GLOBAL LISTENING CENTRE

WHITE PAPER

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Collateral Damage: An Overview of Hearing Loss and Listening Disorders in Pediatric Cancer Treatment

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As humans, we have four modes of communication: reading, writing, speaking and listening. Two of these, listening and speaking, are integrated into our DNA time-line along with the many other milestones that parents across the globe follow as their young child develops. Both listening and speaking are DNA sequenced and occur at the appropriate time for the youngster. Reading and writing, on the other hand, are educationally enabled and will only develop if the child is taught how to read and how to write.

The ability to speak is contingent on the child being in proximity of people who are speaking. This has been demonstrated over time through some pretty gruesome experiments on language deprivation (Shattuck & Candland, 1994). Speaking, reading and writing are all based on the child's ability to hear and understand what is being heard—listening.

A child with listening problems, be it based on physical, cognitive, or treatment-based reasons, can suffer a lifetime of difficulties. Listening disorders have

an impact on learning, communication, school performance, social interaction, and overall quality of life. Listening disorders can lead to academic under-achievement, inability to create or retain relationships, job issues and more.

It is important for all parents, especially parents of children undergoing treatment for any type of cancer, to be aware of the various issues and be strong advocates for ongoing auditory testing and remediating any problems along the way.

We Have Been Listening Forever!

We have been listening since before we were born. Our ability to hear and understand is woven into our DNA and is the basis for learning the three other communications skills that we use on a daily basis: talking, reading and writing. It has been shown that hearing or listening difficulties during infancy can cause many communications and socialization issues as the child grows up.

Each of us is a born listener. According to research done by Patricia Kuhl at the Institute for Learning and Brain Science at the University of Washington, sensory and brain mechanisms for hearing are developed at 30 weeks of gestational age, and the fetus is listening to their mother talk during the last 10 weeks of pregnancy and at birth can demonstrate what they've heard.

> *Within a few days after they're born, they recognize familiar faces, voices, and even smells and prefer them to unfamiliar ones (it even looks as if they recognize their mother's voice at birth based on the muted but still audible sounds they hear in the womb). (Gopnik, Meltzoff, & Kuhl, 2000)*

Since it is a 'built-in' skill, we tend to take it for granted. Parents might monitor and mark the milestone of their child's first words, but they never think about the fact that these words are uttered because the child has the ability to hear and process the sounds into usable information. Just ask yourself "When was the last time you gave any serious thought about how, or how well you actually listen?" The truth is that we don't think about listening and tend to communicate under two key assumptions.

The first is 'when we speak, and the listener acknowledges in any way—by a nod of their head, a slight raising of their hand, a glance directly into your eyes, verbalizing the words "okay" or "yes"—we feel that we have both been heard and understood.

The second assumption turns this around, "when we listen, we are sure that we fully understood what was said—both in words and context."

Of course, neither assumption is accurate all of the time, and generally, either one is correct only a small percentage of the time.

Rhabdomyosarcoma is a rare cancer that tends to form in soft tissue, usually muscle tissue in the arms, legs, head and neck areas, in the hollow organs like the bladder or uterus. It can occur at any age, but most often affects infants and young children.

> *The outlook (prognosis) and treatment decisions depend on the type of rhabdomyosarcoma, where it starts, tumor size and whether the cancer has spread. Treatment may include surgery, chemotherapy and radiation therapy.*
>
> *Major advancements in the treatment of rhabdomyosarcoma have significantly improved outcomes. After completion of treatment, people need lifelong monitoring for potential late effects of intense chemotherapy and radiation. (MayoClinic, n.d.)*

While the Mayo Clinic calls out the need for lifelong monitoring because of the treatment's potential late-effects, it is important to realize, and plan for, the long list of potential side-effects that present during and immediately after the treatment period.

The National Cancer Institute (NCI) provides a somewhat extensive list of the potential side-effects of cancer treatment. It includes:

anemia	appetite loss	bleeding and bruising (thrombocytopenia)
constipation	delirium	diarrhea
edema (swelling)	fatigue	fertility issues
hair loss (alopecia)	infection and neutropenia	lymphedema
memory or concentration problems	nausea and vomiting	nerve problems (peripheral neuropathy)
pain	sexual health issues	skin and nail changes
sleep problems	urinary and bladder problems	

While some of these side-effects might occur at the beginning of treatment, others don't appear until mid- or late in the treatment. Others don't appear until after a prolonged period post-treatment.

Some side-effects disappear (hair loss, neutropenia...) within a reasonable time-frame after treatment ends, and others, like peripheral neuropathy (tingling and reduced feeling in the fingers and toes, neuropathic pain, etc.) might linger for the rest of the child's lifetime.

Each side-effect creates its own set of issues. Most are manageable, even the need to be extremely cognizant of the warning signs of neutropenia throughout the patient's chemotherapy, and a few weeks after, due to the body's inability to fight off any kind of infection.

However, reviewing the side-effects presented in the NIH's list, it is obvious that one very important one has been left out. Important because it can play havoc with the child's socialization and academic achievement once the child completes treatment. This, somewhat hidden side-effect is a variety of potential listening disorders, and topping this list is hearing loss.

Listening Disorders

Listening disorders is a broad topic that focuses on the multitude of factors that make it difficult to understand the words people are saying or to interpret and identify other, non-verbal sounds. Factors include physiological issues like hearing loss; cognitive and neurological issues like tinnitus, auditory processing disorders or auditory dyslexia; psychological issues such as depression and narcissism; and various external issues generally outside of the listener's control such as the understandability of the speaker's voice, the vocabulary being used, room acoustics, etc.

Unfortunately, children being treated for cancer can experience a reduced level of understanding from any one or more of these four categories.

It helps to understand the magic of our auditory system - our ears and the small substructures that connect our ear, the collector of sounds, to our brain, the ultimate interpreter of these sounds.

Our Auditory System

In its simplest form, our auditory system is comprised of two thin membranes (ear drum and oval window), three small bones that make up the ossicles (malleus, incus and stapes), some fluid (cochlear fluid), a few rows of hairs, or cilia (nearly 16-20,000 cilia in total), that look like cowlicks, and a communication

cable to the brain (cochlear or auditory nerve). With this relatively simple setup, our auditory system performs its magic by converting sound energy (slight changes of air pressure) into mechanical vibrations. Then changing the mechanical vi-

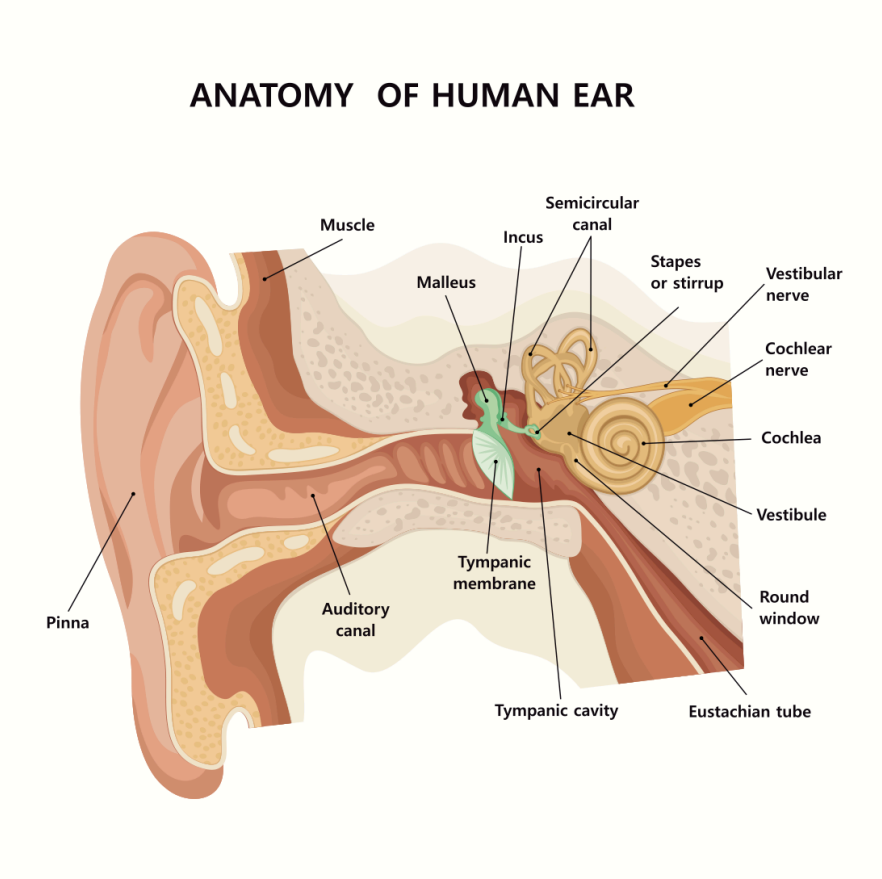

Figure 1. Anatomy of Human Ear | logika5600/Shutterstock.com

brations into fluid waves that flow over the cilia which turns the wave action into neuro-electric impulses that our brain can decode—all of this occurring within a very small space.

Our ears enable us to hear, but hearing is only the first step in the complex set of processes that we call listening. Hearing is about the sounds, while listening is about understanding those sounds. Hearing is not a choice—we cannot turn it off. There is no on/off switch in our ears and no cover that we can pull down over our ears like we have with our eyelids that can close our eyes and block out our

vision. We 'hear' every sound around us 24/7. Listening, however, is a choice. We choose when we want to listen and to what we want to listen to.

How well we hear these sounds depends upon the physical condition of the system. Damage to any of the components, the ear drum, ossicles, cochlear, or cilia, can change or distort the impulses being transmitted to our brain making understanding the sounds difficult.

It is often said that people with listening disorders, can hear people talking, they just cannot understand the words that are being said.

Hearing Loss

Hearing loss is at epidemic proportions around the world and is considered a major public health issue. It is the third most common physical ailment behind arthritis and heart disease. According to the World Health Organization (WHO), over 5% of the world's population suffers from disabling hearing loss. Five percent may seem like a small number, but that totals over 360 million people across the globe. ("World Wide Hearing Loss: Stats from Around the World," n.d.)

Nearly a fifth, 20%, of all Americans 12 years or older have hearing loss so severe that it may make communication difficult, according to a new study led by Johns Hopkins researchers and published in the Nov. 14 Archives of Internal Medicine. (HopkinsMedicine, 2011). That's 12 years or older!

Sound has two fundamental qualities - amplitude or volume, measured in decibels (dB) or sound pressure level (SPL), and frequency which is measured in cycles per second or Hertz (Hz). Hearing loss is the inability to clearly hear sounds softer than a certain volume at different frequencies across the audible spectrum, generally from 20 Hz to 8,000 Hz.

There are two types of hearing loss, conductive and sensorineural. Conductive hearing loss is generally physical in nature, caused by a malformed ear, fluid in the middle ear (otitis media), allergies, infections, foreign bodies in the ear canal (beans, legos, etc.), impacted earwax or otosclerosis (a hardening or malformation of the ossicles). In all but the most severe cases, conductive hearing loss can be reversed leaving the individual with the same degree of hearing acuity they had prior to the incident.

Sensorineural hearing loss is defined by damage to one or more of components of the auditory system: the cochlear, the cilia, or the auditory nerve. Sensorineural hearing loss can be caused by exposure to a sudden extremely loud noises (explosion, gun shot, activation of an automobile's air bags), disease, genetics, head

trauma, tumors, or long-term exposure to excessive noise, chemotherapy or radiation therapy. Unlike conductive hearing loss, sensorineural loss is almost always permanent and requires a technological solution to allow the individual to regain their hearing acuity - hearing aids, personal listening devices, or if the hearing loss is extreme, cochlear implants might be called for.

Effective listening requires that we hear the sound stream with sufficient volume and clarity to discern the words to conceive the speaker's meaning.

In general, an individual with very good hearing can hear sounds at the reference volume of 0 dB, also known as the hearing threshold for the human ear. It does not mean that there is no sound at all, it is just the softest sound that most humans can hear.

Birds chirping is a little louder with a volume of roughly 10-15 dB and a normal conversation between two adults has a volume of around 40 dB. On the loud side, a dog barking measures roughly 70 dB, a lawnmower quite a bit louder at 100 dB and a firecracker creates a sound level of 130 dB. Sounds louder than 130 dB can cause permanent damage to the ear drum.

Hearing loss tends to vary across the frequency spectrum. Most people with hearing loss have, what is known as high-frequency hearing loss which means that they have difficulty hearing the higher frequency sounds like a baby's cry, the sounds of the songbirds, or even their doorbell or telephone ring tone. Far less common is low-frequency hearing loss which is generally reported in individuals with Meniere's disease.

Hearing loss is categorized as a low-frequency, notch, or high frequency loss depending on the range of frequencies most affected. It is also categorized as minimum (between 15 and 25 dB), mild (between 25 and 40 dB), moderate (between 40 and 60 dB), severe (between 60 and 80 dB) and profound (over 80 dB).

To provide a broader understanding of the levels of hearing loss, let's look at the the illustration (Figure 2) on the next page. It places familiar sounds on a chart known as an audiogram, the chart an audiologist uses to graph an individual's hearing loss. The loudness of the sound is noted on the Y-axis, while the frequency is noted on the X-axis.

A person with a mild, 30 dB hearing loss might not be able to clearly discern sounds that are much above the 30 dB line on the chart, such as the birds chirping. They might hear some sound, but to recognize the sound and identify the birds could be very difficult. A person with a 65 dB hearing loss would lose much of the conversation, especially the all important consonants that are softly spoken

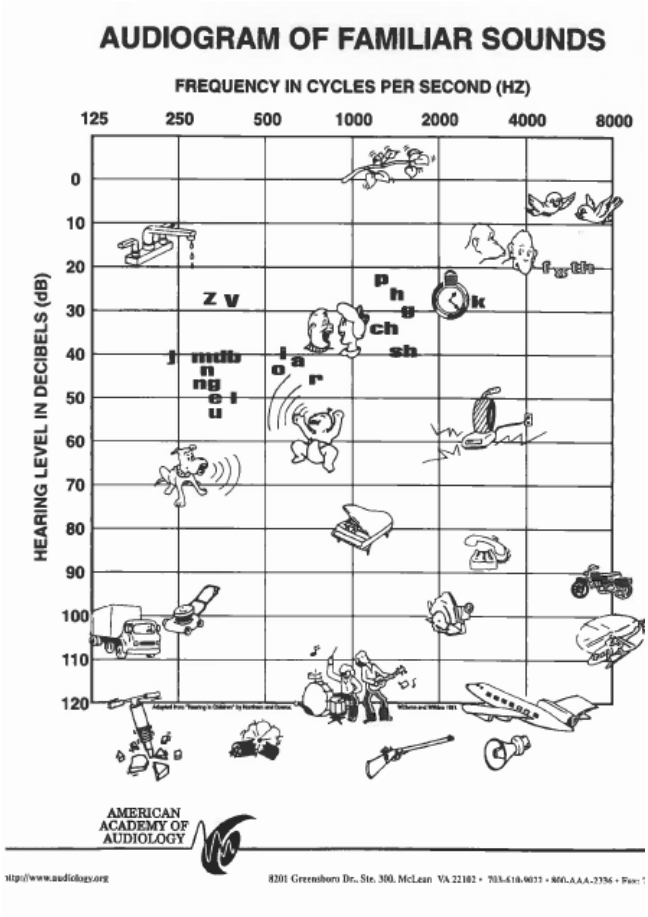

Figure 2. Audiogram of Familiar Sounds

and high in frequency. While we can create loud vowel sounds, it is very difficult to generate loud consonant sounds. Try making a loud /f/ or /s/ sound—difficult and probably messy if not impolite.

Most people tend to believe that hearing loss is just about the reduction in sound volume, but the reality is that it is more complicated. Hearing loss is not just 'loudness' issues per se, but the variation of volume across the audible frequency range. As we'll see in a little while, having a hearing loss at the high frequencies can cause the consonant sounds to be distorted with less clarity — they can hear the people talk, but cannot understand the words being said.

In the classroom the teacher's voice may be loud enough to be heard, but to children with even a minimal hearing loss, may not be intelligible. They will re-

spond when their names are called — a very familiar phoneme stream — yet will confuse or not discern distinctive sounds needed for reading and language skills. Background noise tends to block or garble the speech signal even more, and classrooms, which are not designed for to reduce echoes or reverberation make listening in this early academic setting difficult to the child with any listening disorder.

For students, especially younger ones, this can be academically devastating. Learning requires that the words being spoken be heard with clarity, phoneme by phoneme, so that they can be recognized and understood and then integrated with other information held in both short- and long-term memory.

It doesn't take much of a hearing loss to have adverse affects on children — as little as a 15-20 dB, less than the American Medical Association classification of hearing loss which is set at 25 dB. Minimal Sensorineural Hearing Loss (MSHL) can be the causative agent for a life of academic, social, employment and financial under-achievement.

> *The largest discrepancy between children with MSHL and children with normal hearing was on the subtest communication. The subtest communication focuses on a student's understanding ability, vocabulary, word usage skills, and storytelling abilities - all very important skills for learning in school. In fact, a child with MSHL is 4.3 times more likely to experience trouble in the area of communication than a child with normal hearing. (Bess, 1999)*

Bess added that, in his study, "*37% of children with MSHL failed at least one grade compared to a district norm rate of about 3%.*" Additionally, he notes

> *… that persons with hearing loss are known to expend considerable effort in processing information - especially understanding speech under poor acoustic conditions such as classrooms. Such a situation increases learning effort and, at the same time, depletes the energy available for performing other cognitive tasks. (Bess, 1999)*

As a result, it might be expected that children with even low-level hearing loss will often be tired, frustrated and may 'act out' as a result of their frustrations.

Consonant Confusion

The English language is made up of two types of sounds, vowels and consonants. Generally, the letters a, e, i, o and u are considered vowels while all the rest are labeled as consonants. The difference being that a vowel sound is made with the

mouth and throat not closing at any point and because of this, creating more volume or power than the consonant sounds.

While the vowels provide the volume or power to our speech, the consonants provide us with the meaning of the word. Take, for example, the short phrase "Say Things With Feelings." If we remove all of the vowels, we would have "Sy thngs wth flngs." While not the easiest read, most people would figure out the individual words as well as the sentence's meaning without the benefit of any vowels. However, if we remove all of the consonants, we would have "A i i eei." A totally meaningless gaggle of letters.

It is the consonants that allow us to discern the words in a sentence and create meaning from what we hear (or read!).

If we look at Figure 3: Phonetic Distribution Overlay below, we notice that many of the consonants are in the soft sound, low volume, high frequency region of the chart. This is especially true of the /th/ /f/ /s/ and /h/ sounds. A person with even a mild hearing loss of 30 dB could have trouble discriminating these important

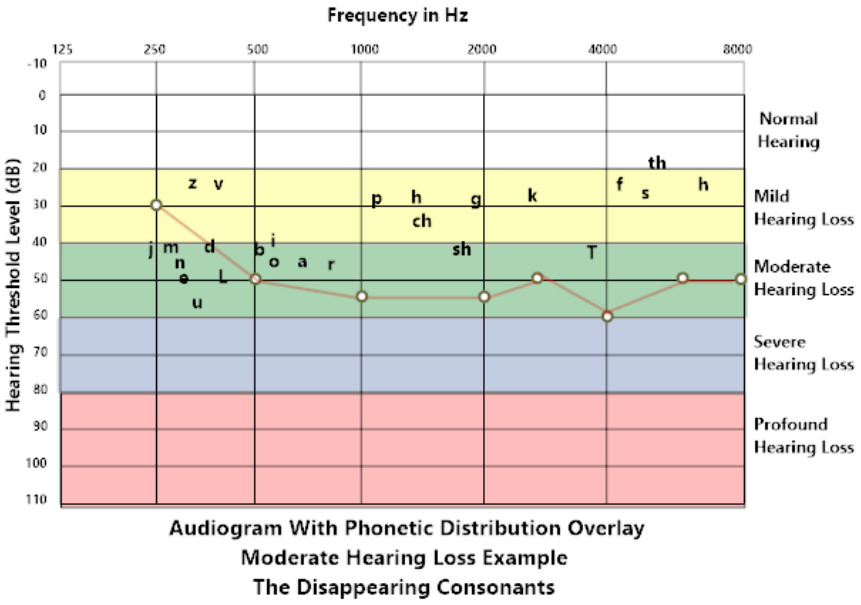

Figure 3. Phonetic Distribution

consonant sounds making it easy for the listener to confuse, say, an /f/ sound for a /th/ or even an /s/ sound. When this confusion occurs, the listener has to spend additional time and cognitive energy trying to recognize the word, when in the

meantime, the speaker has pushed forward with multiple sentences or concepts in the conversation unaware of the listener's comprehension problem.

As adults, our vocabulary is generally comprehensive enough to allow us to predict and 'auto-fill' the words we miss. This is called auditory closure.

> *If a piece of a word—or a word or two—is missed in a conversation, the listener will, unconsciously, fill in the missing parts based upon the context of the conversation and their experiences. This process is so automatic that people never realize that they missed the words at all. (Ehrlich, 2016)*

But for a young child, who is still learning language, prediction is not possible because of limited vocabulary and experience, thus creating a considerable barrier to academic and social success.

Hearing loss is a pretty abstract concept. I find that a good way to visualize it is through the use of harmonic voice prints. Figure 4 is a harmonic voice print of the phrase we used before, "Say Things With Feelings." It is a graphic representation of the vocal dynamics used to create these words. The Y-axis represents the audible frequencies, the X-axis represents time, and the intensity of color represents the auditory volume—from light blue and green being very soft, to deep red being loud.

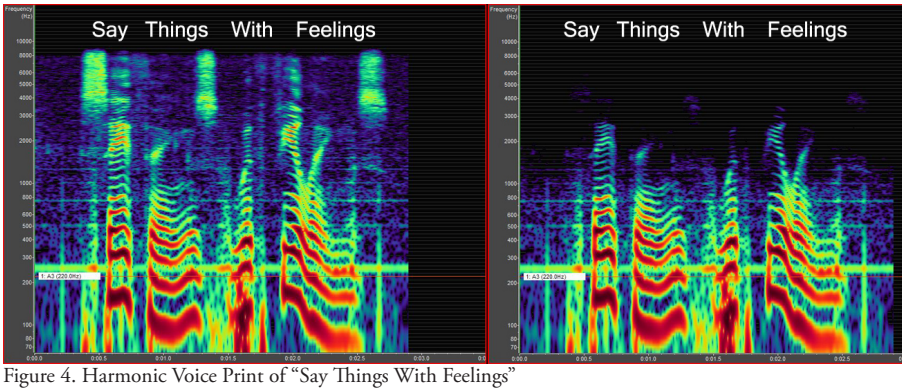

Figure 4. Harmonic Voice Print of "Say Things With Feelings"

The print on the left represents the sentence as it was spoken — with full fidelity. The print on the right is the same audio track run through a hearing loss simulator set to represent a moderate (approximately 40 dB) hearing loss.

Notice that all of the /s/ sounds have all but disappeared along with the /th/ and /f/ sounds. But the vowel sounds retain close to their original (full fidelity) inten-

sity. Someone with this level of hearing loss (mild to moderate), listening to this sentence might have difficulty understanding the words, especially if they heard them out of context or in a noisy environment,

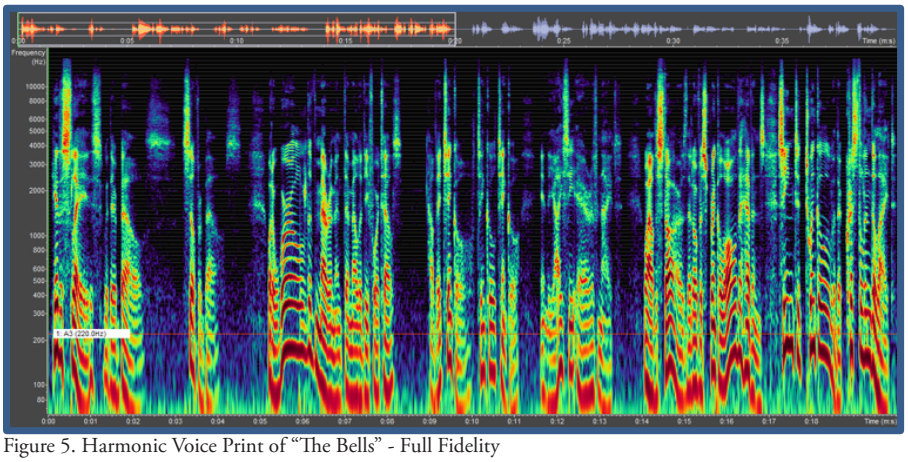

Figure 5. Harmonic Voice Print of "The Bells" - Full Fidelity

The voice print (Figure 5) above is a slightly longer chain of words — the beginning of Edgar Allen Poe's poem "The Bells" read by a professional announcer. This print shows the full fidelity of the announcer's voice.

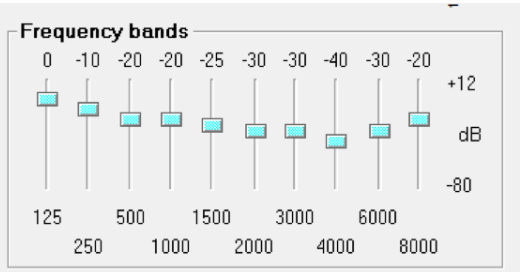

Figure 6 Hearing Loss Simulator - Moderate Hearing Loss

With the hearing loss simulator set for a moderate hearing loss, 40 dB maximum at 4000 Hz, The Bells takes on a very different look as shown in the voice print (Figure 6) on the next page.

The amount of information loss is remarkable, especially considering the relatively low level of hearing loss. Most of the consonants, especially the final /s/ sounds — the plural descriptors — are just barely audible.

High frequency hearing loss also affects the individual's ability to discern the various vocal intonations that indicate that the speaker is asking a question, invoking sarcasm or trying to be humorous. Missing these cues can be devastating both in the classroom, in social situations, or in the workplace.

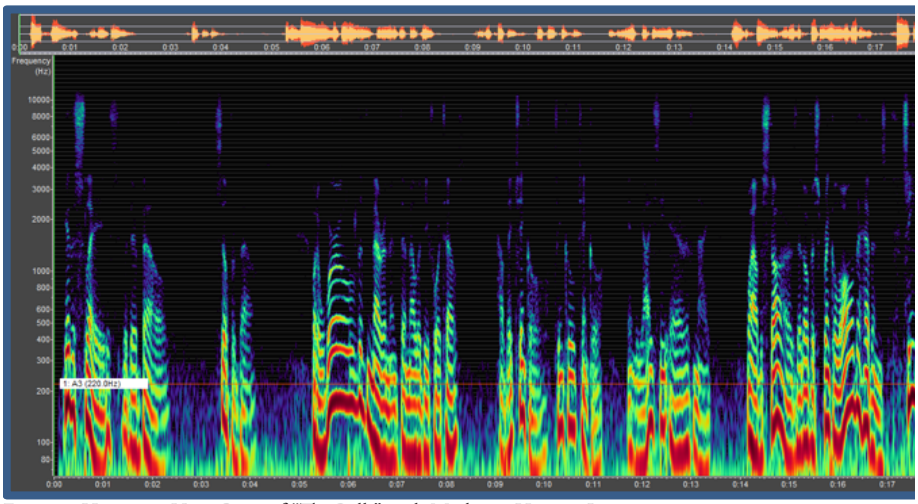

Figure 7. Harmonic Voice Print of "The Bells" with Moderate Hearing Loss

Imagine trying to listen to your teachers and fellow students on a daily basis only hearing part of what's being said. Imagine your teacher trying to understand the students' questions, the waiter taking your order, or your physician trying to understand your problems with the treatment that is being provided.

Hearing loss lends itself to many errors in understanding, academic under-achievement, mis-diagnoses, broken relationships, financial losses, and more.

Ototoxicity

Ototoxicity is the property of being toxic to our auditory system, specifically to the cochlear or auditory nerve, the cilia, or the vestibular system, which contributes to your sense of balance and spatial orientation. Ototoxic damage to any of our auditory system components causes a sensorineural hearing loss which is generally irreversible, and permanent.

Surprisingly, many common drugs are ototoxic. Drugs that we might take every day without giving them much thought — aspirin, NSAIDs and many analgesics can damage our auditory system. These include Advil, Nuprin, Motrin (Ibuprofen), Aleve (Naproxen), Naprosyn and more. Hydrocodone, when combined with an acetaminophen (e.g Vicodin) has also been strongly linked with the development of hearing loss (Hain, 2017).

Some antibiotics, as well, are known for their ototoxicity, Gentamicin, a drug listed on the World Health Organization's List of Essential Medicines, being the

most prevalent. Both neomycin and dihydrostreptomycin are considered to have high levels of hearing toxicity.

All drugs, over-the-counter (OTC) and prescription, have side-effects and, for the most part, we don't realize all of what they can do to us. Many of us know that if we take too many aspirins it will upset our stomach, if we abuse cold medicines (pseudoephedrine) it can cause irregular heartbeat, shortness of breath, high blood pressure, etc. But how many of us truly take the time to read the paperwork that accompanies the medications the we take? How many of us truly listen to the final seconds of the TV advertisements for the latest and greatest prescription medications? If we truly read the papers, or listen to the television commercials for both OTC and prescription medications, we would hear enough about the side-effects to keep us from ever taking the medication. That is if we can understand the rapid-fire speaking they use when describing the various side-effects.

But there is always a balance of risk-reward. While these drugs may have a tendency to hit us with side-effects, we hope that the symptoms for which we're taking the medication will be abated. This is especially true with the chemotherapy drugs that we, our children, friends or family members have to take to cure the cancer inside.

Ototoxicity of Chemotherapy Agents

We live in the world of cancer, here, at this conference, pediatric cancer to be more specific. Ours is a world of medication abundance where more often then not, we are not fully aware of the multitude of side-effects, short- or long-term of the drugs that are being infused into our children. We might, in general terms be advised of some of the most common, or most life-threatening side-effects such as neutropenia, fatigue or nausea, but the list of all potential side-effects is very long and very scary, and like the drug commercials on TV, hearing all of the potential side effects might have us grabbing our child and running for the door.

It seems to be rare for a clinician to talk about the potential auditory side-effects of chemotherapy, at least I haven't heard it. Perhaps it is because of all the potential life-threatening issues that parents and patients have to deal with during their treatment, and hearing health can be dealt with after the cancer has been abated. However, each of the points of the triangle—patient/family, clinician and researcher need to understand that listening disorders present serious and complicated quality of life (QOL) issues that could affect the child throughout his or her lifetime.

A 2010 study by the Children's Oncology Group (COG) on the auditory late-effects of childhood cancer therapy began their abstract with the following:

> *Children treated for childhood malignancies may be at risk for early or delayed onset hearing loss that can impact learning, communication, school performance, social interaction, and overall quality of life (QOL). Survivors at particular risk include those treated with platinum compounds (cis- and/or carboplatin) for neuroblastoma, hepatoblastoma, osteosarcoma, or germ cell tumors and/or those treated with radiation impacting the ear at doses greater than 30 Gray (Gy) for pediatric head and neck tumors.* (Grewal et al., 2010)

The report's introduction begins:

> *With multimodality therapy, 80% of patients diagnosed with cancer in childhood or adolescence are expected to become survivors. Among the functional impairments that result from cancer treatments, hearing loss may be detrimental to speech and language development, educational achievement, communications, social interaction, integration and overall quality of life (QOL), particularly in very young children.* (Grewal et al., 2010)

Hearing loss as a late effect of therapy can occur following exposure to cancer therapeutic agents such as platinum compounds and cranial irradiation. Platinum agents (cisplatin and carboplatin) have improved cure rates of many childhood cancers, but their use may result in irreversible high-frequency sensorineural hearing loss.

Rhabdomyosarcoma is the most common type of soft tissue cancer found in infants and children. While it is considered to be a very rare form of cancer, with approximately 300 new cases being diagnosed in the U.S. each year, it requires a long regimen of multi-agent chemotherapy, the possibility of surgery and the potential for a considerable program of radiation therapy as well.

The most common primary sites for the disease are:

Head and neck region - approximately 25%

Genitourinary tract - approximately 22%

Extremities - approximately 18%

Other less common primary sites include the trunk, chest wall, perineal/anal region, and abdomen, including the retroperitoneum and biliary tract.

The drugs that are used most often in rhabdomyosarcoma treatment are vincristine, actinomycin-D and cyclophosphamide (Sezgin et al., 2015). This is generally referred to as the VAC protocol.

> *Patients with intermediate risk disease are treated with VAC. Successive IRSG and COG clinical trials have attempted to improve the outcome by examining different strategies, such as incorporating different agents (etoposide, ifosfamide, cisplatin, irinotecan, topotecan, and doxorubicin) or intensifying cyclophosphamide during induction, but these strategies have not significantly improved clinical outcome. The greatest need for improvement is in patients with high-risk disease. Recent COG studies have employed the use of a more intensive chemotherapy backbone using vincristine, doxorubicin, and cyclophosphamide that is alternated with ifosfamide and etoposide. Since the survival outlook for high-risk patients has been historically so poor, it appears that a plateau of efficacy has been reached with traditional cytotoxic chemotherapy. Thus, there has been significant interest in the development of targeted and other novel therapies. (Egas-Bejar & Huh, 2014)*

It is very difficult to isolate specific chemotherapy agents and their ototoxic tendencies since they are rarely administered alone but rather in a multi-drug 'cocktail'. While the literature does not indicate high percentages of audiological issues with vincristine and actinomycin-D, there are some indications that they might promote hearing loss in some specific circumstances (Lugassy & Shapira, 1990).

It is understood that vincristine can damage nerves. Some patients complain about tingling and numbness, particularly in the hands and feet. While this is annoying, it is not well know if vincristine affects the auditory nerve. While the tingling and numbness generally fade after some time after treatment has ended, damage to the auditory nerve would prove to be permanent.

At least one study found that cyclophosphamide increased the risk of auditory difficulties. In this study,

> *Cyclophosphamide was the most frequently administered chemotherapeutic agent and was positively correlated with hearing loss. In the population submitted to cancer treatment, a high prevalence of tinnitus and speech understanding difficulty were*

> *found, even in the absence of hearing loss. (Oliveira, Oliveira, Andrade, do Carmo Santos, & de Oliveira-Barreto, 2016)*

While many of the chemotherapy drugs are ototoxic, and have repercussions to the patient's hearing health, the most commonly cited agents with counter-indications to hearing health are cisplatin and carboplatin. These two drugs a part of the 'platinum' group that also includes oxaliplatin and nedaplatin.

Cisplatin is the most commonly used anti-cancer chemotherapy agent and while it has not shown itself to cause vestibular issues, it is cochleotoxic, meaning that it injures or destroys the small hair-like structures, the cilia, inside the cochlear. It is the cilia that converts the sound energy into the neuro-electric impulses that our brain decodes into information.

Cisplatin causes the most damage in the lower turns of the cochlear where the first and second rows of cilia - the ones that convert the higher frequency information (Nakai et al., 1982). High frequency is affected first, with hearing loss eventually progressing to the lower frequencies with increasing cumulative dosage (Li, Womer, & Silber, 2004). As we discussed in the section on consonant confusion, a loss of hearing acuity at the higher frequencies creates a multi-fold problem — difficulty in discerning the words being said and an inability to recognize the vocal intonation of a question (dominant in the English language), hear the final /s/ that represents a plural, or catch the intonations marking irony or sarcasm.

The reality is that protocols and 'cocktails' could change with each patient evaluation. While the VAC protocol is the backbone of RMS therapy, there are times that it does not produce the desired effect and other chemotherapy agents need to be added or substituted into the mix with the goal being a more efficacious outcome.

> *Patients with metastatic RMS were treated with one of two regimens that incorporated a window of either ifosfamide and etoposide (IE) with vincristine, dactinomycin, and cyclophosphamide (VAC) or vincristine, melphalan (VM) and VAC . (Breneman et al., 2003)*
>
> *Ototoxicity is found among people who take Ifosfamide, especially for people who are male, 2-9 old , have been taking the drug for < 1 month, also take medication Etoposide, and have Rhabdomyosarcoma.("Will you have Ototoxicity with Ifosfamide - from FDA reports - eHealthMe," n.d.)*

While the percentage of patients indicating ototoxic affects of Ifosfamide are small, 0.5%, the audiological side-effect happens quickly, 100% within the first month, and then predominately by males (90.6%) in the 2-9 year old age bracket.

Melphalan has not, at this time, indicated any ototoxicity.

It is possible, however, that in certain cases, rhabdomyosarcoma or other cancers, carboplatin may be substituted for actinomycin-D. As we mentioned before, carboplatin, a member of the 'platinum group' has a high indication of ototoxicity and anyone being administered either cisplatin or carboplatin should be monitored carefully for auditory issues.

It is important for the oncology team to monitor the treatment, not only for the efficacy of the cancer treatment, but also, to look ahead at the overall quality of life issues that the patient might experience. Once the chemotherapy is completed, a review of all agents used and their potential effect on the child's hearing health is important.

Auditory Toxicity of Radiation Therapy

Head and neck cancer is the sixth most prevalent type of cancer worldwide. For those with RMS, head and neck presentation is the most prevalent, accounting for approximately 25% of all cases. Like cancers found in other locations, typical treatment includes chemotherapy, surgery and radiation. Depending on the specific location within the head and neck structure, the size and stage of the tumor, the patient's condition, any or all three of these treatment modalities may be used (Schultz, Goffi-Gomez, Pecora Liberman, Pellizzon, & Carvalho, 2010).

Radiation therapy is routinely used in cases of childhood cancer when the tumors are found in the head and neck. Hearing loss can result when any of part of the auditory system lies within the radiation field. This might include damage to the external ear and/or any of the auditory structures of the middle or inner ear. Thus, hearing loss can present as conductive, mixed, sensorineural, or retrocochlear in nature (Jereczek-Fossa, Zarowski, Milani, & Orecchia, 2003).

> *Up to 40% of patients have acute middle ear side effects during radical irradiation including acoustic structures and about one-third of patients develop late sensorineural hearing loss (SNHL). Total radiotherapy dose and tumour site seem to be among the most important factors associated with the risk of hearing impairment. (Jereczek-Fossa, et al., 2003)*

Radiation therapy is being used with increased frequency, especially on tumors where resection presents significant danger. Quite often the tumor location places the inner ear within the irradiation field, and although there is little choice in whether to or not to irradiate, the potential for sensorineural hearing loss is great.

The combination of radiation and chemotherapy offer a double-dip of potential problems and need to be monitored carefully for years after treatment has ended.

> *Use of RT alone with doses of less than 40 Gy did not result in clinically significant hearing loss. High-frequency SNHL was profoundly damaged in patients who received concomitant cisplatin when doses of 100 mg/m2 were used. The threshold cochlear dose for hearing loss with cisplatin-based chemotherapy and RT was predicted to be 10 Gy. The inner ear radiation dose constraints and cisplatin dose intensity should be considered in the treatment of advanced head-and-neck cancer. (Hitchcock, Tward, Szabo, Bentz, & Shrieve, 2009)*

New techniques in radiation therapy might help mitigate some of the danger. Photon-radiation, the conventional radiation therapy is being replaced in some areas with proton-radiation therapy (PRT) which is showing great promise in increased dose-sparing of the auditory structures.

> *Normal structures received markedly less radiation from PRT plans than from 3D photon plans. The cochlea received an average mean of 25 ± 4% of the prescribed dose from PRT, and 75 ± 6% from photons. Forty percent of temporal lobe volume was completely excluded using protons; with photons 90% of the temporal lobe received 31% of the dose. (Lin et al., 2000)*

Unfortunately, proton therapy is not available in all locations so it is important that the radiation therapist be questioned as to the long-term effects of the therapy that is being provided.

Psychological Barriers to Listening

While hearing loss presents a physiological barrier to listening, stress, depression and anxiety create a whirlpool of psychological barriers that could make listening difficult for the family and especially, the patient.

Not that long ago, when the survival rate for childhood cancer was quite low, parents generally spared their children from many of the facts surrounding the situation. Often, the child was not even told the name of the disease that was de-

stroying his or her body. Yet the child felt the tension and depression surrounding it and were not deceived by the avoidance of discussion or by false reassurances about their prognosis. The silence of the adults left the child alone to cope with their fears. (Patenaude & Kupst, 2005)

Today, with the survival rate of childhood cancer rising, there has been a change towards a more open approach to communication. This has created an opening for psychological experts to join the pediatric oncology team for the benefit of both patient and family.

In times of extreme stress it is important that what is being said is interpreted correctly. Physicians provide explicit instructions that need to be followed to help minimize side-effects and promote the fastest possible path towards a cure. If the instructions are not followed, because of misunderstanding or 'selective hearing,' difficulties could arise in the form of more severe side-effects, near-term recurrence, since the efficacy of the treatment has been diminished.

Listening under stress is not an easy task. There are so many questions and none of them seem to reach your lips. Time seems to be frozen. Everyone involved becomes self-absorbed for a some period of time.

> *The Merrion-Webster online dictionary defines self-absorption as: "only caring about and interested in yourself, absorbed in one's own thoughts, activities, or interests." Everyone becomes self absorbed from time to time. People "in-the-flow," who are depressed, and who are deep in thought, not to mention the narcissists and egocentrics in the world who are forever inwardly focused, are all examples of self-absorption.*
>
> *Self-absorption and self-talk go hand in hand. We use self-talk to clarify our thinking, rehearse what we want to say, or play out an argument. Most of us learned to read by sounding out the words in our head. By using this self-talk we can sound out words that we don't visually recognize to see if they sound familiar.*
>
> *But self-talk can be paralyzing as well, especially to those suffering from depression or high-anxiety levels. These issues can present major barriers to effective listening. Those affected use self-talk to continually churn their problems around in their head—leaving no room for an outside voice. Narcissists and egocentrics are constantly focused on their inner voice with little desire to understand those who are talking to them. (Ehrlich, 2016)*

We listen through sets of filters that we develop as we grow up. In our very early years we accept everything we hear, but as we experience life, we develop strong feelings about certain topics, prejudices, expectation, and beliefs. These are based on our past experiences, influences of key people in our lives, our set of values and our attitude. We often hear other people's words through these filters which is a major cause of misinterpretation. The last thing needed in treating a child with cancer is misinterpretation.

Stress and anxiety also produce another listening barrier—that of selective hearing.

Selective hearing does not involve our hearing at all, but rather the processing of the auditory signals in our brain. It is a term used to describe the phenomenon of filtering the sounds around us and only processing the information that we want to 'here' and ignoring everything else. The ears have no filters, we actually hear everything, but there are times that we unintentionally block out sounds—or even people talking about things that we might not want to hear—regardless of their importance—because we just don't want to have to face what is being said.

This could lead to people hearing only the up side of treatment and selectively filtering out all of the potentially life-threatening side-effects of the treatment plan. It could also be just the opposite, depending on the person's attitude and mental state at the time.

The problem is that we don't know what we didn't hear, and that, in itself, is be very dangerous.

The Warning Signs of Pediatric Hearing Loss

It should be remembered that hearing loss is a late-term affect of both chemo- and radiation therapy which means that it could be a number of years before the symptoms begin to present themselves. Annual audiological examinations should be a regular part of the patient's routine healthcare program.

Parents, friends, and caregivers should be aware of the signs and symptoms of hearing loss, reduced auditory acuity or other listening disorders.

According to Hear-It.org, here are ten signs that your child has a possible hearing loss:

- Your child seems to hear fine some of the time and then not respond at other times
- Your child wants the TV volume louder than other members of the family

- Your child says “What?” more often
- Your child moves one ear forward when listening, or he complains that he can only hear out of his “good ear”.
- Your child’s grades fall or their teacher notes that they do not seem to hear or respond as well in the classroom as other children.
- Your child says that they didn’t hear you. This may seem obvious, but many parents assume that their children are not paying attention when in fact there may be an unidentified hearing loss.
- It seems as though your child is just not paying attention.
- Your child starts to speak more loudly than previously.
- If your child looks at you intensely when you speak to them, as if concentrating, they may be depending more on visual cues for interpreting speech.
- You just have a feeling, but you can’t put your finger on what your concern is. Don’t let that stop you. Ask your doctor for a referral to ease your mind. (HearIt.org, n.d.)

Additionally, you need to be aware of changes in the social interaction that your child is having with family, friends and in school or pre-school. Social withdrawal is a common sign that a person of any age is having difficulties hearing. Conversations can be very stressful and tiring to those with a hearing loss. The amount of cognitive energy that is required to try to interpret messages that are audibly incomplete is very high, thus, very exhausting. Often, people with a hearing loss, especially in a noisy environment, will misinterpret what is being said and respond in an inappropriate manner—saying things that might not make any sense based on the context of the conversation. This can create a very embarrassing situation, especially for young children, adding to their already high level of stress. Ongoing depression can be another indicator of a hearing loss because of how it affects their interaction with those around them.

By instituting annual hearing tests into the child’s healthcare regimen appropriate action can be taken at the first signs of the problem.

Conclusion and Recommendations

A child’s ability to hear and listen are critical life-skills, so critical that they are built into our DNA and not left to a ‘learning’ experience for later in life. We,

the parents, families, and medical professionals, must do everything we can to preserve these skills as the child progresses through their cancer treatment.

It has been shown that both chemotherapy and radiotherapy can adversely affect the ability of a child to hear and interpret verbal messages effectively, and we know, without any doubt, that diminished hearing acuity or other listening disorders can create a lifetime of problems—academic under-achievement, social integration issues, and, as the child ages, employment and relationship issues.

While it is the oncologist's job to create a treatment plan using every technique that they can to preserve the life of the patient, it is the parent's job to be aware of the long list of side-effects that could result from the prescribed treatment. While hearing health is generally not on the top of the list, it is something that needs to be watched and addressed, not only during the treatment process, but for years afterwards.

While some facilities include audiometric evaluations before, during and after treatment, it is important that all pediatric cancer patients have a baseline audiological exam at the start of treatment, one at the end of treatment, and additional audiological evaluations at regular intervals throughout their lifetime. Audiological testing should include both pure-tone tests (press the button when you hear the tone) and word recognition tests that will indicate the child's ability to discern words and understand speech patterns.

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