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PROFESSOR: OK, I guess we'll get started. Last time, we were talking about the auditory pathway in the brain, the central auditory pathway, starting with the cochlear nucleus and going up through the various brain stem, the thalamic and cortical auditory areas. And then we focused mainly on the cochlear nucleus, which is the very first of those many auditory central nuclei.

And we talked about the diversity of cell types or neuron types in the cochlear nucleus and the diversity of response types when you monitor the responses of single neurons to sound. And we did some attempts at correlation between the two. And those are firmly established in the cochlear nucleus, much better than anywhere else in the auditory pathways certainly. So any questions from last time?

So today's lecture is on hearing loss and implants that restore our sense of hearing if we happen to be deaf. And I've written a little summary of what I want to cover today on the board. So we'll start out with the first 2/3 of the lecture being on hearing loss. And we've mentioned a little about the conductive apparatus, the eardrum, the three ossicles in the middle ear, conveying the vibrations to the inner ear.

And I think we had an example of one type of conductive hearing loss. If you have, obviously, an interruption of that ossicular chain, then the vibrations are going to be reduced in the inner ear in the conduction path-- because the conduction path is interrupted. So those are relatively straightforward concepts, and so consider those covered.

Today, I want to talk about the, perhaps, more common types of hearing loss that are grouped under the name sensorineural because the sensory cells, or the nerve

fibers themselves, are damaged. And in that case, it's not so easy to understand how we might correct them by putting in an artificial middle ear ossicle or something like that.

This is a bit of a misnomer in that perhaps 99% of hearing loss and deafness of this type was really based on the sensory cells, so the hair cells are the prime culprit in people who have sensorineural hearing loss.

The most vulnerable, of the two types of hair cells we've been talking about, are the outer hair cells. Any of the various causes that we'll talk about that damage our hearing affect the outer hair cells to a much greater degree than the inner hair cells, and the reason for that is not known. For some reason, the outer hair cells are more vulnerable.

As we'll see in the very first slide of today's lecture, those hair cells in the basal turn of the cochlea are more vulnerable than those in more apical regions. Reason for that is not known either. It's a very interesting phenomenon with no basis that we know about. We'll talk about permanent and temporary hearing loss, the various causes of hearing loss, and then, at the end, we'll talk about the various neural prostheses, or implants, that are used to restore hearing. And the most famous of those, of course, is the cochlear implant.

We hope to have a visit from a subject who's deaf, who uses a cochlear implant, and she'll be able to demonstrate her implant to you and answer questions if you want to ask them of her about her cochlear implant. We'll also cover a couple other different types of implants that are used to restore hearing.

So this first slide talks about sensorineural hearing loss in general. And a very common pattern of sensorineural hearing loss, which comes from the basal turn being most affected. This is an audiogram, if you will, a graph of hearing level in terms of sound pressure level, hearing threshold as a function of sound frequency for, in this lower curve, a normal hearing human and, in this upper curve, a typical pattern for someone who has a mild to moderate sensorineural hearing loss.

And so as you can see, this individual with the hearing loss has perfectly normal hearing thresholds up to the middle frequency, 1,000 Hertz, but then their threshold of hearing deviates from the normal so that by about 10,000 Hertz, they have a hearing loss of 60 dB or so. This is a very common pattern of hearing loss that arises because, for some reason, the basal turn is more affected. The basal turn is where you have the responses to the very highest sound frequencies.

This person will come into the Massachusetts Eye and Ear Infirmary, for example, and complain to the doctors and audiologists there when the hearing loss becomes noticeable, when they have a problem understanding speech. Hearing loss is intimately entwined with our perception and understanding of speech. And so when people have problems understanding speech, they often seek medical advice.

Now, the most important frequencies for those in speech are between about 300 and 4,000 Hertz. So you can see this person's hearing loss is clearly getting into the speech range, and they may have problems discerning the more high frequency parts of speech. So what are those? So typically vowels, which have the formants that we talk about, have very low frequency, so something like ahhh and ooh. They are very low frequencies.

But I think if you could read this diagram a little better, you'd understand that high-pitched sounds like the "sss" sound of an s, or something that has an abrupt onset, like a "t", has a lot of high frequencies in that sound. And so those are going to be the first types of speech sounds that are hard to understand for the person with the impaired graph on the top slide there.

Now at first, you might say, well, what we should do is get a hearing aid that amplifies the frequencies that are in loss area OK. So to do that, you'd have to have a pretty sophisticated hearing aid. You'd have to, for each sound frequency, dial in the exact amount of amplification. And hearing aids are very good these days, and there are hearing aids that can be used on a frequency specific manner, that is don't amplify anything at low frequencies and amplify exactly the amount of loss at high frequencies.

So at first, it sounds like a good idea, but we'll get into the reason that that doesn't always work later on. So that simple solution, just install a hearing aid-- a hearing aid, which everybody has seen one probably in older people-- is simply an amplifier. It has a microphone. It picks up sound. It boosts the sound in whatever frequency ranges the audiologist programs.

And then it has a little speaker and it speaks or plays the boosted sound into the ear canal of the person. So it's just an amplifier. So you can have hearing aids that work very well and their frequency tailored. And they especially work very well for the type of hearing loss that's called the conductive hearing loss because, simply, the problem is getting the sound into the inner ear, and amplifying the sound, in a person with a conductive hearing loss, works very well. It doesn't work so well in sensorineural hearing loss for reasons we'll get into in a little bit.

Now how do these hearing losses happen? There are a variety of causes that can damage your hearing. We all have fun with sounds, and we tend to have a lot of fun when the sounds are very intense. And these are so-- this is an old transparency obviously. But this is a graph of sound pressure level here. Remember the thresholds of hearing are way down here.

And these are some example sounds that have very high level, and most of these are damaging, at least if you listen to them long enough. Obviously, gunshots, firecrackers are very damaging. Those sounds are in excess of 120 dB. So a single gunshot, if it's close to your head, can be damaging.

So we had-- we're going to have an example of that in just a minute. Some of these sounds are more moderate, around the region of 100 dB SPL, for example, a chainsaw, a leaf blower, the symphony orchestra here. So everybody goes to the symphony, right? So obviously, these things depend on how close you are to the object that's generating the sound, right?

So if you go to the Boston Symphony, you're not going to endure a hearing loss. But if you have good seats and are looking down on the symphony, you'll see that a lot of the woodwind players who are sitting right in front of the brass, for example, the

trumpet players, they have a little screen behind them, a plexiglass screen that's pretty invisible unless you're looking for it. That causes a sound shadow, and so it protects their ears from the blast of the brass.

And I've also been in the symphony where, sometimes, the woodwind players would actually put in ear plugs when there's a big brass solo, and brass is blowing like crazy. And then after that big solo, they take them out, and they play their own little solo. So professional musicians are obviously very worried about their hearing. And it can be, if you're close to a trumpet or a brass instrument, deafening-- or in front of a big timpani or snare drums-- of course, these things depend on how long you listen to them, so the damage is cumulative.

It may take many years of exposure at 90 dB to produce a hearing loss even though exposure to a really high sound level, like the 160 dB, may give you hearing loss after just a single exposure. So legally, employers are supposed to provide hearing protection for their workers if you send a worker in to an 85 dB sound pressure level environment, like is common in a factory, you are supposed to provide the workers with hearing protection if it's an 8 hour shift. If it's only a 4 hour shift, you don't have to.

If the sound level is 95 dB, it's something like 2 hours. If it's 100 dB, you can expose someone to an hour of that without hearing protection, but if it's longer than that, you have to provide hearing protection. So here's some example. Movie theaters, Godzilla is 118 dB because it's a terrible roar. It can be deafening if you are right near the loudspeaker. And if you go to Godzilla 100 times. OK?

All right. So loud sound is one of the causes of hearing loss, so let's just make a little list here. High level sound is certainly one of the causes of hearing loss, and I think we have some examples here. So this is an example from some research that was done by one of the professors I had in graduate school, Joe Hawkins. And he studied temporal bones where the cochlear is in humans.

So he would get temporal bones after a subject had passed away and had donated their body to science. And they were useful if he knew something about the

individual, like if they had their hearing tested or if you knew a little bit about what activities they liked. These particular data are from a human who is an active hunter, fired a gun a lot.

And the specimens shown in the photomicrographs here are looking down onto the surface of the inner ear, or cochlea, on the left side and the right side of the subject. The bone that's on the snail shell, or cochlea, has been thinned away with a dental drill, and you can see very nicely the basal turn. The apical turn, you can't really see very well from that, but you can thin the apical turn as well. Sometimes. It's cut off and thinned in a different dish.

But anyway, what you're looking at here-- I should get out my pointer, so I point a little better. So this is the very basal end of the cochlea and spiraling up. And the human has about 2 and 1/2 or 3 complete turns of the cochlea. And this white structure here is the organ of Corti sitting on the basilar membrane.

This specimen is stained with a stain called osmium, which stains lipids and especially myelinated nerve fibers, so you can see a lot of myelinated nerve fibers. They look like threads coming out. And here's some more threads up here. And I said the organ of Corti is here, but actually, it's completely gone here on the left side, and you can see it begin right about here and go apically here up into the apical turn.

You can see a very little bit of it in the extreme basal part of the cochlea, and that's diagrammed here on this graph. This is the length along the basilar membrane from the base over here on the right to the apex. And this y-axis graphs the percent of the hair cells that are remaining. And in the basal turn, they're almost zero hair cells remaining. They're all gone. Maybe a couple little islands here and there, but it's virtually 100% hair cell loss.

And as you go around the upper basal turn, you have most of the hair cells remaining in the case of the solid line, which refers to the inner hair cells. And then you have, in the dashed lines, the three rows of outer hair cells, and there, maybe between 30% and 70% remaining depending exactly where you are.

But here again, something has damaged these hair cells, completely wiped them out in the basal half of the cochlea. And wiped a lot of the outer hair cells out and not very many of the inner hair cells are wiped out. Here's the subject's right cochlea. And in this case, you can see-- you don't even need the graph-- you can see that the organ of Corti is pretty intact. Here is a little island of loss, and then another little island of loss, but then you have an intact organ of Corti all the way up to the apex, and that's reflected in the counts here where you have, except at the very basal part of the cochlea which doesn't appear in the micrograph, you have a pretty normal complement of inner hair cells.

Outer hair cells are not in such good shape, but they're present throughout the cochlea in this right side. Now, also on here are graphs of the nerve fibers. Those are these little thread-like stained elements here that appear very nicely in this osmium stain, and they're pretty much intact through the cochlea.

Maybe in places here where the hair cell loss is really bad, some of the nerve fibers are gone, and that's indicated by this interruption here. But this is another example where you can have whatever damaged this fellow's hair cells, left the nerve fibers relatively intact. And this offers some hope to somebody who wants to install a prosthesis like the cochlear implant and stimulate the remaining nerve fiber just because they're going to stick around even if a lot of the hair cells are gone.

So this subject, as I said, was an enthusiastic hunter, and a he was right-handed. And as you can see right here, this is a top view of a person firing a rifle. The left ear of the subject is pointed toward the tip of the gun, and that's where the bullet emerges, and that's where the shock wave of the rifle, when it fires, comes out.

This is a modern rifle, not a flintlock rifle where you have a lot of smoke and sound coming out down here. Most of the sound comes at the tip of the gun. And this subject's left ear is pointed right to that and has taken the brunt of the blast in terms of the loss of hair cells. The right ear of the subject is pointed more away from the tip of the gun and is protected and has a pretty normal complement of hair cells.

Now, that's not saying that this person didn't go to lots of rock concerts, and didn't take lots of drugs that damage your hearing, and isn't an 80-year-old person, so we're going to add a few things to our list here. There are some drugs, for example aminoglycoside antibiotics-- they are really great antibiotics, but they have this side effect of damaging the hair cells.

Three, the aging process damages hearing. And in this kind of a study where you're using a human, you cannot control for these other factors and others that I haven't, but what you can do then is compare left to right. Because presumably, a subject took drugs, and they appeared in both the left and right in your ears. And obviously, the subject had the same aging in the left and right side, so whatever differences there are between the left and the right, we attribute then to the blast from the rifle that the subject shot. So this cause of left right difference would be attributed to the high level sound.

Here are some pictures from an experiment animal that has undergone a high sound level, or an overexposure. This is a normal-- I think, in this case, it's a Guinea pig cochlea. And you see the row of inner hair cells here. There is 1, 2, 3, 4, 5, about a dozen inner hair cells. That's just one row of inner hair cells.

And then there are three rows of outer hair cells looking down onto the tops of the hair cells where you have the stereocilia sticking up at you. And there are 12 or 15 outer hair cells in each of rows 1, 2, and 3. And it's such a regular pattern, and they're all perfectly there. After listening to the overexposure of sound, there are quite a few inner hair cells lost.

Those that are remaining sometimes have abnormal stereocilia. There are number of outer hair cells, in this case, in row one lost. And some that are remaining are indicated by these arrows to have abnormal stereocilia. And here's another example from a different place in the cochlea where almost the entire third row of outer hair cells is wiped out by the overexposure to noise.

So what happens when you lose a hair cell? Well, the nearby supporting cells go fill in its space, and they take over. In mammals, such damage is permanent. Once the

hair cell is killed, it never grows back. And there's a lot of interest in trying to coax the nearby supporting cells to, in these damaged cochleas, become hair cells.

But so far that has not been possible. The field was really excited about 20 years ago when this type of damage in a bird cochlea, if left for a month or so, you see reemerging small hair cells. And if you wait long enough, they become full hair cells. In the bird cochlea, the surrounding supporting cells, after damage to the hair cells, can then divide and become new hair cells, in the chicken cochlea, for example.

And this was a serendipitous discovery where people were working on damaging chicken hair cells, and they were always waiting a couple days after the exposure to look at the cochleas. And there was a holiday vacation where they exposed the animals before, and they went out of town and came back three weeks later, and they found something must have gone wrong with the exposure because the hair cells are here. They're fine. But they figured out later that, actually, the supporting cells nearby had grown back.

So that doesn't seem to help us in the mammalian pathway. There's some sort of growth factor or growth pathway in birds where these hair cells grow back, but not in the mammal unfortunately.

So this is an example from a cochlea that's been treated by an aminoglycoside, and this is just to remind me to tell you that, once again, you can count hair cells along the cochlea. This is a plot of hair cells present where lots of black bars means lots of hair cells. And this is a beautiful example of this particular drug treatment, which I believe is kanamycin, and a certain dose doesn't affect the inner hair cells at all.

But look at the outer hair cell loss in the basal part of the cochlea, virtually complete outer hair cell loss showing that the outer hair cells are more sensitive, they're more labile to this drug treatment than are the inner hair cells. And once again, the most vulnerable part of the cochlea is not the apex. 0% distance from the apex is up here. And the basal region would be down here, and that's again the most vulnerable part of the cochlear for some reason.

We can speculate about why this might be the case for drug treatment. We don't know this, but maybe the drug appears in more in a higher concentration in the basal part of the cochlea. In the cochlea, like you have in the brain, you have a blood-brain barrier. You have a blood-cochlea barrier. Obviously, some drug has gotten into the cochlea, but maybe the blood-cochlea barrier is more permeable down here in the base. And in the apex not as much drug got in. That's an idea.

It hasn't been borne out by experimental evidence, but it's an idea that people have in mind. Or, it could be that the outer hair cells are just, for some reason, easier to kill in the base. That's more suggestive that all of these things affect the hair cells in the base more than the apex. Now, these were some of the original experiments that showed what outer hair cells did for us in the sense of hearing.

So earlier in this course, we had the effect of knocking out the outer hair cells by knocking out the gene for Prestin. OK? In this case, the outer hair cells are knocked out by the drug treatment. So you've lesioned the outer hair cells in the very basal part of the cochlea. The inner hair cells are present.

Let's look at the tuning curves from auditory nerve fibers in that preparation. Now let me remind you again what's happening here. So you have the inner hair cells, and you have the outer hair cells, which have been killed by the drug treatment. And then you have most of the auditory nerve fibers coming from the inner hair cells in the auditory nerve going to the brain.

And the experiment then is to if you're recording electrodes, record from the auditory nerve fibers, get a single nerve fiber, and take its tuning curve. And that's what's shown on this top graph. So tuning curves from the normal region of the cochlea are normal shaped. They have sharp tips and tails, normal sensitivity.

In the region of the cochlea when the drug treatment has lesioned the outer hair cells, the tuning curves look extremely abnormal. There's a tail, whatever tip there is is a tiny little tip, and there's a tremendous loss of sensitivity, as much as 60 or more dB lost. Basically, these are tipless tuning curves.

And now we know that the outer hair cells have their electromotility function. They are the cochlea amplifier. Without the amplifier, you lose the tip on the tuning curve. So that should be a mini review. This is the way the outer hair cells originally thought-- or discovered to be important in the sense of hearing, to provide the normal sensitivity and a sharp tuning.

You can get all kinds of tuning curve abnormalities depending on whether you, in this case, lose all the outer hair cells. You cause disarray of the stereocilia. You have partial loss of the outer hair cells. All these kinds of things can be found after noise damage depending on the place of the cochlea you look at, the type of noise, the length of the noise exposure, and the animal.

There's a lot of variability in noise damage from exposures to 10-- 10 different animals, you can have 10 different types of loss of hair cells. Noise damage is tremendously variable from subject to subject.

Now, we also had-- this is another review. We also had the example of a psychophysical tuning curve. So this is a normal psychophysical tuning curve. Can somebody explain to me what the paradigm is? A psychophysical tuning curve, it's taken from a human listener, right? What's the paradigm?

We had this in class, so we should all know what this is. A psychophysical tuning curve, you have a probe tone. I think that, in this case, the probe tone is right at the tip of the arrow. And the subject is instructed to listen to the probe tone and say when you hear the probe tone.

Give the probe tone. Yes, I hear that definitely. Give it again. Oh, yes, I hear that. No problem. Then, you add a second tone, maybe a little bit higher in frequency than the probe tone. Probe tone was-- let's say, in this case, 1 kilohertz. The second tone, masker tone is 1.5 kilohertz, let's say. Introduce that. Person, yeah, I still hear the probe tone. I hear this other tone too. Oh, don't pay attention to that. Just listen to the probe tone. Sure, I hear that.

Then, you boost the level of that second masker tone up to, in this case, 90 dB. The

person says, I can't hear that probe tone anymore. Can you turn it up? And you plot that on your graph. That's a hit. That's a point. In that case, the masker has made inaudible the probe. And you go on varying your frequencies and levels until that masker masks the probe and the person says I can't hear the probe anymore.

And you get the so-called psychophysical tuning curve, which has this very nice tip to it and a long low frequency tail from a normal hearing person. But a person with a sensorineural hearing loss often has a psychophysical tuning curve like this. This should remind you of the tuning curves that we just saw from auditory nerve fibers in the damaged cochlea, which is basically a tiptless tuning curve.

Perhaps in this case, the outer hair cells have been damaged by fun with sounds, and you have just the tail of the tuning curve. Now, here we come to the crux of why, in this person who has a sensorineural hearing loss-- they still have hearing, but they have a big loss-- why won't just a hearing aid work?

You can certainly install a hearing aid into this person's ear canal and boost their threshold from what they used to here down at 0 dB to what they now here at 60 dB. You can amplify the sound at 60 dB. OK, fine. Then, they'll start to say, yeah, I hear it no problem. What happens when this person goes to a crowded restaurant, and there's all this low frequency DIN? Well before, all the low frequency DIN was here. It didn't get into the response area of the sharply tuned tuning curve.

Now, you have all this low frequencies that's amplified by the hearing aid. It now gets into the response area of the nerve fiber. That low frequency signal, which you don't want to pay attention to because you're listening at 1 kilohertz, is a competing, or masking, stimulus along with the signal. And so now, the person with the hearing aid and sensorineural hearing loss goes into the crowded restaurant and says I hear very well, but I can't understand the person across the table speaking to me.

All I hear is this big noise. And no matter what I-- how I adjust my hearing aid, it just sounds noisy. I can't understand anymore. I can hear. They're certainly not deaf, but they can't understand anymore because before they had sharply tuned frequency tuning, and now they have no frequency tuning at all. It's very broad.

That's the problem that a hearing aid can't deal with in terms of restoring normal hearing to a person with sensorineural hearing loss.

Before I start to talk about implants, let me just remember to say what other processes affect our hearing. And we have a list just so I don't forget anything. And one of the important things is genetic causes. So maybe you can't see that from the back of the room, but number four here is genetic causes. There are babies who are born deaf, and in the state of Massachusetts, in most states, it's mandatory to test infant hearing at birth because you want to install a hearing aid or install a cochlea implant at a young age if the baby has hearing loss.

And another cause that we should list are certain kinds of infections and disease processes. Number five, cause of hearing loss is diseases, for example, meningitis. And one of the MIT students that I used to use for demonstration of cochlea implant is deaf because at age 12, he got very sick with meningitis.

And when I asked him, how did you go deaf? He said, well, I got sick with meningitis. And I was so sick that my MD's treated me with aminoglycosides so that they would kill the meningitis bacteria. And he isn't sure whether it's the meningitis or the side effect of the aminoglycosides that made him deaf. But when you woke up, he was cured, but he was deaf. So in some cases you're not sure which of these agents caused the hearing loss.

So that's a pretty complete list now. Do we have any questions about what things cause hearing loss? And you might imagine that, during our lifetime, some of these things will be understood in a better way. It's clear why loud sound causes hearing loss. I mean the mechanical action. These things are moving. You could damage the very sensitive apparatus, like the stereocilia.

Drugs, aminoglycosides bind to some of the membrane channels in hair cells. And maybe a therapy for this ototoxicity, this hearing loss created by these aminoglycosides, could be to install some competitive binder that would occupy the binding sites while you gave the drug therapy.

We don't know at all what causes the hearing loss with aging. That's a very active subject in today's research. Genetic causes, same way, usually these are some sort of developmental factor or protein that's necessary for normal hair cell development and it's lost, in the case of recessive genetic problem. That's pretty clear how that arises.

Meningitis, it's not clear how those diseases kill hair cells, but they certainly do. But there's certainly room to imagine that will be worked on quite actively in the next 10 or 20 years. It's not known right now how the hair cells are lost in meningitis.

So let's talk about, now, people who have complete hearing loss and are eligible for the so-called cochlear implants and other types of implants that restore hearing. So this is a nice slide from, I think, the paper that we're reading for today.

And actually that reminds me, besides that paper, which is a very short one, easy to read, the textbook reading that I've assigned for today, which is most of chapter 8 on auditory prostheses is excellent. It's really up to date. It tells you a lot about cochlear implants and coding for speech, which I probably won't have time to get into. But this is a really-- I mean hearing aids past and present, that's not so important. But it has a lot of good information on cochlear implants, so I'd encourage you definitely to read that textbook passage today.

And the research report by Moore and Shannon is a very simple, easy to read paper. It shows you the sites where these various implants go. So the cochlear implant, obviously, is installed into the cochlea, right here. For people who have lost their hearing because of a problem with their auditory nerve, you put a cochlear implant in, and it's not going to do any good because the messages aren't going to be conveyed by the nerve into the brain.

And so what's an example of someone like that? Well, a disease process called neurofibromatosis type two, or NF2, is a disease process where the subjects get tumors that grow on various nerves. And a very common type of tumor in NF2 patients is called a vestibular schwannoma. And a schwannoma is a tumor of the schwann cells that normally provide the myelin covering of peripheral nerves. And it

grows on the vestibular branch of the eighth cranial nerve.

Obviously, that's quite near the auditory branch of the eighth cranial nerve. And these tumors grow and grow. They probably rob the nerve of the blood supply. They probably put pressure on it, and they certainly infiltrate the tumor cells in amongst the fibers. And when the surgeon goes in to remove that type of tumor invariably the eighth cranial nerve is cut.

So in that case, the subject has no nerve conveying messages from the cochlea into the brain. Well, the surgery is right here. You're removing a tumor from here, so it's fairly easy to go ahead and install an implant into the cochlear nucleus of the brain. The cochlear nucleus is visible. And that's what's called an auditory brainstem implant.

It should be called a cochlear nucleus implant, but it's called an ABI. And an ABI-- I'm not going to talk too much about it-- but just suffice it to say, it's an array of surface electrodes. There are two companies making these. One has 15, and one has 21 in a checkerboard pattern. And the electrodes go onto the surface of the cochlear nucleus, and their placed there during the surgery.

There was an experimental penetrating electrode array, or PABI, but that's been discontinued because of side effects. Some of these patients got trigeminal neuralgia, or pain sensations from nearby nerves, maybe by the fact that these electrodes penetrated into the brain. And so that underwent an FDA trial, but that's no longer used.

But this surface ABI electrode is used in cases of NF2 or in other cases where the nerve function is compromised. Those implants don't work very well. So if you look at this graph here. This is a graph of the different types of implants, especially I'll call your attention to the cochlear implant and the auditory brain stem implant.

In the cochlear implant, you've got a lot of people who can-- if you do in a word recognition test, how often they get the words correct, a lot of them are placing at 100% of the words. So the task here is you stand behind the subject, or the

audiologist stand behind the subject, and they say repeat after me, baby. And the person says baby. Sunshine, and the person says sunshine. And the person says, Red Socks. And you say, Cardinals. And they got one wrong.

But anyway, you can do these tests without-- it's important to stand behind the person to make sure they're not lipreading. But a lot of cochlear implant users can get 100% on these tests. Now, the ABI, auditory brain stem implants, you've got many of the subject, if not all of them, saying the wrong word or not giving you any response here. So what good is the ABI?

The real success story of these prostheses is that the person can understand speech. If the person can't understand speech, this thing isn't doing them too much good. So that's not to say that the ABI isn't successful in certain ways. The ABI is sometimes thought of as a lipreading assist device. So it helps these subjects read lips better.

For example, if you guys are deaf and you look at my letters, and I make two different sounds, pa and ba. That looks exactly the same if you're trying to read my lips. But it sounds different to you. You guys have good hearing, and it may sound a little bit different to the ABI user, and it may give that ABI user a little bit of a step up and help versus someone who's just using lipreading.

Now, just for completeness, I'll talk about the auditory midbrain implant. The idea here is to put the implant higher up in the pathway. Why would you want to do that? Well, some people think that the ABI doesn't work because there's been this tumor here. And surgeon has been hacking on the tumor to try to get it out, yanking and pulling on it.

If the tumor didn't damage the cochlear nucleus, well, the hacking and tugging on it did. And so maybe you should put the implant further up where you haven't been hacking and everything's normal. And so that's the idea behind the auditory midbrain implant, which goes into the inferior colliculus. And there have been five patients who've gone undergone the auditory midbrain implant-- actually six, five very well documented.

And the outcomes have been no better than the ABI, but that's because four out of the five well-documented didn't hit the right spot. The inferior colliculus is pretty small, and the part that you really want to go into is the tonotopically organized spot so that this needle electrode y-- this is a long electrode array with about 16 contacts on it, in this needle.

And that's put into the tonotopic part of the IC, and it didn't get into the right place in most people. But even in the one individual, got it in the right place, it wasn't any better than the ABI. But there is going to be another clinical trial in which they implant five more subjects. And hopefully, the outcomes will be better on that.

So that's the various types of electrodes. And, obviously, the cochlear implant is the real winner here. And we have been having readings-- Hi, Sheila-- we've been having readings in our class, and I'll do a reading now about the cochlear implant.

This is from-- this is not made into a book form yet because this is from the esteemed academic publication called Yahoo Finance, on the web. And this is dated September 9, 2013. And the subject of this column is the Lasker Award.

So the Lasker Award, does anybody know what the Lasker Award is? Sometimes, called the American Nobel Prize, so it's a very prestigious honor. It's given in several different fields, mostly in medicine and biomedical areas, and so there are sub-groups. And this one was given in clinical medical research award.

So the 2013 Lasker Clinical Medical Research Award honors Graeme Clark, Ingeborg Hochmair and Blake Wilson for developing the modern cochlear implant, a device that bestows hearing on profoundly deaf people. The apparatus has, for the first time, substantially restored a human sense with a medical intervention. Blah, blah, blah.

Throughout the world today, there are about 320,000 people outfitted with cochlear implants. Most recipients can talk on their cellphones and follow conversations in relatively quiet environments, and an increasing number of patients with severe age-related hearing loss are taking advantage of this marvelous invention.

So the three people here, two of them are actually founders of cochlear implant companies. So you can think of Nobel Prizes and these prize being awarded to people who made big discoveries. And certainly, in the third case, Blake Wilson did. But in the first two, it's really conveying a technology to the masses that was recognized by this award. So that's the 2013 Lasker Award.

So let's look a little bit about what a cochlear implant is, and that's shown in the next couple of slides. So the cochlear implant has an internal part, which is a series of electrodes that go into the cochlea, and the electrode comes out from here and goes into a so-called internal coil-- sorry about that-- and this is sometimes called the receiver because it gets messages from the external coil, or sometimes called the transmitter, across the skin here.

So there's skin between the external and internal coils. On the outside, you have a microphone which picks up the sound and sends the microphone messages to a so-called speech processor. The speech processor sends transforms that sound wave form into a series of electrical pulses that are sent down the electrodes and stimulate the remaining auditory nerve fibers in the cochlea.

So the cochlear implant has the electrodes, the internal part, the external part, and the speech processor and microphone. And I have a demonstration cochlear implant here. And I'm going to pass it around. These things are very valuable, so as demonstration models, they strip off the electrodes.

So the part I'm passing around is just this tube that goes down here but not the electrodes themselves, and I think it has the internal and external coil, and obviously not the microphone or the speech processor, so just to give you an idea of the size. And I think this one, the tube comes down, and it coils around a little like the electrodes do as they coil in the cochlea.

Now, this next slide is pretty important because it shows the electrodes coming into the cochlea in a cutaway diagram. And so the electrodes come in the basal turn of the cochlea. Remember there's an area in the bone that has a little membrane over

it called the round window. Surgeons can go in there and make a tear in round window and put the implant in there.

Or, they can drill a hole a little bit apical from the round window and start in the base of the cochlea, which is the big part of the cochlea and then thread just by pushing the electrode array more and more apical into the cochlea. Now, the cochlea gets pretty small as it goes very apically. And the electrodes don't fit into the apical region so far.

So current cochlear implants only can be pushed in about to cover the basal half of the cochlea, the basal 50%. So that seems like a huge limitation. It's a bit of a limitation. Fortunately, it's not an extreme limitation because the spiral ganglion doesn't go all the way to the apical part of the cochlea. The ganglion is where the cell bodies of the auditory nerve is.

And so there is ganglion that ends about 3/4 of the way out, so the last quarter wouldn't be helpful anyway. And here are the various electrodes along the cochlear implant. And modern cochlear implants have 22 electrodes.

And they are hooked up. I'll show you how they're hooked up in just a minute. Actually, I'll show you how they're hooked up right now. The way this works is the microphone signal comes into the speech processor here, and the microphone signal is split up into various bands. The microphone might pick up only high frequency, in which case, this band would be active, or it might pick up middle frequencies, in which case these bands would be active, or it might pick up low frequency or it might pick up all frequencies.

It depends on what the sound is. The output of those filters is sent to some processing schemes, which eventually result in little electric pulses, and those are shocks that are sent down into the cochlear implant electrodes. And this is supposed to be-- actually something's not happening here automatically.

This is supposed to be electrode number one, which is the most apical electrode, and so on and so forth. And this scheme only ends in electrode 18, so this is an old

diagram here because current cochlear implants have 22.

So if you are hearing very low frequencies, you're going to be stimulating very apical electrodes. And if you're hearing the highest frequencies, you're going to stimulate the most basal electrode. And this is a recapitulation of the place code for sound frequency where base of the cochlear transduces in normal hearing, the high frequencies, and the apex transduces the low frequencies.

So when we said the cochlear implant doesn't go all the way apically, it can't fit there. So what happens? Well, the apex isn't very well-stimulated in these designs. And so you will hear descriptions of people who have their implant turned on for the first time, and they'll say it sounds like Donald Duck. It sounds really shrill and very high-pitched. Well, a lot of the apex-- not drawn here-- is not stimulated.

So what happens? So these people, after a month or two, say oh, yeah, it's sounding better and better. And so there's some sort of learning or plasticity that makes things settle down, and the voices sound a little bit more normal, maybe not normal, but more normal. And perfectly, as you saw from the graph before, normal word recognition scores can be achieved even though you're stimulating just a portion of the cochlea.

Now, I have a movie here, and this gets on my nerves, but I want to show it to you because this is what's shown to patients who are about to get a cochlear implant. Gets on my nerves because you see hair cells in here that have stereocilia that are just waving around, but the stereocilia are really rigid.

But anyway, I thought it would be interesting just to see what someone sees when they are getting this stuff from a cochlear implant. Let's see if this movie will play.

[VIDEO PLAYBACK] In normal hearing, the hair in the inner ear--

PROFESSOR: I hate this. I mean the best membranes way over here. The hair cells--

-The hearing nerve still remains functional, but the hair cells have been lost or damaged. In a cochlear implant system, sound enters a microphone and travels to

an external mini computer called a sound processor. The sound is processed and converted into digital information. This digital information is sent over a transmitter antenna to the surgically implanted part of the system.

The implant will turn the sound information into electrical signals that travel down to an electrode array inserted into the tiny inner ear. The electrodes directly stimulate the auditory nerve, sending sound information to the brain. Bypassing the damaged inner ear, the cochlear implant provides an entirely new mechanism for hearing.

[END VIDEO PLAYBACK]

PROFESSOR: So that's what the patient's see. And how well does it work? So we can ask a demonstrator that we have today. Sheila come on up in front of the class. This is Sheila [? Zu ?], who is a MIT undergraduate. You're a senior now, right? What's your major at MIT?

SHEILA: I'm the only in this major at MIT. I'm in [INAUDIBLE] technology and [? society ?] and [INAUDIBLE] is a joint major between Humanities and [? Chinese. ?]

PROFESSOR: Are you an overachiever?

SHEILA: I don't know. Maybe.

PROFESSOR: So has anybody in the class ever spoken to a cochlear implant user before?

SHEILA: I know some of them.

PROFESSOR: You know some of these people?

SHEILA: We're in the same dorm. [INAUDIBLE] in my sorority.

OK. Great! So we can do this whatever way you want to. You can ask Sheila questions if you've already asked them to her. I'll ask her questions. Does anybody have any questions? Yes?

AUDIENCE: How old were you when you got your implant?

SHEILA: So I was born deaf, but I got implant when I was 3 years old. Actually, I got surgery when I was 2 years old. [INAUDIBLE] when I was 3 years old.

PROFESSOR: So one question I often get about implants into children is how young can a child be and still be implanted successfully. So the surgeons at Mass Eye and Ear say that the cochlea is adult size by age 1 and 1/2, so typically, that's the age when a person who is born deaf is implanted these days, age 1 and 1/2.

The idea to implant early is so that the subject can grow up and enjoy normal hearing, especially during a critical period for language formation, which was maybe starting at 1 and 1/2, 2 years old. So if you implant a person later, in their teens, and they haven't heard sound, they have a lot worse chances of acquiring normal language skills than someone like Sheila who has been implanted early. So the trend is to try to implant as early as possible.

SHEILA: I want to point out that I may have been implanted when I was 3 years old, but I didn't start speaking until I was about 5 years old. And I didn't start learning math or learning how to read until I was 7 years old, so I was really delayed back then.

PROFESSOR: Did you have a question?

AUDIENCE: So I was just wondering, are you like reading my lips right now?

SHEILA: Yes, I am. So the way it works, I have to see people's face, like how to read their lips, and I listen too at the same time. I could read your lips alone, but maybe not 100% accurate. Or, if I don't look at you lip, and listen to you, maybe not really understandable, so it's like I have to read lips and listen at the same time in order to understand you.

PROFESSOR: But if you don't read lips, for example, in situations like talking on the telephone, can you understand someone on the telephone?

SHEILA: It depends on the person. If I'm familiar with your voice, like I know my dad's voice. I can understand him pretty well, but if I'm talking to a stranger on the phone, then maybe not. And also, don't forget, there's a lot of background noises, so that makes

it harder for me to hear people on the phone.

PROFESSOR: When I-- let's say about 10 years ago in my lab, I hired a research assistant who used a cochlear implant, and she wanted me to shave off my mustache. It was because she had a little trouble reading my lips with my mustache. Now, my wife also has told me I should shave a mustache, but she has normal hearing.

SHEILA: I actually had a professor at MIT when I was a freshman, I comment one day I had hard time understanding him because he had like a full beard. Then, next day, he shaved off everything. So he came up to me, I was like, who are you? [INAUDIBLE]

PROFESSOR: That's very nice. Wow, interesting! I didn't shave off my mustache, neither for my assistant, nor for my wife.

SHEILA: [INAUDIBLE] half is better.

PROFESSOR: Maybe. Yeah. So if an audiologist were to test your speech comprehension, do you think you'd get every word correct or do you think you'd miss some?

SHEILA: I think I probably miss some words or may not pronounce some words correctly, because the way I hear words may sound differently from what you hear. And sometimes, in English language, some words don't sound exactly the way it's written down. So I think my speech is not bad because, based on my interaction with people, they seem to understand me most of the time. Yeah?

AUDIENCE: Do you know any other languages?

SHEILA: I know another language. Yeah. I know a couple of languages. I know American sign language. I use it often to help, in some cases, when cochlear implant don't work. For example, if I'm in a loud bar or party and I can't hear people, but if I use sign language, I understand people. I know British sign language too, but that's another sign language.

PROFESSOR: So you mentioned when you're in a party and you can't hear people, does that mean that there's a lot of noise that masks speakers and that's a hard situation for you? Right.

SHEILA: So like the speaker's voice will blend into other speakers voices or background noises, so I tend to rely on lipreading or some other method to communicate.

PROFESSOR: Right. So for example, in cochlear implants, a common problem is when there is an environment where there's many, many frequencies of sound, like a crowded restaurant or a party, and there's one speaker that you're trying to pay attention to and the subject gets overloaded on every single electrode. And so some kinds of cochlear implant processors try to circumvent that by trying to pick out in the spectrum the important peaks of the spectrum.

So if you're listening to the vowel aa, you'd have three formants. The processor tries to pick out those formants and only present electrodes corresponding to those formants and turn all the other electrodes off so that there's a huge difference between where the formant is and where the nothing is. Really in theory, it's nothing, but actually, it could be a noisy background.

So that is one kind of speech processor design. It's called the speech feature extractor, sometimes the speak chip. It's trying to pick out formants so that it can understand vowels. And it's supposed to be less sensitive to noise masking, which is a huge problem in cochlear implants.

A cochlear implant user doesn't have the sharply tuned filter of the normal auditory nerve tuning curve that normal hearing people do. What about listening to music? Do you listen to music?

SHEILA: Yeah. Like last month, I went to hear Yo-Yo Ma play. Like when-- I can hear music, but I'm not sure. I think I hear music differently from you guys because there's a whole range of frequencies, like you said, but yeah I can listen to music.

AUDIENCE: How often do you go to the doctor for updates?

SHEILA: How often do I go to--

AUDIENCE: You're doctor.

SHEILA: Oh, you mean audiologist. I see audiologist like maybe once every year just for a checkup and remapping.

PROFESSOR: So do you get a remapping or do they just bill your insurance company?

SHEILA: Yeah.

PROFESSOR: Yes.

SHEILA: It's expensive.

PROFESSOR: But do they-- do you know if they change the mapping for your electrodes?

SHEILA: Yeah, they change it, but they told me it's not really a lot of changes. So I think the older you get, the less change is made than when you were younger.

PROFESSOR: Perhaps, yeah. So that's interesting. So how do they do that mapping? Do they say here's electrode 1, and then here's electrode 2. Which is higher? Do they do that?

SHEILA: Yeah, so I had to go into a special sound booth. So it's like a cell that is completely soundproof. And they will test me on a bunch of sounds like saying stop if it's too loud, or which one is louder or softer, can you repeat words after me, and so on. And they use all of that input to create a new map.

PROFESSOR: Interesting. So apparently with cochlear implant users, the frequency mapping of the electrodes doesn't change in a big way. But in the auditory brain stem implant, they go through yearly checkups and, evidently, the mapping can change a great deal. So it's completely different. In cochlear implants, usually the most apical electrode evokes the lowest sensation of pitch and more basal electrodes get higher and higher sensations of pitch.

AUDIENCE: How easy is it for you to differentiate between two voices? Like if you didn't see who was talking and if I said something and then Professor [? Brown ?] said something, how different would our voices sound to you?

SHEILA: His voice is deeper, and you're farther away from me. So I think I can tell the

difference between you two. I can tell difference between male and female voices.

PROFESSOR: Right. Female voices sound higher usually.

SHEILA: Higher pitched. Yeah.

PROFESSOR: Do you know Mandarin Chinese?

SHEILA: Yeah, a little bit. I can speak some Chinese, but not so good because I haven't used Chinese for a long time.

PROFESSOR: It's a tonal language, right?

SHEILA: Yeah. Oh my God!

PROFESSOR: Does that give you--

SHEILA: It's like I went to China 4 years ago. I stayed in China for about a month. So my grandma, she couldn't speak English, so I had to speak to her in Chinese. But it's interesting how it's-- when I talk to people, like when I speak myself, I have to remember how use the tones, but if I listen to them, I can't tell the difference between tone. So what I do is I read their lips and listen.

And I use context clues like so if the sound goes with this sound, so I think those sounds form a certain word. That's how I did, but I believe I can learn Chinese with a matter of practice and getting used to the sound.

PROFESSOR: Apparently, cochlear implant users have a lot of problems with melodic intervals, octave matches, and tonal languages. The temporal code for frequency that helps us appreciate musical intervals is not present at all in any cochlear implant scheme that's used now. So you only have the place code for sound frequencies, you don't have the timing code in current generation cochlear implant users.

And so the goal, remember, is to allow the users to understand speech. It's not in terms of recognizing musical intervals. Now, if cochlear implant companies were based in China, maybe the goal of understanding Mandarin Chinese, which is total,

would be more important, but so far, that hasn't happened.

AUDIENCE: Are you more comfortable with speaking with people or are you more comfortable with not speaking with people?

SHEILA: Well, I'm more comfortable using sign language, but I don't mind going up in front of people and speaking.

PROFESSOR: So one time, I had a demonstrator get asked this question. What's the stupidest thing you've ever done with your cochlear implant? And he had a response right away. He said when I first got my implant, I went to the beach. And I was 13 years old, and I was a typical teenager. And I saw someone else with a cochlear implant, and that was great because it was the first person I had ever seen.

And so I said, let's swap processors. And that was actually a very stupid thing to do because each cochlear implant user is not only programmed for their coding for frequency, but they're coding for how much shock goes into auditory nerve. And some people who have electrodes close to the auditory nerve don't need much current all, but if your electrode is far away you need a lot of current.

And this fellow got a processor that had been dialed in a lot of current, and so he got a big severe shock when you turn the other person's cochlear implant on. So that's something they tell you not to do, right?

SHEILA: I don't think anybody told me that. But clearly I was like, OK, total wipe out. That's a bad shock.

PROFESSOR: You did that also?

SHEILA: Well, we both did. We exchange at the same time.

PROFESSOR: Kids don't usually listen to adults, right? So are there a lot of students at MIT who use a cochlear implant?

SHEILA: So far, by now, I think I'm the only one. But last year, there were two of us, but he graduated. So this year, I'm the only one. But I'm not the only deaf student. There

are like two or three other deaf student, but they wear hearing aids.

PROFESSOR: Question.

AUDIENCE: How often do you turn it off-- or how often is it off?

SHEILA: Oh, I turn it off every night. [INAUDIBLE] I go to bed because there's no point when I go to sleep, right? And when I take a shower or go swimming or if I want to have a [INAUDIBLE] day. On campus sometimes, I would get so tired of listening to people, I would just take it off.

PROFESSOR: Which classes do you turn it on and which classes do you turn it off? That's OK. How long does your battery last?

SHEILA: My battery last like 3 or 4 days, disposable battery, 3 or 4 days, but rechargeable battery it's like one day.

PROFESSOR: And do you have an implant on one side only, or both sides?

SHEILA: In my right ear, it's just one side.

PROFESSOR: Are you going to get it in the other ear?

SHEILA: I'm not so sure because it takes time. I had to go through a surgery, to see doctors, and so on, so I'm not sure at that time because I'm so busy at MIT.

AUDIENCE: What kind of alarm clock helps you to wake up?

PROFESSOR: Do you have an alarm clock?

SHEILA: Oh, yes. I have a special alarm clock. So I know you guys use a typical alarm. They make loud noises. But for me, I use alarm clock and a flashing lamp, so it just flash light on me that helps to wake me up. But some other people say it doesn't work for them, so what they do, they take a small vibrator thing and tuck it under their pillow or mattress, so it's like that then shocks them awake.

PROFESSOR: What other kinds of problems do you have with your implant besides noise?

SHEILA: I wish it was really waterproof because if I go swimming with my buddies who are not deaf, then how can I hear them. But right now, it's like a computer, so obviously, I can't just jump into water.

AUDIENCE: I was going to ask who taught you sign language.

SHEILA: Do you know some sign language?

AUDIENCE: A little, but where did you learn?

SHEILA: [INAUDIBLE] I learned when I was here at MIT. That was about like two years ago, so I took a class at Harvard. And then from there, I met a lot of deaf people here at MIT and outside of MIT, so I was able to be comfortable in sign language. I don't know. I guess it's not really hard for me to learn sign language compared to, let's say Spanish, because it's more official. You don't need to listen or speak, so it's really like all hands and [INAUDIBLE]. So it was pretty natural for me to pick it up.

And I use sign language on a daily basis with my boyfriend or with my friends or whenever I ASL interpreter for my class.

PROFESSOR: So you often have an ASL interpreter?

SHEILA: Yeah, not all, but it depends on the class. For example, if the class is math or science lecture based, like one hour long lecture, then I use [INAUDIBLE] like real time closed captioning. Someone sit next to me, and on the computer screen, I read whatever professor saying in real time, and that person type out everything.

Another class, like more of a lab or a hands on class or more moving around, then I use ASL interpreter because it's just awkward to carry around a laptop reading words on a screen.

PROFESSOR: What do you want to do after you graduate?

SHEILA: Right now, I'm applying to one Ph.d program at Harvard that's a program he is a part of, so he may be my professor next year even.

PROFESSOR: Yeah. If you graduate. What's the program? This is a little sales pitch. You can tell them about it.

SHEILA: The program is part of Harvard, but it was a part of MIT before. But it's a Ph.d program called Speech and Hearing Bioscience and Technology. Right?

PROFESSOR: Right.

SHEILA: And it's a program that focus on hearing, cochlear implant, hearing aids, or anything related to hearing and speech. So right now, I'm applying to that program. We'll see how it goes.

PROFESSOR: Good.

AUDIENCE: This is personal, but did your boyfriend already know sign language?

SHEILA: Oh, he's deaf himself, so he knows sign language. But he's like me. He could speak and sign. But difference is he had cochlear-- no wait-- he had hearing aid, I have cochlear implant.

AUDIENCE: Do you think that you've become a faster reader? Like do you think you're faster at reading than most people because you rely on it more?

SHEILA: I would be more what? Faster?

AUDIENCE: Faster at reading.

SHEILA: Faster at reading lips?

AUDIENCE: Like reading words on a screen or reading text.

SHEILA: That's a good question. I never thought of that. It's a possibility because yeah, you're right. Have you seen it in person?

AUDIENCE: I haven't seen it.

SHEILA: You haven't seen it. So it's like on that comp screen, where she type out words really fast. So I have to read fast. But after one hour, I got too tired to read, so I just

look around the room. The good thing is after class, she send me a transcript, so I will go back and look at it again. So I mean, it's really tiring to look at computer screen, for one hour straight, reading words really quickly.

PROFESSOR: OK. So the cochlear implant is sometimes called the most successful neural prosthesis, and here we have an example. So let's give Sheila a hand. Thank you very much for coming. And we'll talk next time about brain stem reflexes. So we'll hang around if you have any other questions.