortable in my own skin. So I think, as I say, the last couple of years I've come such a long way. And so I think that really does reflect, probably, one of the happiest moments of my life, really. Just knowing that I could actually get far in life now that I've got these qualifications, going to university. So, yeah.

CHLOE JOYNER: Uhm, for me two things come to mind. Swimming lessons are quite comical in our family. Uhm, me desperately signing on the edge of the pool, uhm, and every week they create new, uhm, tricks for the kids to do, and there is me desperately trying to make up signs, and she is like "can I jump now? Can I jump now?" So that is always good for a laugh.

( Laughter )

And just thinking slightly more profoundly. I think I feel very strongly that the process, uhm, this all the families in this room, and all the people who support people with Usher Syndrome go through and their adjustment to being all that person needs, or to be all that child needs is a thing of beauty. And I really just see that in all of the different examples I can see around the room. And I take so much strength from that. Uhm, I really do. In any, uhm, moment when I'm finding it challenging, and it gives me a lot of happiness and strength to see that beauty in action of people providing support to other people.

MIKE WALSH: Speaking at Harvard.

( Laughter )

( APPLAUSE )

( Laughter )

I mean it is Harvard.

( Laughter )

Happiest moment. I guess what has been fascinating, uhm, so I'll -- up until, ah, late January I have always kind of never really thought about Usher Syndrome, you know, something that my brother and I had. But the last six months have been amazing with the campaign and all the people that reached out to me. They want to learn more about it. And it forced me to, like, learn more about it so I could teach them. And, uhm, just all the people that I've met have made me very happy. Uhm, and, you know, this is an excellent room of great people, and panelists. Like Ryan and Molly. I've seen them online the last couple months. Here they are live, and we are talking, and I have made new friends. So it is just -- this is great. It is the community, you know, and the more we work together and go forward and, you know, and let's be happy. What is the happy song? All right.

( Laughter )

MARK DUNNING: Great. Thank you very much.

So I have one more question for you guys. Uhm, so what are your plans for the future? Elaine, do you want to go first?

ELAINE DUCHARME: Future plans? Hmm. Let me see. I would say my future looks like to continue to be a supporter and advocate for the deafblind community. Uhm, I enjoy working with the deafblind community. There is some people who, uhm, still have vision left and I really enjoy working with them and supporting them through the transition. I feel like I have a lot to offer. I feel like, uhm, my part and my mind are really open to them and that's -- and that's really my calling. It is the people I love to work with.

If and when I do retire, I'll certainly continue to volunteer, to train people to make sure that people, ah, continue to have a positive attitude about their life with Usher Syndrome, that it is important that they know who they are, and what their identity is. And not to let, uhm, ah, depression get them because I don't know if you've heard, but Usher Syndrome doesn't kill you. So everything is good from there.

( Laughter )

( APPLAUSE )

RYAN THOMASON: Uhm, I'm kind of at a bit of a crossroads at this point, you know, 32 years old and, uhm, my wife and I are talking about going back to school. Either getting my MBA or, ah, re-training, ah, in a totally different profession. And starting in a, ah, in a different career path than what I'm doing now. Uhm, so, uhm, so, you know, I'm trying to figure out, you know, if we are going to go that way, or what we are going to do, and, uhm, and, you know, and just enjoying all of my time with my wife and my kids. And that's pretty much all I really have for my future. I just want to be with my wife and kids and have fun because that is what we do every single day.

MOLLY WATT: Awwww, a cutie.

( Laughter )

Future? Uhm, yeah. I, hopefully, if I pass, I find out my results in, uhm, in August. Uhm, I will be starting university in September. Uhm, to basically become a teacher. Uhm, yeah, I want to teach around nine or ten-year-olds. In England we call it primary school. I want to teach that age group because they will be talking human and not like monkeys.

( Laughter )

And, ah, and I will have my own classroom, so I will have my own big fancy chair.

( Laughter )

And I will be able to teach the class, I reckon. I don't think I will be teaching that long, oddly enough. I really do want to carry on doing my motivation will talking for my family's charity that we created. Uhm, I really, actually, wish that, hope, that one day I will just be traveling and talking because I would

love to see the world, while I can, and talking to people, and meeting people with Usher Syndrome is such a privilege. Uhm, so yeah. So two kind of objectives, really.

( APPLAUSE )

CHLOE JOYNER: For us, our plans, uhm, well really it is up to my daughter. I have a lot of faith in her strength and spirit. She is a very determined young girl. So, uhm, so I'm just going to watch as a bystander, I guess. But I'm going to also personally learn from the people in this room and try to make as many connections as I can to understand, uhm, as a bystander and someone in the wings supporting her, to give her all the chances she needs to become the woman she will be.

( APPLAUSE )

MIKE WALSH: Barbecue.

( Laughter )

Future. So the last six months, ah, I've been traveling all around the world. Thirteen countries. Twelve states. Something like that. Uhm, and I want to keep going. And, ah, and keep meeting people. And blogging about them. And posting that. And so I'm at the point where, ah, I've had some great support from Delta Airlines, and I'm -- and I will be finding some more sponsors, and I will be using crowd funding. We have all heard about Kickstarter. And so, uhm, so that is the future. Hopefully more traveling in the next six months, and, ah, you know, it has been great. And I look forward to meeting you all.

( APPLAUSE )

MARK DUNNING: Great. Well, thank you very much, guys, for everything, uhm, up here.

Normally we try to do a Q&A right now. But Mike mentioned -- who on the panel is going to the barbecue? Everybody going to the barbecue? Yes? All right. Excellent.

So how about if we do our Q&A at the barbecue? So that we can get to the barbecue, eventually.

RYAN THOMASON: Can we do it before I get barbecue sauce all over myself?

( Laughter )

MARK DUNNING: We'll do it before you bump into the trees --

ELAINE DUCHARME: I have the interpreters with me, so come on over and talk to me.

MARK DUNNING: Yes. Absolutely.

Thank you, guys. Thank you very much.

( APPLAUSE )

Okay. So as we try and stay on schedule here, uhm, we have breakout sessions now. Uhm, and so the breakout sessions are going to go from now until five o'clock when you guys are all going to come back here. You have a choice of three breakout sessions. We have a breakout session for partners and spouses of adults with Usher Syndrome.

We have a breakout session for, ah, for Parents Knowledge Exchange.

And then we have a breakout session for young adult, college and career chat. Those are upstairs.

They are not on the second floor. They are on the mezzanine. So up in the mezzanine area up there.

We also, in this room here, are going to be having a, ah, a road map discussion for, ah, for professionals as we are going to try to put together the structure for a road map, uhm, for research based on the last two days of discussion.

Uhm, so, ah, uhm, and then after that we'll meet back here at five, ah, and we'll say some final words and then we can all go, en masse up the road.

## Concluding Remarks

MARK DUNNING: Hello, everybody. If we can get everybody back in here for a few minutes. And then we can get to the barbecue and have a grand old-time.

If I can get everybody to come on in and take their seats. I think I see -- there's my wife. Julia, is there a crowd out there still? Is someone ringing a bell and bringing them in?

Hi, everybody. If you want to take a seat we'll get you out of here in just a jiffy.

I just have a couple of housekeeping items. Housekeeping items. I've lost my voice at the very end. A couple of housekeeping items for everybody. If you have Assistive Listening Devices, you need to make sure that those get returned and I saw Marilyn around here a second go. Oh, there she is. So there's Marilyn. So the loops go to you, Marilyn?

MARILYN NEAULT: Just put everything back there.

MARK DUNNING: If you just take everything to the back-door where the glass is, please put that there. Please don't take it home because we need to make sure it stays here with Harvard and Marilyn. So I want to make sure that you guys keep that stuff.

The second thing is that we are going to head over to the barbecue after this. And we are going to go as one big parade. That is probably the easiest way to do it. It is literally a five-minute walk. And Krista, our -- what's the plan for walking people over there? Are we going to meet and just walk? Do we have a map for people?

KRISTA: We have maps and we'll guide people.

MARK DUNNING: We have maps. And we'll guide. But it is a very, very short walk. It is on the Simmons College Quad, and they will have food for us. And it will be fun. And the kids can run around.

Kids, did you have fun?

MARILYN NEAULT: Jessica would like to give a brief report on the Museum of Science.

JESSICA CHAIKOF: Everyone stand up. This is for you, Mark. Thank you for lighting the way.

( APPLAUSE )

MARK DUNNING: That's great, guys. Thank you. I can't wait to see that thing in the hotel in the middle of the night.

MARILYN NEAULT: Just one more thing you'll see in the middle of the night. I think that we should recognize a young man who managed to raise $45,000 on Stink Week. Mr. Jack Dunning.

( APPLAUSE )

His award is for the eyes.

MARK DUNNING: Excellent. Thank you very much.

So -- and then there was -- so, ah, so there are maps, and we are going to walk on over there.

One other thing I wanted to mention to everybody, we sat here with all of the researchers and talked about the key -- the key pieces that are missing to keeping us from getting a cure for people. And the biggest thing is finding all of those people with Usher Syndrome. And we need you to do that. That is why I asked everybody to do that. You are the key. I have this bracelet on my list right here. It says "I am the cure." You are the cure. If you guys go out, and you continue to maintain relationships with people that contact you about -- through the Family Network so that we keep in touch with them. If you encourage everybody you know who has Usher Syndrome to join the Usher Syndrome Registry. If you educate your physicians. And I can't stress this enough. Your physicians don't know about the Coalition. They were not here the last two days to see all of these treatments that are on the horizon. You need to tell them about that stuff. You need to get genetically tested so that we have that information. And we need -- and it is -- and you need to contact your Congressman about this stuff if you are here in the U.S.. I'll let Moira talk more about that.

MOIRA SHEA: I just wanted to add my two cents. Having worked on Capitol Hill for five years, uhm, money doesn't necessarily buy everything. And what money does not buy is your vote. And your vote is priceless. And so I strongly urge you, now that we really feel empowered from hearing all this good news, go home and contact your district person of your Senator. And they have places all over the district. You don't necessarily need to meet the Congressman, the staff has the ear of that Congressperson. So I strongly encourage you to reach out to your Representatives, educate them about

Usher Syndrome, and educate them about the need for funding at NIH. And, you know, to get the support behind us on Capitol Hill. And that will be most appreciated and highly effective. Thank you.

( APPLAUSE )

MARK DUNNING: Okay. Does anybody have anything else they want to say?

>>: Mark, just tell them to register to vote because they check your voter registration before they read your letter.

MARK DUNNING: Gotcha. So make sure you register to vote if you are not registered to vote because they won't talk to you unless you are registered.

It looks like we have one more thing to say here.

>>: Hi. This is Ava and we've been up in child care working really hard today. And she has something to tell us.

>>: We made a gift and want to say thank you.

>>: We made bracelets for all the members of the planning committee to thank them for their hard work.

( APPLAUSE )

MARK DUNNING: So all of us should see Ava and Julie to get our bracelets. I will wear that to work on Monday, I promise you.

Okay. Thank you, everybody. This has been a fantastic three days. It is not quite over yet. We are going to walk over and there was a lot of talk about mini pigs, the scientists were talking here, we are looking for aN animal model. Let's go eat some pig.