Auditory Development in the Fetus and Infant

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Auditory development in the fetus and infant entails the structural parts of the ears that develop in the first 20 weeks of gestation, and the neurosensory part of the auditory system develops primarily after 20 weeks' gestational age. The auditory system becomes functional at around 25 weeks' gestation. The cochlea of the middle ear and the auditory cortex in the temporal lobe are most important in the development of the auditory system. They are both easily affected by the environment and care practices in the newborn intensive care unit (NICU). The period from 25 weeks' gestation to 5 to 6 months of age is most critical to the development of the neurosensory part of the auditory system. This is the time when the hair cells of the cochlea, the axons of the auditory nerve, and the neurons of the temporal lobe auditory cortex are tuned to receive signals of specific frequencies and intensities. Unlike the visual system, the auditory system requires outside auditory stimulation. This needs to include speech, music, and meaningful sounds from the environment. The preterm as well as the term infant cannot recognize or discriminate meaningful sounds with background noise levels greater than 60 dB. The more intense the background noise, especially low frequency, the fewer specific frequencies (pitch) can be heard and used to tune the hair cells of the cochlea. Continuous exposure to loud background noise in the NICU or home will interfere with auditory development and especially frequency discrimination. The initial stimulation of the auditory system (speech and music) needs to occur in utero or in the NICU to develop tonotopic columns in the auditory cortex and to have the critical tuning of the hair cells of the cochlea occur. The control of outside noise, the exposure to meaningful speech sounds and music, and the protection of sleep and sleep cycles, especially rapid eye movement sleep, are essential for healthy auditory development. The environment and care practices for the fetus in utero or the infant in the NICU are critical factors in the development of the auditory system.

Keywords: Auditory development; Fetal development; Infant; Hearing; Sound

The human auditory system is unique and different from other animals. It differs from all others because it develops the capacity to receive, interpret, and respond to complex language. It also develops the capacity to hear, discern, and respond to music. The auditory system supports development of language as well as musical skills. Unlike the visual system where actual visual experience begins after birth at term, the auditory system requires auditory experience with voice and language, music, and meaningful environmental sounds during the last 10 to 12 weeks of fetal life (28–30 weeks' gestational age) whether in utero or in a newborn intensive care unit (NICU). Thus, auditory development and the potential for interference with auditory development are critical issues for the care of preterm infants in the NICU or the care of postterm infants in day care or home environments.

The Structure of the Auditory System

The structure of the external and middle ear is shown in Fig 1.[1,2] The external ear canal leads to the tympanic membrane (eardrum). The middle ear contains a chain of three bones that connect the tympanic membrane to the cochlea. Vibrations of the tympanic membrane are transmitted to the cochlea. The cochlea (Fig 1) contains three parallel fluid chambers. The vibration of the tympanic membrane creates fluid waves in the cochlea. Within the cochlea, between the fluid chambers, is the organ of Corti. The organ of Corti contains the hair cells that have a hair-like projection from their apex (stereocilia). It is the physical movement of the stereocilia that is converted into a nerve signal that is then transmitted through the spiral ganglion and the relay nuclei in the pons and midbrain to the auditory cortex in the temporal lobe (Fig 2).[3] The neurons of the temporal lobe connect to
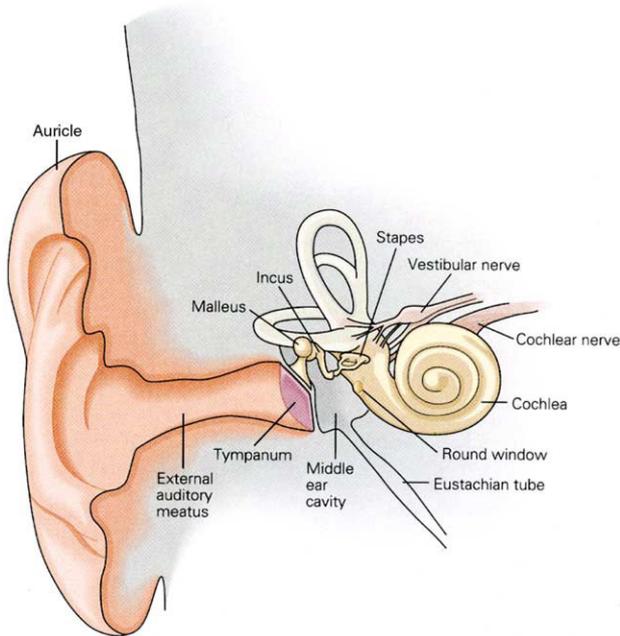
Fig 1. The structure of the human ear. The external ear, especially the prominent auricle, focuses sound into the external auditory meatus. Alternating increases and decreases in air pressure vibrate the tympanum. These vibrations are conveyed across the air-filled middle ear by three tiny, linked bones: the malleus, the incus, and the stapes. Vibration of the stapes stimulates the cochlea, the hearing organ of the inner ear (Reprinted from Kandel ER. *Principles of Neural Science, Fourth Edition*. New York: McGraw Hill; 2000:591; with permission).

other parts of the cortex, limbic system (emotions), and hippocampus (memory and learning).

Development of the Auditory System

The auditory system in the human fetus and infant has its own developmental sequences. The anatomical or structural parts of the system develop early. The structural parts of the cochlea in the middle ear are well formed by 15 weeks' gestational age and are anatomically functional by 20 weeks' gestation.[1,2] The somaesthetic (touch), kinesthetic (movement), proprioceptive (position), vestibular (motion-head), and chemosensory (smell and touch) systems all are both structurally and functionally operative before 20 weeks' gestation. The auditory system follows those systems in the sequence of development.[4]

The auditory system becomes functional at around 25 to 29 weeks' gestational age when the ganglion cells of the spiral nucleus in the cochlea connect inner hair cells to the brain stem and temporal lobe of the cortex.[2] The earliest evidence of an auditory evoked response is at 16 weeks' gestational age. At this age, the ganglion cells in the cochlea are connected to nuclei in

the brainstem that stimulate a physiologic response. At 25 to 26 weeks' gestation, a loud noise in utero or in the NICU will produce changes in autonomic function. The heart rate, blood pressure, respiratory pattern, gastrointestinal motility, and oxygenation can all be affected.[5] The neural connections to the temporal lobe of the cortex are functional at around 28 to 30 weeks' gestational age. This begins the development of tonotopic columns in the auditory cortex. They are needed to receive, recognize, and react to language, music, and meaningful environmental sounds.

The two parts of the auditory system that are most important in the developmental processes are the cochlea (the receptor organ) and the auditory cortex. The cochlear nuclei, superior olivary nuclei, nucleus of the lateral lemniscus, inferior colliculus, and medial geniculate nucleus all undergo organization of the ganglion cells and neurons in response to stimulation, both endogenous and exogenous (Fig 3).[3] However, they all relate to the signals received from the neurons of the spiral ganglion and cochlear nuclei of the cochlea. It is the cochlea and auditory cortex in the temporal lobe that are most affected by the environment and the care practices of the NICU.

The Cochlea

The differentiation of the hair cells in the cochlea begins early in gestation (10–12 weeks). The development of the stereocilia on the apex of the hair cells follows. It begins first on the inner hair cells and later on the outer hair cells. The development of hair cells proceeds from the base of the cochlea to the apical regions. This is true for both inner and outer hair cells. There are an excess number of hair cells created early in development, and some disappear if not connected or used. It is a phenomenon very similar to the excess ganglion cells of the retina. Nature starts the infant or fetus with an excess of potential receptors and connections. The outer hair cells are the last to develop, at around 22 weeks' gestation and beyond.[2,3] They connect to some of the neurons of the spiral ganglion, but most receive feedback connections from the nuclei in the pons and brainstem. These are feedback connections, many of which are not functional until near term. The fetus and preterm infant have limited ability to modulate or reduce an intense auditory signal.

The movement of the tympanic membrane (eardrum) varies with the intensity and frequency of the sound stimulus. This is transmitted to the oval window in the cochlea where a wave is created in the fluid chamber. The wave causes the basilar membrane beneath the hair cells to be driven up. The hair cells are in contact with the tectorial membrane above them. As the basilar membrane rises, the hair cells are excited. The location of the rise along the course of the cochlea depends on the sound frequency or pitch. The extent of the rise in the membrane depends on the intensity. The higher the intensity, the more the hair cells are stimulated, resulting in more frequent firing. Each hair cell has a specific frequency at which it achieves maximum stimulation. On the average, adjacent hair cells should differ in their prime or characteristic frequency by only 0.2% (1/30 of
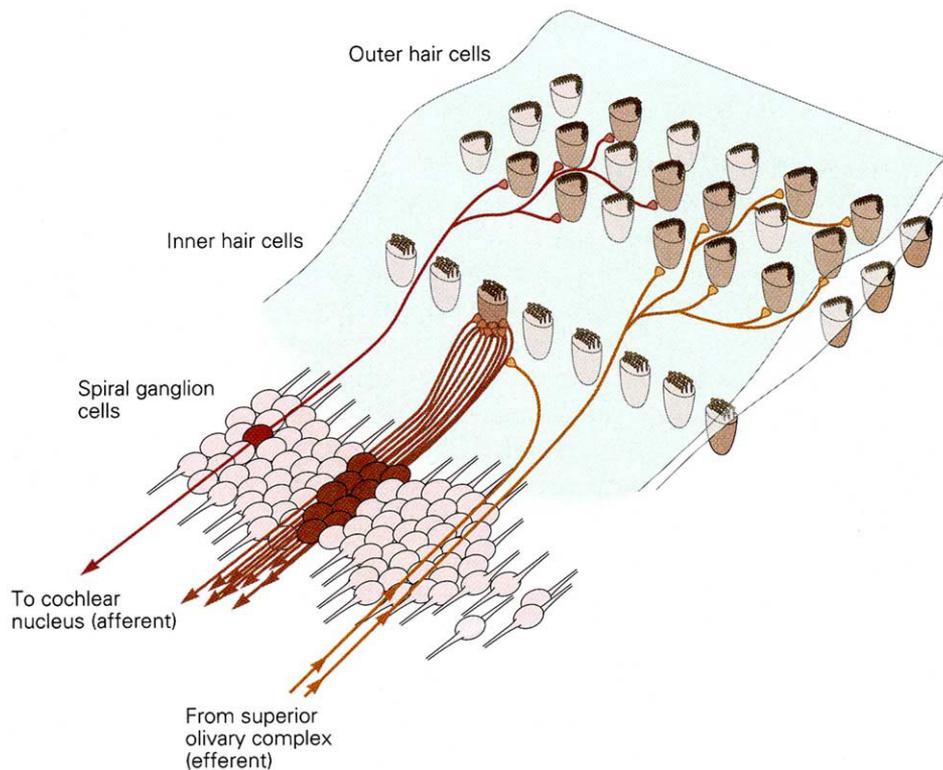
Fig 2. Innervation of the organ of Corti. Most afferent axons end on inner hair cells, each of which constitutes the sole terminus for an average of 10 axons. A few afferent axons of small caliber provide diffuse innervations to the outer hair cells. Efferent axons largely innervate outer hair cells and do so directly. In contrast, efferent innervation of inner hair cells is sparse and is predominantly axoaxonic, at the endings of afferent nerve fibers (Reprinted from Kandel ER. *Principles of Neural Science, Fourth Edition.* New York: McGraw Hill; 2000:602; with permission).

the difference between two piano notes).[6] They are very precise in the very specific frequency that produces the maximal response. The hair cells connect to specific cells of the cochlear nucleus based on the frequency or pitch of the hair cell peak response. The tuning of the hair cells of the cochlea is facilitated by the Kölliker organ that resides in the cochlea. It functions throughout gestation and early infancy but disappears later in development. Most of the tuning of the hair cells of the cochlea occurs between 28 weeks' gestational age and early months of infant life.

Sound energy is actually amplified by the hydrodynamic and mechanical properties of the cochlea.[6] It is also strongly affected by the original intensity of the auditory signal. The greater the intensity of the auditory signal or sound is, the less the sensitivity is for tuning of the hair cells. The sensitivity of the basilar membrane to 80-dB stimulation is less than 1% that for 10-dB stimulation. Although 60 to 80 dB of auditory noise may not cause damage to adult hair cells or pitch discrimination, it can severely interfere with the initial tuning of the hair cells in the fetus or preterm infant. Thus, the environment of the NICU can profoundly affect the tuning of the hair cells of the cochlea.[6]

More than 90% of the cochlear ganglion cells innervate inner hair cells. Each axon innervates a single hair cell, but each inner hair cell directs its output to up to 10 nerve fibers. The neural information for hearing originates almost entirely from inner hair cells. At any point along the course of the spiral ganglion in the cochlea, the neurons respond best to the optimal or prime frequency of the inner hair cell. Thus, the tonotopic organization of the auditory cortex as well as relay nuclei begins with the postsynaptic site on the inner hair cells.

The acoustic sensitivity of axons in the cochlear nerve mirrors the innervations pattern of the spiral ganglion cell. Like the hair cells, each axon has a characteristic frequency of sound for maximal response. There is a tuning curve for the ganglion cell nerve fibers, just as there is for hair cells.

The auditory nuclei that are in the pons and midbrain areas function in sound localization and interaural sound differences. Because the fetus in utero receives sound by bone conduction, there is no interaural sound difference until birth at term. Preterm birth creates interaural sound differences and exposure to high-frequency sound. Most high-frequency sound is filtered by the uterus, amniotic fluid, and mother's tissues in utero. In utero, the hair cells that are tuning to high-frequency sounds are protected from intense high-frequency sounds, but are exposed to low-frequency sounds that permit fine tuning of the hair cells. The hair cells lose their sensitivity to pitch in the face of intense background sound levels of 60 dB or greater.[6,7]
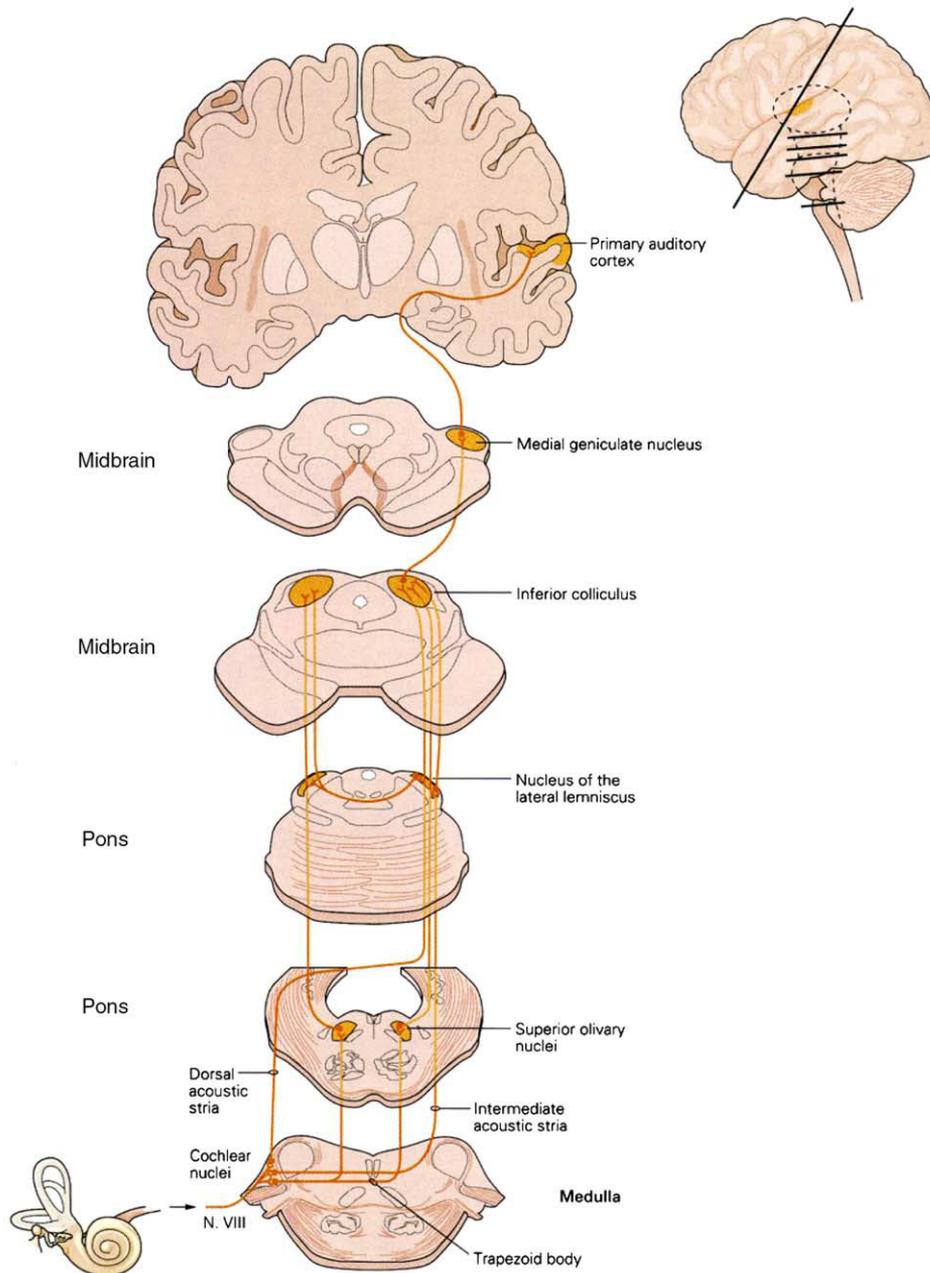
Fig 3. The central auditory pathways extend from the cochlear nucleus to the auditory cortex. Postsynaptic neurons in the cochlear nucleus send their axons to other centers in the brain via three main pathways: the dorsal acoustic stria, the intermediate acoustic stria, and the trapezoid body. The first binaural interactions occur in the superior olivary nucleus, which receives input via the trapezoid body. In particular, the medial and lateral divisions of the superior olivary nucleus are involved in the localization of sounds in space. Postsynaptic axons from the superior olivary nucleus, along with the axons from the cochlear nuclei, project to the inferior colliculus in the midbrain via the lateral lemniscus. Each lateral lemniscus contains axons relaying input from both ears. Cells in the colliculus send their axons to the medial geniculate nucleus of the thalamus. The geniculate axons terminate in the primary auditory cortex (Brodmann areas 41 and 42), a part of the superior temporal gyrus (Reprinted from Kandel ER. *Principles of Neural Science, Fourth Edition.* New York: McGraw Hill; 2000:604; with permission).

The auditory cortex is on the outer surface of the temporal lobe.[3] It develops as an area with tonotopic cell columns or clusters that represent the characteristic frequencies. The neurons tuned to the high frequencies are in the caudal region, and the neurons tuned to the low frequencies are in the rostral or front end of the auditory cortex. This creates a spread of cell groupings that are responsive to specific frequencies or pitch. The auditory cortex is also divided into two types of alternating zones that are at right angles to the axis of the tonotopic columns. The first is summation columns that are half of the zones and are responsive to either ear (EE cells), and the alternating cortical bands (EI cells) are primarily stimulated by one ear and inhibited by the other ear. Thus, the auditory cortex is partitioned into columns that respond to separate frequencies and from one or both ears.[8] The summation bands respond to different intensities from one or both ears.

The auditory system must be able to receive and recognize small differences in frequencies or pitch, differences in intensity or loudness, interaural differences in sound, sound patterns, and timing or rhythm. With these capabilities, the human can use language, hear and feel music, and recognize meaningful sounds from the environment to avoid danger and manage the events and activities of daily living.

Processes Involved in Auditory Development

The building of the human auditory system involves four basic factors that are essential to the process.

Genetic Endowment, Activity Independent

The basic structures of the auditory system are the result of cell multiplication, migration, differentiation, and basic cell position. These are directed by genetic code or genetic endowment. These events will proceed without stimulation or outside facilitation. Some gene expression is altered by environment and outside stimulation; but the basic structure, cell locations, etc, are the result of genetic code. It is possible to interfere with genetic processes but not to improve them. In the case of the auditory system, the structure and shape of the ears, the middle ear, the basic structure of the cochlea, the nerve tracks, and the nuclei are also genetically coded.[2,9]

The expression of individual genes that direct the development of the auditory system may be altered by exposure to factors emanating from the environment. The expression of any single gene can be altered without changing the structure of the DNA. This process is termed *epigenetics* and is the basis for major genetic research in the past few years. The alterations in gene expression result from the exposure to three types of environmental factors. Gene expression can be altered by chemical or toxic exposure, nutritional deficiencies or excesses, and intense or constant abnormal sensory stimulation. These exposures or stimuli not only affect the mother and her fetus but can also alter the gene expression in the eggs in the ovary of the female fetus to transmit the effect to the next generation. Mothers exposed to diethystilbestrol had both daughters and granddaughters affected. The development of the auditory system can be altered by epigenetic processes.

Endogenous Stimulation Dependent

Endogenous stimulation is nerve cell activity that originates in the brain, sensory organs, or peripheral nerves without outside stimulation. The first stage of this endogenous activity is spontaneous irregular firing of ganglion cells of the spiral nucleus and the cochlear nuclei. This is needed to promote growth of axons for cell-to-cell connection. In the human, this starts before the 20th week of gestation. The irregular firing becomes regular; and with further maturation at around 22 weeks, they become synchronous waves of ganglion cell firing. This is essential for targeting of axons and midbrain nuclei. They continue to the temporal lobe of the cerebral cortex by 28 to 29 weeks' gestation. These endogenous stimuli can be blocked by drugs, alcohol, and toxic chemicals from the environment. The effect of intense noise or loud sounds on the endogenous ganglion cell activity is not known.[9]

Exogenous or Activity-Dependent Processes

Unlike vision where visual experiences and stimulation are not needed until after birth at term, the auditory system needs auditory stimulation as part of development during the last 10 to 12 weeks of fetal life (28–40 weeks' gestational age) and continuing for several years after birth. Starting at 28 to 29 weeks, the hair cells and their connections in the cochlea are sufficiently mature to begin tuning for specific sound frequencies. The hair cells for the lower-frequency sounds are tuned first. The fetus is protected from most high-frequency sounds in utero. The internal in utero environment is sufficiently quiet to permit the recognition and response to sounds, internal and external. Exposure to outside intense low-frequency noise (70–80 dB) will block the ability to tune the hair cells to the very specific prime frequency in utero or in the NICU. The differences in prime frequencies of adjacent hair cell should be 0.2%. This requires a very quiet background noise level either in utero or in the NICU.[6]

The fetus is capable of in utero learning such as mother's voice, simple music, or sounds common to the environment. In utero learning of sounds, voice, and music has been demonstrated at as early as 32 weeks' gestational age.[10] Infants in utero learned mother's voice or a particular melody and were able to discriminate it from others after birth. The auditory learning and memory from fetal (or NICU) life must include recognition of difference in pitch, pattern, intensity, and rhythm. They cannot discern or respond to harmony or note relationships in cords. For the fetus to learn to recognize a voice or melody, he or she needs to have protected sleep cycles with particular attention to rapid eye movement (REM) sleep. Rapid eye movement sleep generates the brain waves needed to create long-term synapses in the auditory cortex and brain stem nuclei[11] that become the auditory memories.

For in utero learning or NICU learning, a preterm infant must hear the voice or music when awake or when in quiet sleep followed by a period of REM sleep. It will take multiple exposures and multiple cycles with REM sleep. It must occur with the background noise level at less than 50 dB and no loud spikes in noise level. In utero, the fetus will primarily hear voice or music sounds with pitch or frequency around middle C and below (<300 cps frequency).[11] The exposure to voice, music, and meaningful sounds between 30 to 40 weeks' gestation is needed for the fine tuning of the hair cells and their neuron connection to the spiral ganglion and cochlear nuclei. The fetus that is exposed to intense (<80 dB) low-frequency sound with television, boom boxes, machinery, or room noise interspersed with quiet and absence of voice will arrive at 40 weeks' gestation with 2 months of language delayed. The infant will be behind in tuning of hair cell frequency specificity. He or she will not have developed circuits for recognition of phonemes, speech patterns, pitch, and special characteristics of mother's voice as well as other voices close to the infant. If the same tape of music or voice is played repeatedly, the fetus or infant will habituate to the tape and not attend to it.[11]

All speech, music, and meaningful sounds from the environment are not only created as memory circuits in the auditory and language areas of the cortex but have direct neuroconnections to the limbic system (emotional memories). Pleasure, joy, fear, sadness, anxiety, or other parts of emotional memory are recorded and stored as part of auditory memories but in the limbic system. Even a fetus at 34 or 36 weeks will distinguish different moods or emotional qualities to speech and music that are retained as part of accumulated memories.

With in utero or NICU preterm infant learning, the speech or music must have and repeat some familiar parts; but to retain interest and expand recognition, new material needs to be constantly added, and changes must be made. Head phones should **NEVER** be used directly on the abdomen of a mother during pregnancy because in utero sound is nondirectional and the sound from each earphone is additive. It is easy to have each earphone at 60 or 70 dB, which is 120 to 140 dB to the infant. When it is frequencies below middle C, this will damage and even destroy hair cells with as little as 1 to 4 hours of exposure.[12]

Effects of Environment and Sensory Interference

Factors in the environment have a clear impact on auditory development for the fetus in utero and the infant in an NICU, in a day care, as well as at home.

In Utero All intense (>60 dB) low-frequency noise should be avoided and especially after 20 or 22 weeks' gestation. The fetus in utero, after 28 to 29 weeks, needs exposure to mother's voice, family voices, music (simple melodies), and meaningful sounds of the family and environment. The background noise level needs to be kept to less than 50 dB, especially in the lower frequencies, for the infant to discriminate the speech or music.

Newborn Intensive Care Unit The background noise level should be maintained at or less than an Leq (average sound level, a weighted, slow response scale over one hour period) of 50 dB and at or less than an L_{10} (upper sound level 10% of the time over a one hour period) of 55 dB. The 1-second maximum should not exceed 70 dB, a weighted, slow response. This will provide an environment in which the infant can hear and learn the mother's voice, music, and meaningful sounds. It is also an environment with as little disruption of sleep and sleep cycles as possible. Learning auditory patterns requires REM sleep after 32 weeks' gestation to create long-term memories. Sleep cycles with REM sleep, especially protected, are important throughout infancy and childhood. This applies to home, day care, or NICU.[13]

It is important in the care of infants in the NICU to teach and demonstrate to parents and caregivers the requirements for a developmentally supported environment, to control background noise, and to ensure the appropriate auditory experience (parents' voice, etc). This includes the support for and protection of REM sleep and sleep cycles. This requires the selection of and timing of care and care procedures to support the developmental processes and protect sleep as much as possible.

Early learning of mother's voice and ability to discriminate it from other voices are important in the attachment process as well as in providing comfort. The environment of the preterm and postterm infant is an important factor supporting auditory language and music learning. It can, with loud, low-frequency noise or unusual vibration and motion, create significant interference with healthy auditory development.

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