Chapter 8: Hearing and Ear Abnormalities in Fanconi Anemia

Introduction

Hearing and ear anomalies are prevalent among patients with Fanconi anemia. About 3 of every 20 patients with FA have ear malformations [1], and reported prevalence of hearing loss in patients with FA ranges from 11% up to 50% [2-3]. Although the hearing loss in patients with FA is typically mild, it can impair an individual's communication abilities and interfere with language development and learning.

This chapter will describe the normal anatomy and function of the ear, common concerns related to the ear and hearing in patients with FA, amplification tools, surgical management, routine auditory monitoring, and useful resources for the hearing impaired.

In particular, this chapter will explore the following three concerns in patients with FA:

- *Abnormal ear anatomy and function*
- *Hearing loss*
- *Impaired learning and development of speech, language, and communication skills as a result of hearing loss*

The ear and hearing clinical care team should include an **otologist** (an ear specialist) and an **audiologist** (a hearing specialist) and, when needed, a **speech-language therapist**. This team should work in close collaboration with other FA specialists and the primary physician, usually the hematologist/oncologist, to coordinate care.

Anatomy and Function of the Ear

The ear is made up of three main sections: the outer, middle, and inner ear (Figure 1). The two main portions of the outer ear are the pinna and the ear canal. The pinna collects sound waves and directs them down the ear canal to the eardrum.

The middle ear consists of the eardrum, which is also known as the tympanic membrane, and three tiny bones known as ossicles: the malleus, incus, and stapes (commonly called the hammer, anvil, and stirrup, respectively). The malleus is attached to the eardrum, the stapes is connected to the inner ear, and the incus lies in between the two; together, the three ossicles vibrate, converting sound energy into mechanical energy that is transmitted into the fluids of the inner ear (Figure 1).

The inner ear is composed of two parts: the balance-sensing system called the vestibular apparatus, which includes the semicircular canals and vestibule (utricle and saccule); and the sensory organ of hearing, known as the cochlea. The cochlea resembles a snail-like structure and is filled with tissue and fluid.

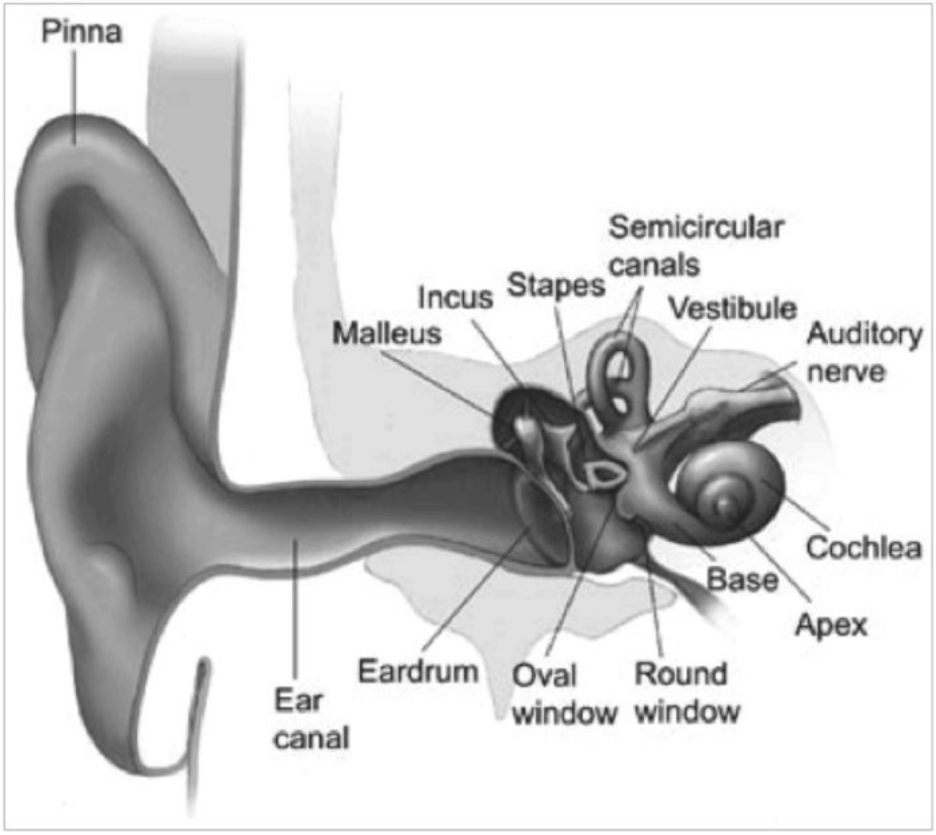

Figure 1. Anatomy of the ear.
Source: http://www.nidcd.nih.gov/health/hearing/Pages/noise.aspx

Sound waves enter the ear canal and cause the eardrum to vibrate like a drumhead. The vibrations move the ossicles, which amplify and transmit sound to the inner ear. When the stapes vibrates against the inner ear, the fluid within the cochlea moves and stimulates the thousands of tiny sensory structures called hair cells that line the inner surface of the cochlea. The hair cells then transform the sound vibrations into electrical impulses, which travel along the auditory nerve from the cochlea to the brain. The brain translates these signals and allows us to comprehend speech and recognize various sounds. Sounds can vary in terms of intensity (volume) and frequency (pitch).

Types and Degree of Hearing Loss

There are three main types of hearing loss:

- ***Conductive hearing loss*** is caused by problems in the outer and/or middle ear that prevent sound waves from being carried, or conducted, efficiently into the inner ear. Conductive hearing loss can be caused by, among other conditions, fluid in the middle ear, a middle ear infection, excessive wax accumulation in the outer ear canal, and a hole in the eardrum. Although uncommon, conductive hearing loss can also be caused by malformation of the ossicles, the absence of an ear canal at birth (a condition known as congenital aural atresia), or restriction of ossicular movement due to the formation of abnormal scar tissue or bone.
- ***Sensorineural hearing loss*** typically occurs when the hair cells in the inner ear are damaged and unable to transform sound waves into electrical signals. Common causes of sensorineural hearing loss include genetic predisposition, the aging process, excessive exposure to loud sounds, and certain drugs, such as some chemotherapeutic agents or intravenous antibiotics. Sensorineural hearing loss can also result from damage to or congenital absence of the auditory nerve.
- ***Mixed hearing loss*** is a combination of conductive and sensorineural hearing loss that involves problems in the outer and/or middle ear as well as the inner ear and/or auditory nerve.

Good to Know

A **decibel** is a measure of sound intensity.

Soft sounds correspond to low decibel levels (e.g., 0-15 dB HL).

Loud sounds correspond to high decibel levels (e.g., 90 dB HL).

Any patient who experiences hearing loss should be referred to an audiologist, who can perform a hearing test (audiogram) to determine the:

- ***Degree*** *of hearing loss, an indicator of how much hearing loss exists*
- ***Type*** *of hearing loss (conductive, sensorineural, or mixed)*
- ***Configuration*** *of the hearing loss, or the overall pattern of hearing loss across the test frequency range*

There are several measurement methods that, collectively, identify the degree, type, and configuration of hearing loss. These methods include behavioral audiologic tests, otoacoustic emissions tests, and auditory brainstem evoked response tests (ABR, sometimes referred to as BAER). Hearing can be assessed at any age; however, the patient's age and ability to cooperate will determine which methods are appropriate. Several tests and test sessions may be required to clearly characterize the hearing of very young children.

To determine the degree of hearing loss, an audiologist performs a hearing test to identify the softest level of sound a person can detect, known as the *audiometric threshold,* for a variety of pitches (frequencies). In a hearing test, hearing sensitivity is measured in terms of decibels hearing level (dB HL). People who have normal hearing are able to hear sounds as soft as 0-15 dB HL. The degree of hearing loss is classified according to severity:

- ***Slight hearing loss***: the softest sound the person can hear ranges from 16-25 dB HL
- ***Mild hearing loss***: the softest sound the person can hear ranges from 26-40 dB HL
- ***Moderate hearing loss***: the softest sound the person can hear ranges from 41-70 dB HL
- ***Severe hearing loss***: the softest sound the person can hear ranges from 71-90 dB HL
- ***Profound hearing loss***: the softest sound the person can hear is greater than 90 dB HL

Even minimal hearing loss can negatively impact a child's social and academic development. A slight to mild degree of hearing loss can make it difficult to understand speech that is not presented at close range, or that is obscured by background noise. Moderate, severe, and profound hearing loss impairs the ability to understand speech under any conditions, and will significantly affect

learning and the development of speech and language abilities unless the hearing loss is identified and treated by 6 months of age [4].

Signs and Symptoms of Ear and Hearing Abnormalities in Patients with FA

Only a few scattered case reports of ear and hearing abnormalities in patients with FA have been reported in the medical literature. To systematically examine and define the ear and hearing abnormalities in patients with FA, a team of researchers at the National Institutes of Health in Bethesda, Md., conducted a study of 31 patients with FA who ranged in age from 3 to 56 years old [5]. Out of 62 ears in 31 patients, 4 ears in 4 patients with FA were excluded from the analysis because of prior ear surgery. Thus, the results reflect data obtained from 58 ears.

All patients underwent comprehensive hearing testing and evaluation of the ears, nose, and throat. Microscopic examination of 54 ears revealed abnormalities in 31 ears (57%), and one case of an undeveloped, absent ear canal (aural atresia). Abnormal eardrum findings included a small eardrum, a short malleus that was abnormally positioned on the eardrum, and the presence of abnormal bony islands (bony plate) under the eardrum (Figure 2).

Comprehensive audiologic information was available in 52 ears. Hearing loss was detected in 24 ears (46%), and the majority was classified as mild in degree. The remaining 28 ears had normal hearing. The most common type of hearing loss was conductive, which was found in 11 ears, or 46%. An additional common finding in 8 ears (33%) was the presence of subclinical conductive hearing loss, in which hearing thresholds fell within normal limits, but evidence for a conductive component was still present. Sensorineural hearing loss (which was found in 3 ears, or 13%) and mixed hearing loss (which was found in 2 ears, or 8%) were less commonly observed. These findings suggest that the most common type of auditory dysfunction in patients with FA is mild conductive hearing loss, which is probably due to an abnormally developed eardrum, ossicles, or both.

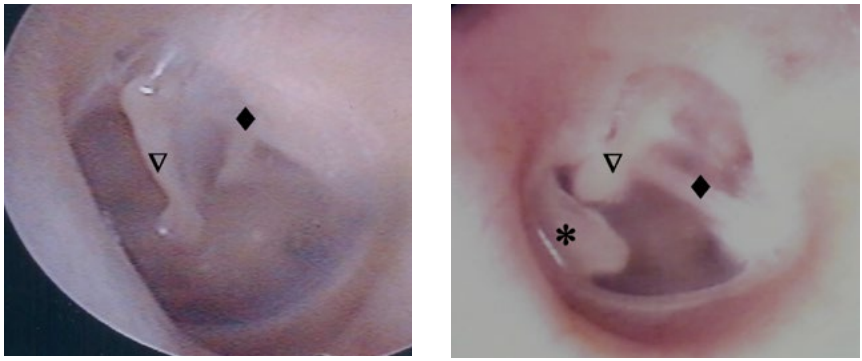

Figure 2. The left eardrums of a healthy individual (left) and a patient with FA (right) and bony plate (*), manubrium (∇), chorda tympani nerve (♦).

In summary, this research found that hearing loss was present in almost half of the ears (24 out of 52) of patients with FA, and the majority of the ears with hearing loss (19 of the 24, or 79%) had conductive or subclinical conductive hearing loss. Of the 54 ears that underwent microscopic examination, 57% had congenital abnormalities of the tympanic membrane and middle ear ossicles. The incidence of hearing loss and congenital ear malformation observed in this study is much higher than previously reported [1-3]. The findings suggest that abnormal features can be present even if hearing is normal or only slightly reduced.

Consequences of Hearing Loss

Hearing loss in adults can impair an individual's communication abilities, especially if the listening situation is not ideal. It can make a person reluctant to participate in conversation and avoid social situations, and can cause fatigue if visual and contextual clues are required to fill gaps between what was said and what was heard.

Children use their hearing to develop speech, language, and communication skills, and to facilitate learning. Consequently, hearing loss can interfere with language development and learning. Even slight or mild hearing loss makes it difficult to hear a teacher or peers who are not within close range, especially in environments with a lot of background noise, such as a typical classroom. Left untreated, hearing loss can cause delays in language development and gaps in education. Even if the hearing loss only occurs in one ear and the other ear is normal, a child can have enough trouble hearing in school or in other situations that it impairs his or her social interactions and academic potential [6,7,8,9].

Early Identification and Intervention for Hearing-Impaired Children

Any child diagnosed with FA should undergo comprehensive assessments of his or her ears and hearing by an otolaryngologist (an ENT specialist) and an audiologist, respectively. Newborn hearing screening tests can miss slight or mild degrees of hearing loss; therefore, all children with FA, including those who are not diagnosed with hearing loss at birth, should receive follow-up audiologic testing. The earlier hearing loss is identified and treated, the less severe possible permanent effects may be. Research has shown that early identification and treatment (e.g., speech therapy, amplification devices, and educational accommodations and interventions) within the first 6 months of life can alleviate the long-term adverse effects of hearing loss on learning and language development [9].

Children with hearing impairment often require some form of special education or related services [10]. The federal Individuals with Disabilities Education Act (IDEA) [11], Part B, mandates the development of an Individualized Education Plan (IEP) for any student with a disability who needs special education. This document details educational goals for the child, and specifies the services that will be implemented in the school setting. Part C of the IDEA describes early intervention services available for eligible infants and toddlers from birth up to age 3 years, and the development of an Individualized Family Service Plan (IFSP). This document defines the services needed by the child and his or her family to enhance the child's development. The services must be provided in the child's natural environment, which can include the home or childcare center. Early intervention and academic support teams should work in conjunction with health care providers, such as audiologists and speech therapists, to identify intervention and academic needs. Section 504 of the Rehabilitation Act contains provisions for a school-aged child with hearing loss who needs accommodations, such as assistive listening devices, to access the educational curriculum, but who does not need one-on-one special education teaching or therapy services [12]. This act also contains provisions for workplace accommodations, which should be sought out as needed by employees with hearing loss.

Examples of accommodations or special education services that a school-aged child with hearing loss might require include the following:

- *Favorable classroom seating located near the teacher and with a clear view of the teacher's face*
- *Assistive listening device*
- *Modifications to the classroom to improve acoustics*
- *Speech and language therapy*
- *Educational audiology consultation with classroom teachers to explain the impact of a student's hearing loss on school performance, and to suggest strategies for communication*
- *One-on-one teaching with a specialist, such as a teacher of the hearing-impaired or special education teacher*

Amplification

If hearing loss is identified in a child or an adult, an audiologist should evaluate the patient's need for hearing aids and/or assistive listening devices (see below). There are many different types of devices available. The audiologist will make a recommendation for the appropriate device based on the patient's lifestyle, type and degree of hearing loss, and the environment in which the device will be used. For example, a school-aged child may need different features on his or her device than an adult in the workforce.

Hearing aids

Hearing aids are devices that make sounds louder, and are worn in or behind the ear. Hearing aids can be beneficial for all types of hearing loss (conductive, sensorineural, or mixed) and almost all degrees of hearing loss. Hearing aids can be used by patients of any age—even babies in their first few months of life [13].

The audiologist programs the hearing aid specifically for a patient's degree and configuration of hearing loss and can reprogram the device later if the patient's hearing changes. Hearing aids differ in technology, size, power, and availability of special features, but all hearing aids have the following components:

- *A small **battery** that powers the hearing aid*
- *A **microphone** that picks up sound*
- *An **amplifier** that increases or magnifies sounds that are inaudible to the hearing-impaired listener*
- *A **receiver** (or speaker) that delivers the amplified sound into the ear*

A baby or child with hearing loss will be fitted with a hearing aid that sits behind the ear and has the ability to connect with other assistive listening devices if needed. The hearing aid directs amplified sound into the ear canal via the earmold, a plastic piece that is custom-made to fit each ear. Children require frequent replacement of their earmolds—as often as every 2 to 4 weeks during the first year of life, every 1.5 to 4 months as toddlers and preschoolers, and every 6 months to a year until they are teens—due to their growing ear canals.

Assistive listening devices

Assistive listening devices (ALDs) help hearing-impaired individuals function in daily communication situations. They may be used alone or in combination with hearing aids. ALDs are typically only used for specific listening situations, such as environments with a lot of background noise (e.g., school classrooms, restaurants, movie theaters, and conferences). The most common type of ALD, known as a frequency-modulated (FM) system, captures the audio of interest using a microphone (which is often worn by a speaker such as a teacher or presenter) and transmits the sound wirelessly, much like an FM radio signal, to a receiver used by the listener. The receiver can be integrated into a hearing aid or used as a stand-alone listening device similar to a personal music player. If used in a classroom, for example, the device brings the teacher's voice directly to the student's ear at a consistent volume that is above the typical background noise, regardless of the distance between the teacher and student.

An ALD known as a sound-field amplification system can be a good option for children with hearing loss that is mild or only affects one ear, as well as children with stable or fluctuating conductive hearing loss. With this type of ALD, the teacher wears a wireless microphone that transmits sound via FM or infrared waves to a speaker or speakers, which evenly distribute the teacher's voice to all parts of the classroom. A sound-field amplification system can help to ensure that a hearing-impaired student can hear what the teacher is saying, even if the teacher isn't directly facing the student or is speaking from the other end of the classroom.

Surgical Management of Hearing Loss in FA

Evaluation
Some types of hearing loss can often be corrected with surgery, though it should be noted that sensorineural hearing loss from inner ear or auditory nerve damage cannot be restored by ear surgery.

Below are a few causes of conductive hearing loss that may be surgically corrected in some patients:

- *Fusion of the malleus to a bony island under the eardrum*
- *Fixation of the ossicles to the bony walls of the middle ear cavity*
- *Discontinuity of the ossicles (one of the ossicles is not attached to the others)*
- *Scarring or bone growth around the stapes*
- *An absent ear canal*
- *Fluid in the middle ear*
- *Hole (perforation) of the eardrum*

Before choosing a middle ear surgery, the otologist, the patient, and the patient's family must consider multiple factors and all of the alternative treatment options, such as hearing aids, to optimize the child's rehabilitation. Surgery is not suitable for every patient with conductive hearing loss. Individuals with serious medical conditions such as heart problems, bleeding tendencies, and a high susceptibility for infection due to bone marrow failure are probably not good candidates for surgery.

To be considered a candidate for middle ear surgery, the patient must have normal inner ear function as demonstrated by a hearing test called bone conduction testing. Patients with moderate, severe, or profound sensorineural hearing loss are typically not candidates for middle ear surgery. The otologic surgeon should carefully evaluate the anatomy of the patient's middle and inner ear using high-resolution thin section CT scanning. This procedure enables the surgeon to determine the possible cause of the conductive hearing loss and gauge the potential success of surgery. In some patients, poor middle ear anatomy or middle ear fluid precludes surgical intervention.

Timing of surgery

Middle ear surgery can be performed in children ages 7 years or older, who are typically capable of cooperating in the office for the necessary postoperative care and are beyond the age of frequent childhood ear infections. In patients with an ear deformity known as microtia (in which the external part of the ear, known as the pinna, is underdeveloped or absent), the timing of surgery will depend on the family's decision regarding reconstructive surgery for the pinna. The options for management of microtia include the following:

- *Microtia can be repaired using **cartilage** from the patient's ribs, a traditional method that has withstood the test of time. This procedure should be performed prior to middle ear surgery.*
- *Microtia can be repaired using a **synthetic implant**, which is often made of high-density polyethylene. This procedure should be performed after middle ear surgery.*
- ***A prosthetic ear** can be applied before or after middle ear surgery.*

Middle Ear Surgery

If the middle ear bones are immobile or absent, a surgical procedure called ossicular chain reconstruction can be performed to replace the defective or missing ossicle(s) with a prosthesis. The prostheses are typically made of artificial bone, titanium, or other biocompatible composite materials. Surgery can be done using either local anesthesia and sedation or general anesthesia, and typically takes about 1 to 3 hours.

If the ear canal is absent or very narrow, it can be reconstructed in a surgical procedure called canalplasty. During this procedure, the otologist uses an otologic drill to remove bone, thereby opening or widening the ear canal and freeing the ossicles. To restore hearing to the ear, the surgeon constructs a tympanic membrane using a piece of connective tissue. Then the reconstructed eardrum and bone of the ear canal are carefully lined with a very thin skin graft called a split-thickness skin graft. The outer opening of the ear canal, called the meatus, is widened, and the outer edge of the skin graft is delivered through the meatus and sutured to the native skin of the pinna.

In the general population, middle ear surgery improves conductive hearing loss in 75% to 90% of carefully selected candidates [(14)], but it is important to understand that not all patients with conductive hearing loss and associated middle ear abnormalities are candidates for surgery. It is through both the

hearing test and the temporal bone CT scan that a patient's candidacy for middle ear surgery or canalplasty is determined.

Complications associated with ear surgery are uncommon but may include:

- ***Further hearing loss or no hearing improvement*** *(in less than 10% to 20% of surgeries). Total deafness is extremely uncommon.*
- ***Injury to the facial nerve*** *that runs through the ear, which can cause facial paralysis. This is extremely uncommon. Surgeons should use a device called a facial nerve monitor during ear surgery to minimize this risk.*
- ***Altered taste perception*** *on the side of the tongue, which can last for a couple months.*
- ***Persistent post-operative dizziness or ringing in the ears****, both of which are quite uncommon.*
- ***Renarrowing (stenosis) of the ear canal****, which requires additional surgery.*

Bone conduction hearing devices

A bone conduction hearing device may be useful for patients with conductive hearing loss who cannot use conventional hearing aids due to problems such as a congenitally undeveloped ear canal, or for individuals who are not good candidates for traditional middle ear surgery [15]. For children who fall into this category, such a device can be essential for normal speech and language development [16]. A bone conduction hearing device transmits sound waves directly to the inner ear by vibrating the bone of the skull, which transfers the sound energy to the fluids of the cochlea. A traditional bone conduction hearing aid consists of a bone oscillator or vibrator affixed to a fabric or metal headband that is worn around the head with the oscillator tightly applied to the mastoid bone or cortical bone above the ear. Alternatively, a bone conduction hearing device can be surgically implanted into the bone behind the ear in children age 5 years and older. This type of device is known as a bone-anchored hearing device. Bone-anchored sound conduction systems have been used in Europe since 1977 and were approved in the United States in 1996 as a treatment for conductive and mixed hearing losses. Table 1 lists the implantable hearing devices that are currently commercially available. The patient and his or her family should consult with an audiologist and otologist about whether to use a traditional bone conduction device or a bone-anchored hearing device for conductive hearing loss in one ear.

Table 1. Bone-implantable hearing devices.

Implantable Hearing Device	Baha	Ponto	Sophono	SoundBite*
Manufacturer	Cochlear Ltd. Sydney, Australia	Oticon, Inc. Somerset, NJ	Sophono, Inc. Boulder, CO	Sonitus Medical, Inc. San Mateo, CA

**A non-surgical bone conduction device via a dental appliance. This device has been FDA approved for individuals 18 years of age and older.*

Family Members of Patients with Hearing and Ear Abnormalities

When a patient is diagnosed with FA, his or her siblings must also be tested for FA. However, if a sibling of a patient with FA does not test positive for FA via a chromosome breakage test on the peripheral blood but displays classic signs of FA-related ear and hearing abnormalities [17], the hematologist should perform additional genetic tests to rule out FA (see *Chapter 1*).

Regular Periodic Auditory Monitoring

Children who are diagnosed with FA should be referred for audiologic and otologic consultation as soon as possible. Children of any age can undergo hearing testing by an audiologist. Before the age of 3 years, such testing can rule out hearing loss that may affect speech and language development [16]. By the age of 5 or 6 years it is typically possible to obtain very complete testing for each ear to establish hearing thresholds of 15 dB HL or better across the speech frequencies, and therefore rule out a hearing loss that may have subtle effects on communication and learning.

Once hearing loss is identified, the patient's hearing should be monitored regularly [18]. Babies and toddlers should be seen by an audiologist every 3-4 months, whereas older children should be seen every 6 months until age 6 or 7, after which an annual audiological assessment may be sufficient. If the child's hearing loss is not stable or if other hearing related issues arise, more frequent monitoring may be recommended. Adults with hearing loss should receive annual audiologic monitoring, or immediate evaluation if they suspect a change in hearing.

It remains unclear whether FA is associated with progressive hearing loss. Therefore, patients with FA who have been diagnosed with normal hearing

should have their hearing monitored regularly (approximately every 2-3 years). Hearing tests should be performed more frequently in children, because they are unable or unlikely to self-report concerns about difficulties hearing or communicating. Patients with FA are likely to undergo medical and surgical treatments that can potentially affect hearing. Many patients with FA will be treated with medications that are potentially ototoxic (having a damaging effect on the ear), such as intravenous antibiotics (e.g., aminoglycosides such as gentamicin), iron-chelating agents (e.g., desferoxamine), and chemotherapy agents (e.g., cisplatin). Furthermore, patients with FA are susceptible to recurrent infections due to neutropenia, multiple blood transfusions for severe anemia, and malignancies of the blood and solid tissues; these conditions increase the risk of exposure to ototoxic medications. It is important to establish the patient's baseline hearing level before he or she is treated with ototoxic medications, and monitor the patient's hearing closely during treatment. Lastly, the genetic instability associated with FA has been associated with premature aging processes [19]; therefore, patients with FA may be at risk of developing age-related hearing loss at an earlier age than the general population.

Conclusions

- Congenital hearing loss and/or malformations of the eardrum and middle ear are more commonly associated with FA than reported previously. The hearing loss is typically mild and conductive.
- All patients with FA should undergo a comprehensive ear examination and audiologic evaluation by an otolaryngologist and audiologist, respectively. Preferably, these medical providers should be familiar with FA.
- FA-related hearing problems can often be successfully treated with either appropriate amplification and/or surgical correction.

Useful Resources for the Hearing Impaired

Alexander Graham Bell Association for the Deaf and Hard of Hearing
3417 Volta Place, NW
Washington, DC 20007
202-337-5220
www.agbell.org

American Academy of Audiology
11480 Commerce Park Drive
Suite 220
Reston, VA 20191
800-222-2336
www.audiology.org

American Academy of Otolaryngology-HNS
1650 Diagonal Road
Alexandria, VA 22314
703-836-4444 (V)
www.entnet.org

American Speech-Language-Hearing Association
2200 Research Boulevard
Rockville, MD 20852
800-638-8255 (V)
301-296-8580 (TTY)
www.asha.org

National Institute on Deafness and Other Communication Disorders
National Institutes of Health
31 Center Drive, MSC 2320
Bethesda, MD 20892-2320
800-241-1044 (V)
800-241-1055 (TTY)
www.nidcd.nih.gov
nidcdinfo@nidcd.nih.gov

Hearing Loss Association of America (formerly Self Help for Hard of Hearing People – SHHH)
7910 Woodmont Avenue, Suite 1200
Bethesda, MD 20814
301-657-2248 (V)
www.hearingloss.org
info@hearingloss.org

Boystown National Research Hospital
555 North 30th Street
Omaha, NE 68131
402-498-6511 (V)
www.babyhearing.org

Descriptions of IEPs and Section 504 of the Individuals with Disabilities Education Act
Wrightslaw Special Education Law and Advocacy: www.wrightslaw.com
National Dissemination Center for Children with Disabilities: www.nichcy.org

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