Neurofibromatosis, Late Deafness and ALDA

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Roy Miller: First here is some medical information about myself. In 1972 I had a right-side acoustic neuroma removed at the Mayo Clinic in Rochester, Minnesota. At the same time I lost both the eighth and the seventh cranial nerves on that side. The seventh nerve is your facial nerve. So at that time they did an eleven to seven anastomosis. That is basically connecting the nerve that activates your shoulder. It's a dead nerve and the only thing that I can do is close my eye, but it's at least closeable.

About 15 years later in 1987, I had a left-sided acoustic neuroma removed again. On this particular operation, I lost the seventh and the eighth cranial nerve. At the time the doctors did what's called a 12-7 nerve jump. That's an interesting kind of operation because that hooks a nerve that activates the left half of your tongue. My tongue has two cranial nerves working it that activate the left half of my tongue. This allows me to close this side by gritting my teeth. Weird, but that's that.

Later on, I had all kinds of facial work done. I had springs put in my upper eyelids to help my eyes close. I had transposition surgeries done, a nasty operation where they cut part of your facial muscle out and route it down to your cheek to pull your cheeks up so they don't droop to the floor. It's a good thing. I had Gore-Tex sling put in both cheeks. Then a few years later the Gore-Tex sling on one side had to come out because the body rejected it. When they took it out, that destroyed the nerve junction so that eye no longer worked at all. Anyway, that's some stuff about my medical situation.

Let's go directly to the topic that we have for today.

Neurofibromatosis. What is that? Well, neurofibromatosis is a general term that actually now covers three different genetic disorders. NF1 and NF2 and more recently they recognized a third one and that's called Schwannomatosis. What's NF1? To start with, it's a genetic disorder that means if a person has NF1, everyone of their children has a 50 percent chance of inheriting the gene and developing the same disorder, NF1 .

NF1 has a lot of things associated with it. Of course the main symptom is a variety of tumors on and slightly under the skin anywhere on the body. For a long time people talked about the elephant man syndrome as being the same thing. But he had another

disease that is not part about our discussion here. Tumors occasionally develop anywhere in the brain and along the spinal column with people with NF1. NF1 is primarily tumors on the skin. Optic gliomas are associated with NF1. Those are tumors on the optic nerve of the person. So vision often is involved. About 50 percent of the people with NF1 have learning disabilities. For whatever reason, it happens.

We are going to focus on NF2, which is what most of our ALDA people are involved with. Again, it's an autosomal dominant genetic disorder with a 50 percent chance of your children inheriting the disease. It's characterized by multiple tumors on the central nervous system and by other lesions within the brain and along the spinal column. Its central hallmark is bilateral acoustic neuromas, tumors of the eighth cranial nerve.

For some of you here who've had experience with NF2 operations may have heard a different term. Not an acoustic neuroma but a cynoma. They're the same but right now I will use the term acoustic neuroma. Normally speaking, acoustic neuromas begin in your teenage years or your early 20s. NF2, as I say, can be inherited or it can be a mutation. I have actually no family history of NF. My NF2, like many others, are genetic mutations. People ask how does that happen? When a man and a woman get together, contributing one sperm and one egg, those cells pass information back and forth. If that information matches correctly, everything is fine. Once in a while the egg and the sperm will clash and the information gets distorted. This occurs at the genetic level. What happens to start the NF2 gene is that gene got messed up in the embryonic stage.

Some facts. The average age of NF2 onset of findings is 18 to 24 years. Almost all people with NF2 develop bilateral acoustics by age 30. I had my first operation when I was 32. It's likely that the tumor that was removed at that time started about age 16 or age 17. Two-thirds of NF2 patients also develop spinal tumors and about half of the NF2 patients develop intracranial meningiomas. Those are different tumors at different places in the brain. About one-third of NF2 patients have decreased acuity in their eyes which affects their vision a little bit. NF2 has absolutely no sexual, ethnic or racial predilections. Black people get it the same as white people. People in India and the Soviet Union get it the same as in America. Women and men can get it the same. There are no particular biases.

The first case of bilateral acoustic neuromas was studied in 1822 in Edinburgh, Scotland. The tumors themselves are benign. They are not formally cancerous although they can become so if not treated. But that's not normally an issue. They are normally benign tumors but it is where they are located that can cause major problems

to a person. A person may have multiple tumors requiring surgeries over and over again.

The average age of death for people with NF2 is 36 years old. We don't think about that much here because we see just a few of the older people. We rarely see the kids with NF2. The actuarial survival time is estimated at 15 years after diagnosis. Boy, are we lucky.

Let's talk a little bit about the third, Schwannomatosis. It's characterized by Schwannomas, nerve sheath tumors, under the skin. In one sense it's closely linked to NF1 that also produces tumors on the skin. Very seldom do you ever see vestibular tumors on people with Schwannomatosis. It's been only recently that this was recognized as a separate and distinct kind of a neurofibromatosis. It's characterized by extreme pain; these tumors under the skin can be very painful for the person.

How often does it occur? NF1 occurs one out of 4,000 people. These numbers may vary a little bit, depending on which website you're reading. I have seen it in numbers as low as one out of 3,500, one out of 4,000, one out of 5,000. NF2 occurs about one person out of 40,000. I have also seen that reported also as one out of 50,000. NF2 with only bi-laterals and no other tumors--that's me, only bi-laterals that's it--I'm one out of 800,000 people. In other words, I am a very unique person, right? I hope so. For Schwannomatosis because of its recent discovery history, there really isn't consensus about its frequency of occurrence. But I have seen a figure that is say, one out of 40,000 for it.

How does a doctor know you have got NF2? Well, again, if you have got a bi-lateral eighth nerve acoustic tumor, you have got NF2. Or if you have a first-degree relative a parent, a brother or a sister with NF2 and either a unilateral eighth nerve tumor or two of either a meningioma, gliomas, Schwannoma or a posterior sub-capsular, lenticular opacity, meaning a little dark and fuzzy with the eyes, those are what the doctors use to diagnose NF2.

What is this thing, an acoustic neuroma? It's also called a neurilemmoma, a vestibular Schwannoma or a neurinoma. Technically the tumors have a different microscopic history but in a sense we don't care if it's a Schwannoma or a neuroma. It doesn't matter. It's a tumor. It's a benign tumor on the eighth cranial nerve and it grows in the angle between the cerebellum and the pons in the posterior fossa, which is the back of the skull. That tumor grows next to the brain stem and this is the important part about that tumor. It's located next to the brain stem so as it grows, it puts pressure on that brain stem. The first thing that you notice when this happens is headaches. But if you

let it go, you let it go untreated, that tumor will grow and the pressure will be so great you will have problems swallowing food, drinking and ultimately breathing. You can die. So somebody asks, “Can I leave that tumor alone forever and just play it's not there?” Huh-uh. You don't want to do that.

Now we get into the technical items. These tumors usually grow very slowly. The tumor arises from the myelin forming cells, the Schwann cells on the eighth cranial nerve. That is where the cortical part of the nerve joins the central part of the nerve, called a Hensen's node. Hensen’s node is usually located in the inner ear canal that leads to our hearing apparatus, the acoustic meatus. That eighth cranial nerve is really three nerves in a sense in one. There are two vestibular nerves and one acoustic nerve, the hearing nerve. Immediately adjacent to these nerves, though, is the seventh cranial nerve. Running in that same canal from the outer ear to the brain are the eighth and the seventh cranial nerves. So when you get a tumor on the eighth nerve, it often hides itself and grows around the seventh nerve as well. That's why you will see people like me who say I lost both the eighth and the seventh in the surgery because the doctor had to take them both in order to be sure to get all of the tumor out.

Larger acoustic neuromas may also involve the swallowing nerves that are below the fifth cranial nerve, the nerve that controls sensation. For example, when I touch this side (touching face) that feels good. When I touch this side, I can't feel that. I have a little bit of numbness on this side of the face because of the nerve that was one of those vestibular nerves has been sacrificed.

How do we treat people with NF2? There are basically three things the doctors will do. One, they will say, “Don't do anything. We want to observe it. It's a slow growing tumor. Right now it's very small. It may be years before we have to do anything about it.” Usually that means an MRI every year or every couple of years to observe and monitor the tumor’s growth until it becomes essential to treat it.

The second treatment is known as stereotactic radiation known as the gamma knife. That's done in a single or a multi-dose treatment. In the single dose treatment, the person is zapped with radiation from all different angles, which intersects on the tumor. Then, you’re done; you go home. Multi-dose treatment means a person goes in one day for radiation to zap one part. Go home. Come back the next day and zap another. Go home. Go back the next day and zap it from a different direction. The multi-dose treatment may continue for a couple of weeks.

The third form of treatment of course is the surgery, involving one of two different kinds. Surgery either aims for partial de-bulking or complete removal of the tumor. There are reasons why people choose one or the other.

Why on earth would anybody just sit there and watch this tumor grow? There are a couple of reasons for that. Remember that these are benign tumors that produce the symptoms by exerting pressure as they grow. Some patients might be in a situation where it might be quite reasonable just to watch it grow. Older patients for whom the tumor is not really expected to ever cause serious damage before the person dies just leave it alone and watch it grow. Also patients prefer to just watch with a tumor on their only functional hearing nerve, particularly if that tumor is the size that hearing preservation with removal would be unlikely.

Some personal history. A tumor was removed from this side, gone. On that side I am deaf. On this side I still had hearing. Like many of us, the tumors are not operated on at the same time because they don't grow at the same time. So when this one was discovered, the question for me was what do I do? I could go into surgery now. But then I thought, oh, I can't communicate with anybody. I don't know sign language. I can't speech read worth a diddle. I couldn't communicate. The tumor is not hurting me yet; I don't get any headaches. I know that when they take this other one out, I will probably be deaf. So what do I do? I chose to watch it for three years and let it grow. There are times observation is ta choice that the patient may make.

Stereotactic radiation is radiation therapy, sometimes referred to as radio surgery. The technique is based on the principle that if you pinpoint radiation on the tumor, you are going to do one thing: stop the tumor from growing anymore. The tumor is still there. It's the same size; you are just stopping its growth rate. Well, if you are in a position where the tumor is not hurting you, maybe that's reasonable to do. Maybe in other circumstances it's not. As I said, there's a single dose and the multiple dose treatment. Except maybe I should highlight that in some cases the hearing can be preserved with a radio therapy. If the radio surgeon is good enough and accurate enough to only hit that tumor and not in any way damage that acoustic nerve, then once in a while you can save your hearing. But never take that particular option thinking hey, I'm definitely going to come out of it with my hearing. Huh-uh. Most of the time you are going to lose it just as with surgery.

Now, let's talk about surgery. Partial removal of the neuroma may be indicated in some patients. But again, why would somebody choose to have only part of the tumor removed? Possibly, for older patients with a large tumor causing a threat to life, removing the entire tumor may be too difficult for that older patient to withstand. Instead

the surgeon decides take out half of it or a quarter of it, just enough to relieve the pressure that the tumor is causing on the brain stem.

For a long time Boston General Hospital was the clinic known for doing partial removals most of the time. Partial removals were for patients who had large tumors in their only hearing ear. I could have elected that once this tumor was discovered. When you do a partial removal, you know you have to have surgery again in the future because that tumor is still going to grow with partial de-bulking. Partial removal may greatly reduce the risk of facial nerve involvement. If that becomes the most important consideration for you, maybe you decide on de-bulking.

As for total removal, the micro-surgical techniques and those instruments along with the operating microscope have tremendously reduced the risks of these surgeries. People opt for total removal when preservation of the facial nerve is primary to prevent permanent facial disfiguring. Preservation of hearing, of course, in the affected ear is also a primary goal but inevitably it's not one that is accomplished most of the time. Several surgical approaches are used for total removal. There are the trans-labyrinth approach, the middle fossa and the retro-sigmoid or sub-occipital approaches.

With the trans-labyrinth approach, the surgeon makes a cut here (showing skull), removes a part of the bone covering the tumor and takes out that tumor. Now, why is this good? It's good because it facilitates the identification of that facial nerve. The surgeon can easily see that facial nerve, and as a result, most of the time can save that nerve. But what's wrong with that approach? It results in the patient being totally deaf on that side. So you go for in trans-labyrinth, you are going to be deaf on that side.

With the middle fossa approach, the insertion is a little bit further back and higher. It's utilized for the primary purpose of saving a person's hearing. It too has its good and not so good sides. A small window in the bone is removed allowing the surgeon to see things from an elevated angle and expose that tumor. They can take it out but it can only be used with very small tumors. That's the negative. If your tumor is not discovered until its three centimeters big, surgeons are not going to go in the middle fossa because three centimeters is too big.

The major use of the sub-occipital approach is to remove large tumors, as in my case. This approach creates an opening in the cranium behind the mastoid part of the ear. The surgeon can observe both the vestibular canal and the brain stem. Neither of the other approaches allows for brain stem observation, observing that tumor in relation to the brain stem. When removing large tumors through this approach, the facial nerve can

be exposed at times. Small tumors can be removed with the hope of preserving hearing.

How large is a tumor? When this tumor (visual) was removed it was a six-centimeter tumor. That's about the size of a walnut in the middle of my head. This tumor (shows picture) was basically a three-centimeter tumor. These are considered larger tumors. Small tumors are little teeny tumors.

Possible results. What can happen after the surgery? After the surgeon does his job and sends you home, what problems might you have? Number one, you can have tinnitus. That's not unusual. A lot of hard-of-hearing people with hearing aids and people with hearing loss to one degree or another have tinnitus. This is an interesting thing: GET, gaze-evoked tinnitus. I have gaze-evoked tinnitus. Does anybody else here have GET? With GET, when you look in one direction, sound is different from when you look in a different direction. When you move your eyes and look in different directions, the sound changes. I can create a symphony in my head just by rolling my eyes around. It's kind of cool. It took me a long time to figure out what was happening. But that's GET.

We all suffer balance problems especially after dark or on uneven surfaces that we are walking on. Swallowing difficulties may occur in some patients. Underwater disorientation is there. You want to be very careful about spending time under water. Stop if you are a person with NF because balance disorientation is easy. Facial numbness as I say occurs; one side of mine is numb. Loss of taste happens. Such is life.

What other things could happen to you? That facial nerve could be damaged. A damaged facial nerve is going to result in a side of your face drooping. Eye problems is an area that I don't think when it happened to me I knew a darn thing about. In a way the doctors never talk much about what could happen to your eyes. What can happen? Number one I have dryness because I can't blink my eyes. Normal human beings blink many times a day to lubricate. If you don't blink your eye, it stays open all the time and gets very dry. You are probably going to use drops for the rest of your life. No tearing. I can't tear, which means I can't cry. Even if I am sad inside, I can't show it by tears. Because that eye is always exposed and it's dry, you can develop ulcers on your corneas, or ulcerated corneas. They can be very painful. You have to treat them over and over again. I guess I have had maybe five different ulcers. Retinal abnormalities. Interestingly enough, do you realize that two-thirds of the patients with NF2 have cataracts? I have had cataracts removed. Are there others in the room who have had cataracts? Marta, do you have cataracts? Cleo? All have cataracts.

There could be eating problems. There could be speech problems. What kind of speech problems? For me, I can't close my lips which means I can't pronounce or

enunciate the sounds /p/, /m/, /v/, the sounds that require you to close your lips. So those words that use bi-labial sounds sound a little bit different from me. But in context usually it's okay. With facial weakness there is disfigurement and the inability to show emotions can be there, too.
The last item to talk about is the damage to the acoustic nerve itself. It can result in either hearing loss to one or another degree to total deafness. It can be unilateral or bi-lateral. I am deaf as a doorknob on both sides, I wouldn't know if there was a rock concert in the hallway. Other NF2 people can have some hearing. They can be deaf on one side and not the other. It's all an individual situation.

Radiation treatment. It was 1972 when I had my first surgery. At that time radiation treatment was beginning and exploratory in many ways. Why would a person choose radiation over surgery? There are many reasons. The first is effectiveness. Radiation zaps in from all sorts of directions. Sometimes it works perfectly. Sometimes it doesn't work very well at all. The question is how effective is that treatment going to be. We know that radiation can cause cancer and it can cause tumor growth. Sometimes the radiation that goes into the brain will in fact stimulate tumors and gliomas in the brain. That's a negative a person will have to consider.
Radiation induced necrosis. Necrosis not a tumor. It is like a black hole where a particular soft part of your brain kind of dies. Whether that good or bad depends on what and where the necrosis occurs. Is it where it can control your speech or control your heart, your vision? It all depends on where that tumor is.

Cognitive effects from radiation treatment. I don't remember as well as I used to. It's a cognitive loss. Or a puzzle is harder to put together than it used to be. There can be a great variety of cognitive effects of radiation treatment.

Let's talk a bit about nerve damage. People can be NF2ers and have a cochlear implant or an ABI, a brain stem implant. If you have a cochlear implant and the tumor needs to come out, you will have a radiation treatment, right? But you want to be darn sure that your doctor is good and he misses that internal part of either the CI or the ABI. He can thoroughly destroy that CI if he zaps it with radiation. So you can have a CI and NF2 with radiation treatment but you want to be sure the doctor is good if you are going to do that. Like anybody with radiation treatment, you can have hair loss.

NF2 chemo-therapies are tumor suppressors. Think about the fact you have a tumor here that the doctor is going to go in and take out. But note, that treatment affects that one tumor. That's all. Many of NF2ers may have a tumor here and a tumor there. They may have several tumors. That means having several different surgeries. It would be nice if we could develop something that would in effect attack all of these tumors at

once. So the search continues for the miracle drug. There have been clinical trials but no tumor-suppressing drug has survived clinical trials. If you are interested in the current clinical trials that are going on with respect to NF2 drug therapies, go to nftwois.com. Maybe you would be interested in participating in a clinical trial.

Tactaids with NF2. You can have hearing aids called vibro-tactile aids. Anybody know what a Tactaid two or seven is? Tactaid two is a device that when a person speaks, the frequencies are received at different levels. Tactaids are developed and engineered so that different vibrators vibrate at different frequencies of speech. The company in Boston, Massachusetts, first developed a Tactaid two with two vibrators. You wore it on your wrist wired from a battery down your shirtsleeve. When a person spoke, Tactaid would vibrate on your wrist. It could help you understand what someone was saying. That company later developed the Tactaid seven. This one had seven vibrators on a band that you wore around your chest. They vibrate at different frequencies. I have a Tactaid seven. But like a lot of people with hearing aids, my Tactaid wound up in the drawer. I used it but it was only effective in one-to-one conversation with a person whose speech was very articulate. I just never use it anymore.

Genetic considerations for NF2. As I said both NF1 and NF2 are genetic disorders. They can be inherited from your parent. Each child has that 50 percent chance of inheriting NF. The type of NF that they would inherit would be exactly the same as the parent. They don't inherit and develop a different NF. So if the parent is a NF2er, the child would be a NF2er. Now this is important: the NF2 gene does not skip generations. So let's say I have it. My children don't have it. Could my grandchildren get that gene? No. It never skips a generation.

In 1993 the NF2 gene was isolated on chromosome 22. The NF2 gene is a tumor suppressor gene. It encodes the 587 amino acid protein and the gene product is something that's called a Merlin. For several years there was a lot of talk about how Merlin is going to solve the problems if we can just find something that will work against Merlin. It's also called Schwannomin. Today many scientists are doing research to see if we can figure out something to control that tumor suppressor or gene.

Some resources. Where do you go if you want to know more than what Miller told you today? You can go to any one of these places: the National Institute of Health website, the Children's Tumor Foundation website, the NF Network website. If you are that kind of a person who likes to chat with people with the same disorder, you can join NF2 crew. You can go to NF2 information and services. That's NF2 IS or Advocure NF2, Incorporated.

We don’t need a lot of this discussion on hearing loss because we know about late deafness. I think it is interesting though to think about NF2ers’ shared experiences. Number one, we usually had multiple surgeries, whether it's radiotherapy or just general surgery. Number two, we usually become facially disfigured and have had to deal with whatever that experience produces for us. Three, we have endless eye problems. Number four, like all of ALDAns we have lost our hearing either in part or totally and we have had to struggle with communication problems.
We know about this, okay? How do we communicate? CSL, crappy sign language is one of the things that the NF2ers use a lot. We practically all speak like you have heard me here. Our words may be a little slurred or distorted but we speak. We practically all can write, our handwriting may be nearly illegible. Why? Again, everything depends on where that tumor was and what approach the surgeon used to go in.
In my case when they went in and took out this first tumor, in order to get to the tumor, they had to move a part of the brain, the cerebellum. In my case, they wound up cutting out a part of my cerebellum. The cerebellum controls fine muscle movements. If you think about it, writing requires fine muscle skill to make those letters as little as they are and clear. After my surgery I couldn't write zip. I practiced and practiced and practiced over and over again. I had to learn how to write my name again and to this day, the only thing that I write is my name. For everything else, I print the letters because that doesn't require as fine a muscle skill. Obviously, the development of laptop, tablets and smart phones has helped our group of individuals.

Receptive communication. Most of us can't hear. So trying to communicate with people who only speak, forget it. Communication with most of the world is not our *forte*. Many of us can't sign. So we can't understand people who sign. Communicating with people in deaf culture? Forget it. Most of us can't understand cued speech at all. I learned cued speech a long time ago and I have since forgotten it all but that's okay. We have various communication capabilities, so please be patient when you are trying to discuss things with a NF2er. Don't just talk to us assuming we can read your lips because usually we can't. It’s all “Blah, blah, blah, blah.” And most important, don't say, “Oh, never mind, it’s not important.” A small do-list for chatting with NF2ers includes 1) Offer to write or to type to be sure that that person understands what you are trying to communicate. 2) Ask them how to best communicate with them. 3) It’s always useful to think about the fact that you may be talking with a person who just a few months ago was a lawyer, a doctor, an engineer, a banker, a U.S. senator, or a college professor. So don't think that these individuals with NF2 necessarily have any limited brainpower. They have NF2 and that's it.

ALDA and NF2 and this is the part that I really wanted to get to. ALDA was started by Kathy Hering, a person with NF2. Well, how do I conclude this thing? How do I wrap it

up? I will make the point that people with NF2 have made a very important contribution to the creation and the development and the long time procedures of ALDA. They have been vital to this organization. In fact, without NF2ers, ALDA might never have been born. Remember Kathy Hering started it all. The contributions of NF2ers stretch throughout the entire history of our organization.

Dr. Roy Miller retired from teaching at Southern Illinois University after which he served as Executive Director of the Missouri Commission for the Deaf and Hard-of-Hearing. He is a former president of the Southern Illinois Center for Independent Living, of ALDA, and Hearing Loss and Telecommunications for the Deaf and Hard-of-Hearing. He has served on the statewide independent living Council of Illinois, the Missouri State Rehabilitation Council, the Relay Missouri Advisory Committee, and the Missouri School for the Deaf Advisory Council. Dr. Miller has neurofibromatosis type two.