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The Development of the Auditory System from Conception to Term

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Objectives

After completing this article, readers should be able to:

1. Explain when the fetus begins to respond to sound.
2. Describe the type of sounds to which fetuses and extremely preterm newborns initially respond.
3. Explain why the fetus is exposed to low-frequency sounds.
4. Describe the role of the fetal cochlea and the outer and middle ears in response to sound.
5. Compare and contrast the response to sounds in the fetus of the same postmenstrual age and preterm newborns.

Introduction

For the first half of pregnancy, the fetus is unresponsive to sound. By term, basic auditory capabilities are relatively mature. We review in this article the anatomic and functional developments during that remarkable interval between those two landmarks, which also is a time of increased risk for otologic insult. (1) We also comment on the environmental milieu during this critical period of development in normally developing fetuses and in preterm newborns.

Sound

Definitions

Sound is vibratory energy transmitted by propagating compressions and expansions of a stationary medium. The frequency of a sound (perceived as pitch) is defined by the number of compressions and expansions (cycles) per second or hertz (Hz). Human hearing ranges from 20 to 20,000 Hz, with greatest sensitivity at 1 to 4 kHz. The density and elasticity of the medium determine sound transmission through that medium. For example, the speed of sound in water (and amniotic fluid) is more than four times the speed of sound in air. Acoustic impedance is the complex ratio of the pressure induced by the sound source to the volume velocity of the vibrating medium. The impedance mismatch at boundaries between different media determines how much sound energy is transmitted and how much is reflected at those boundaries. The impedance mismatch in transmitting sound from air to the fluid-filled inner ear or cochlea is about 32 dB. If there were no middle ear, about 1% of the incident sound at 1 kHz would be transmitted to the cochlea of humans because of the impedance mismatch between air and the cochlea. With the middle ear, about 50% of the sound power actually is transmitted to the cochlea at 1 kHz.

Sound intensity and pressure could be expressed in absolute units on a linear scale, but this is not typical. Rather, a logarithmic transformation of sound pressure is used because it makes the enormous range of audible sounds more manageable and corresponds to human sensation. It also is customary to express sound pressures relative to a meaningful referent sound pressure, by convention 20 mcPa (approx-

Abbreviations

AAP:	American Academy of Pediatrics
ABR:	auditory brainstem evoked response
dB:	decibel
GA:	gestational age
HL:	hearing level
Hz:	hertz
IHC:	inner hair cell
NICU:	neonatal intensive care unit
OHC:	outer hair cell
PMA:	postmenstrual age
rms:	root mean square
SPL:	sound pressure level

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imately the threshold of hearing at 1 kHz or 1,000 cycles/sec). The unit of sound constructed in this manner is called the bel, in honor of Alexander Graham Bell, who invented the telephone. Because the bel is a rather large unit, the decibel (dB) is used more frequently (10 dB=1 bel). Sound pressure level in decibels (dB SPL) is defined as $10 \times \log_{10}$ (the measured sound pressure/20 mcPa). (2)

The amplitude of a sound wave can be expressed in peak, average, and root mean square (rms) amplitudes. The relationships among these different measures is straightforward for pure tones (ie, sinusoids) but not for complex signals. The rms is used frequently in sound measurements because it is proportional to the energy of the sound wave measured. Peak SPL measurements are used to characterize impulses and other short-duration sounds. The relationship between peak SPL and the energy of a waveform changes with the complexity of the waveform.

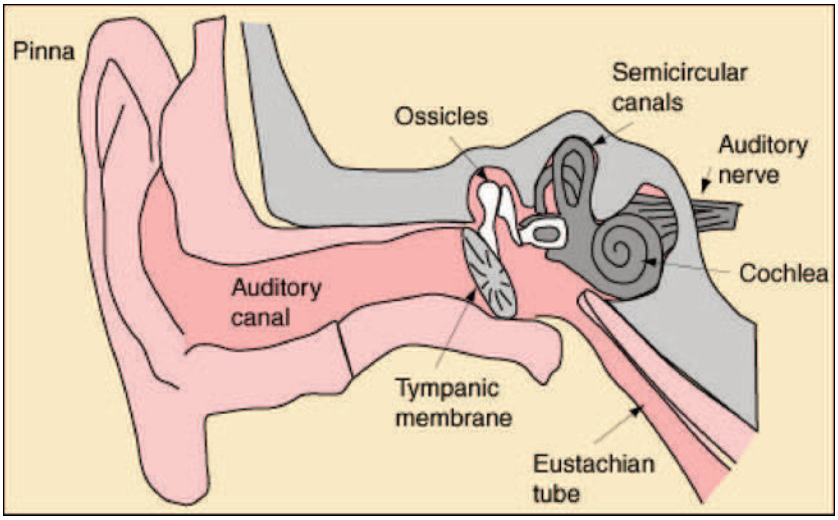

Figure 1. Important anatomic structures of the human adult ear.

Measurement

A variety of instruments are used to measure sound, depending on the purpose of the measurements. The sound-level meter is used most widely for measuring sound levels. Many sound-level meters have frequency-weighting networks (eg, often A, B, C) and a linear weighting (a flat frequency response). Frequency weighting scales more accurately describe the perceived loudness of sounds because the human auditory system attenuates some frequencies and emphasizes others (primarily due to the resonance characteristics of the outer and middle ears). The A, B, and C weighting scales approximate the normal adult human's perceived loudness as a function of frequency at different sound levels. The A-weighted sound level scale approximates the 40-phon equal loudness curve, which describes the levels of pure tones over the audible range judged by human adults to equal the loudness of a 40 dB SPL 1 kHz tone. Low- (<1 kHz) and high- (>4 kHz) frequency sounds are attenuated (39.4 dB at 31.5 Hz, 16.1 dB at 125 Hz, 1.1 dB at 8 kHz, and about 13 dB at 20 kHz). The B and C frequency weightings approximate the 70- and 100-phon equal loudness curves, respectively. The B and especially the C weightings are flatter than the A weighting. The A weighting is most widely accepted and generally used in national and international standards. It correlates better than the other scales with sound levels associated with noise-induced hearing loss in human adults. Weighting scales reflect adult hearing and may not accurately describe infant hearing.

Sound measurements indicate the level of the measured sound pressure relative to a referent sound pressure on a dB (logarithmic) scale. For sounds in the environment, the referent is typically 20 mcPa. Those measurements are properly indicated as dB SPL. In clinical settings, human threshold sound levels are specified in dB hearing level (HL). The referent sound pressures for dB HL sound levels are the frequency-specific threshold sound pressures for normal hearing adults.

Anatomy

The human ear is capable of detecting sound-induced displacements less than the diameter of a hydrogen atom. Evolution has protected the sensitive detectors responsible for hearing by encapsulating them in a fluid-filled chamber (the cochlea) in the petrous portion of the temporal bone (Fig. 1). The challenge of efficiently transmitting airborne sounds to detectors in a deeply embedded fluid-filled chamber is met by elaborate middle and outer ear systems. The resonance characteristics of the head, outer ear, and external auditory meatus modify the intensity and frequency profiles of sound. The ossicles of the middle ear transmit sound-induced vibrations of the tympanic membrane to the oval window, overcoming a considerable impedance mismatch and initiating a traveling wave of displacements along the cochlear partition. The traveling wave peaks where the

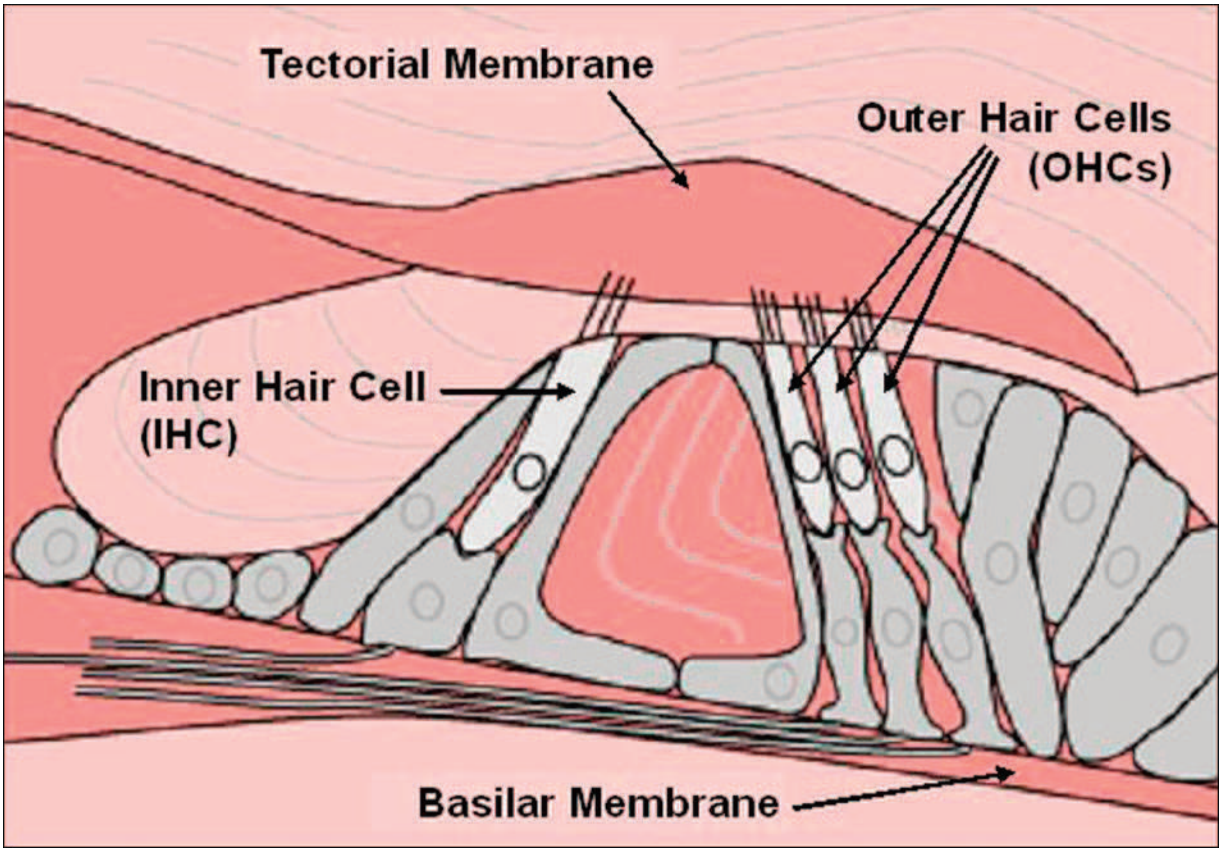

Figure 2. A cross-section of the cochlear partition, identifying the tectorial and basilar membranes as well as the inner hair cells (IHCs) and outer hair cells (OHCs).

impedance due to the stiffness of the cochlear partition is equal to but out of phase with the impedance due to its mass. Because the stiffness of the cochlear partition decreases toward the apex and mass-related inertial forces increase with frequency, the traveling wave peaks nearer the base for higher frequency stimulation and nearer the apex for lower frequency stimulation. The outer hair cells (OHCs) in the cochlear partition act as "cochlear amplifiers," enhancing the peak of the traveling wave displacement, thereby increasing sensitivity (Fig. 2). Displacements of the cochlear partition cause a shearing motion between the overlying tectorial membrane and the hair cells. That shearing movement bends cilia of the inner hair cells (IHCs), opening potassium channels that polarize those cells to initiate neural transmission along the auditory pathway.

Anatomic Development

There are many excellent Web sites on acoustics and the anatomy of the auditory system. For readers wanting additional background, we suggest: http://hyperphysics.phy-astr.gsu.edu/hbase/sound/ear.html#c1.

Different terms are used in the literature to characterize the ages of fetuses and newborns. In embryology, the most common term is gestational age (GA), dating from conception. Because the exact time of conception often is unknown for humans, clinicians most commonly use postmenstrual age (PMA), time from the last menses. We will be consistent with the terminology used in the literature, referring to GA when discussing embryology and PMA for studies that date fetuses and newborns according to the last menstrual period.

Cochlear Embryology

The outer ear, middle ear, cochlea, and neural pathways develop in parallel from disparate embryonic tissues serving other purposes in phylogeny. The onset of auditory function after the 20th week of gestation coincides with developments in the cochlea (Fig. 3). (2) Much attention has focused on the development of the tectorial mem-

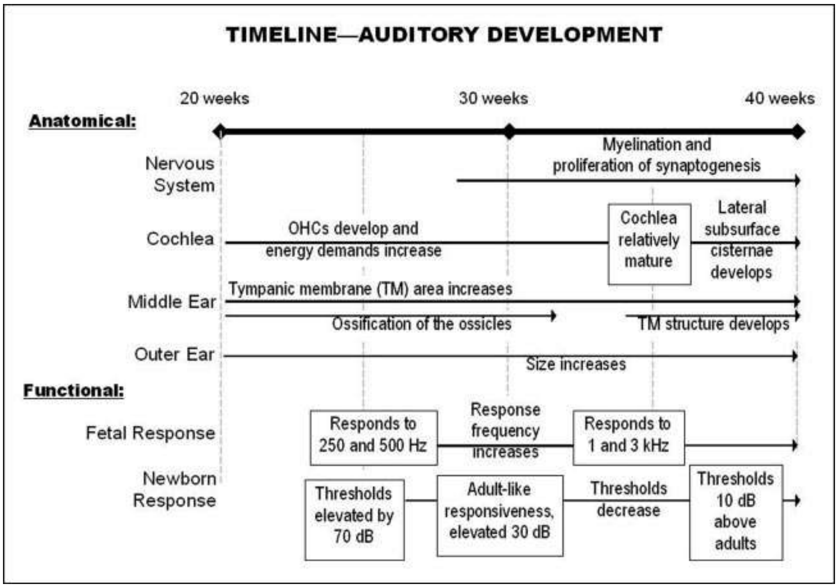

Figure 3. A timeline of auditory development from 20 weeks GA to term, including the important events in anatomic and functional development and their chronological relationships. OHC=outer hair cells.

brane and the underlying cells in the cochlear partition that permit the sound-induced shearing movement between the tectorial membrane and the hair cells. Metabolic demands increase when the cochlea is developing rapidly. (3) Thus, high-risk fetuses and preterm newborns whose metabolic resources are compromised may be especially susceptible to cochlear insult.

Pujol and Uziel (1) hypothesize that the cochlea matures by about 35 weeks GA. Cochlear maturation is not uniform; rather, it begins in the base just beyond the hook region and proceeds basalward and apically. (2) In addition to a base-to-apex developmental gradient, there is a radial developmental gradient that results in the maturation of IHCs before OHCs. The IHCs transduce sound-induced displacements into neural impulses. OHCs are hypothesized to be cochlear mechanical amplifiers, with impaired OHC function associated with elevated thresholds and reduced frequency tuning. Many of the gross morphologic changes that occur between 20 and 35 weeks' gestation concern the OHCs and cells that support the OHCs. In addition, the basilar membrane changes as radially oriented filaments increase and epithelial cells on the scala tympani side thin. These developments likely affect basilar membrane displacement and, therefore, the sensitivity and the frequency response to sound. More subtly, cochlear developments extend beyond the 35th week of gestation in the human, including development of the lateral subsurface cisternae that may play a role in OHC motility. (4)

Cochlear anatomy is inconsistent with the low- to high-frequency functional developmental gradient reported in many laboratory animals. The frequency response of the cochlea may shift. (5) The place that eventually becomes responsive to mid and high frequencies initially responds to low frequencies because of the mechanical characteristics of the immature cochlea. Lesion studies in animals support these hypotheses, but definitive human data are lacking.

Outer and Middle Ear Embryology

Concurrent with development of the cochlea, parts of the embryonic brachial system evolve to form the ossicular chain of the middle ear and the external auditory meatus (Fig. 3). Simultaneously, endoderm from the primitive pharynx evaginates, becoming the eustachian tube, the tympanic cavity, the air cells of the mastoid and petrous portions of the temporal bone, and the inner layer of the tympanic membrane. The remaining components of the inner, middle, and outer ears arise from surrounding mesoderm.

In the adult, the middle ear system provides about 30 dB of gain to overcome the considerable impedance mismatch at the cochlear (oval window) interface. Most of that gain results from the disparity in size of the tympanic membrane relative to the oval window. The tympanic membrane in the term newborn is about 4.5 mm in diameter compared with 7.5 mm in adults. (6) Unless compensated by other factors, middle ear gain in the newborn should be significantly less than in the adult because of the significantly smaller tympanic membrane. The tympanic membrane (especially the fibrous layer) thins with development as it increases in diameter. The skeletal support for the tympanic membrane begins to fuse to the temporal bone at 34 weeks' gestation and is completely fused by term. These changes affect tympanic membrane movement and sound transmission to the cochlea.

There are other anatomic indications that sound transmission by the middle and outer ears changes considerably after 20 weeks' gestation. The 17-mm length of the term newborn's external auditory meatus is significantly shorter than the 27-mm length of the adult. (6) The resonance characteristics of the outer ear change with their changing geometry, shifting from emphasizing high frequencies to lower frequencies with age. Low-frequency sound also is absorbed by compliant cartilaginous canal walls of the newborn rather than transmitted to the middle ear.

The ossicles begin ossification by the 16th week, a process largely completed by 32 weeks GA. Increasing weight due to ossification attenuates the transmission of high-frequency sounds. The fetal stapes is fused medially to the otic capsule and is much thicker than the adult stapes, approaching adult dimensions by term. The middle ear cavities and air cells are far from adult size in the fetus and newborn; their developmental process continues into infancy and childhood.

The stiffness of the middle ear is determined largely by the middle ear cavities and fibrous structure of the tympanic membrane. For low-frequency sounds, stiffness limits sound transmission. Therefore, the smaller immature middle ear cavities of newborns indicate reduced low-frequency input to the cochlea. Mass (principally of the ossicles) limits high-frequency transmission by the middle ear. The ossicular joints, annular ligaments supporting the stapes in the oval window, and the cochlear fluids are the resistive components of the middle ear that dissipate transmitted sound energy by frictional forces. As coupling of the ossicular chain improves with development, loss of sound energy due to friction should diminish. Anatomic considerations indicate that at the onset of auditory function, the middle ear is relatively less efficient than the adult middle ear. Furthermore, relative to adults, high-frequency sounds are emphasized and low-frequency sounds are attenuated.

Development of the Auditory Neural Pathway

A rudimentary nervous system begins to develop by the third week postconception. By term, most neurons are present. Neuropil and supportive tissue continues to grow postnatally. (7) Neuronal migration from periventricular proliferation zones begins about the eighth week and is complete by the second month in the brainstem, but it continues postnatally in the cerebral cortex. (8) Synaptogenesis and the elaboration of pre- and postsynaptic circuits are especially intense from the 28th week PMA until early childhood (Fig. 3). After cell multiplication and migration have ended, myelination begins, and it continues well into adulthood. (9)

Innervation of the IHCs commences by 11 weeks and is complete by 14 weeks GA. In contrast, efferent innervation of the OHCs is not complete until after 22 weeks. The roots of the eighth nerve are completely myelinated by the fifth month postconception. Myelination continues in the cortical auditory pathway into the second postnatal year.

Functional Development

The onset and development of human auditory function has been studied in the fetus and the preterm newborn (Fig. 3). Each presents its own measurement challenges, and each provides answers to different, but complementary developmental questions. Although the incidence of congenital hearing loss is 1 to 3 per 1,000 newborns in the United States, (10) the incidence of hearing impairment in graduates of neonatal intensive care units (NICUs) is 10 times greater, (10)(11) and in the sickest, most preterm newborns, it is 100 times greater. (12)(13)(14)

Fetal Auditory Capabilities

MODE OF HEARING. The fetus develops in an aquatic (uterine) environment. Because the peripheral auditory system does not participate in underwater hearing as it does in terrestrial hearing, (15) it is not surprising that the outer and middle ears do not participate in fetal hearing. (16) Gerhardt and colleagues (16) recorded the cochlear response to sound in fetal sheep with the fetal head uncovered, covering the fetal head with a sound-attenuating Neoprene® hood, and with a Neoprene® hood modified to cover the head but expose the ear canal. The cochlear responses were reduced in the two hooded conditions, suggesting that head vibration and not middle ear transmission is the effective uterine sound stimulus.

ONSET OF A RESPONSE TO SOUND. Real-time ultrasonography makes it possible to observe the responses of human fetuses to sound. Birnholz and Benacerraf (17) detected the first distinct response to intense vibroacoustic stimuli (110 dB) at 25 weeks PMA; after 28 weeks, the auropalpebral reflexes were consistently present. The earliest response that Hepper and Shahidullah (18) detected was to a 500-Hz tone at 19 weeks PMA, with virtually all fetuses responding to 250- and 500-Hz tones by 27 weeks. In contrast, responses to 1- and 3-kHz tones were not detected until after 29 and 31 weeks, respectively. The intensity levels required to elicit these responses decreased as age increased. The response to the high-level auditory and vibroacoustic stimulation used to elicit responses from fetuses may stimulate the somatosensory system. Fetal cutaneous receptors mature earlier than the auditory receptors. At the high levels of stimulation necessary to elicit responses in fetuses, it is unclear which sensory modalities are responding. (19)

Figure 4 illustrates the elevated threshold levels of the fetus compared with newborn and adult thresholds. This figure is speculative because definitive data do not exist, but it communicates current thinking on fetal and newborn thresholds. The fetal data are from Hepper and Shahidullah (18) (converting dB(A) to dB SPL). The preterm newborn data were generated from adult thresholds (20)(21)(22) shifted up in frequency to account for their higher outer ear resonance frequency and up in level to account for their higher thresholds.

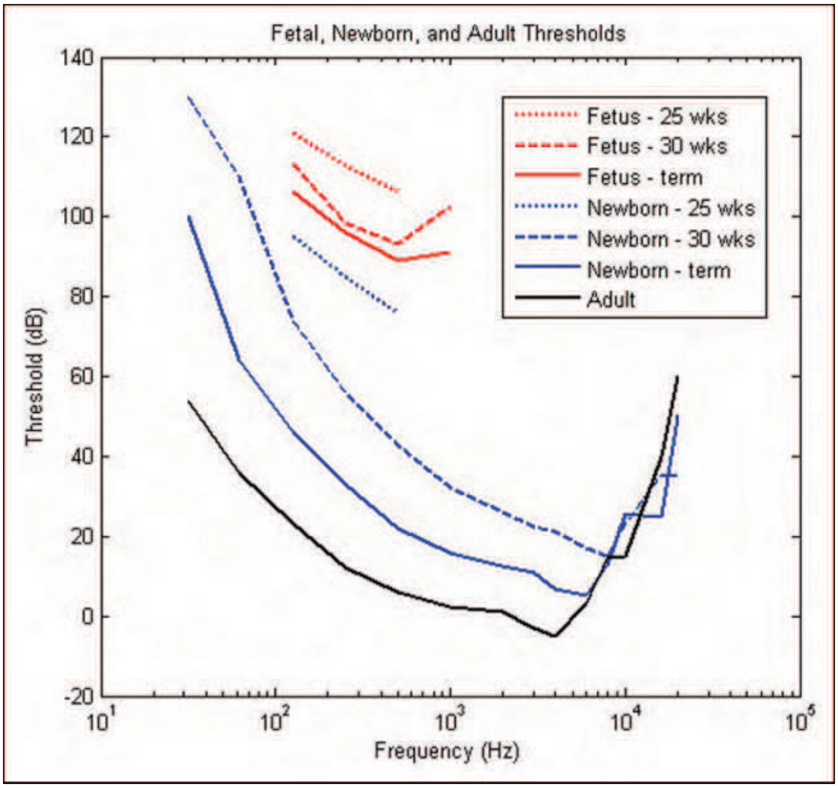

Figure 4. A characterization of frequency-specific auditory thresholds for fetuses (in weeks PMA), newborns (in weeks PMA), and adults. The fetal data were reported by Hepper and Shahidullah (18) (their reported sound levels in dB(A) were converted to dB SPL). These data for newborns do not exist. Newborn values were extrapolated from adult values according to known shifts in frequency and threshold levels in newborns as reviewed in this article. Adult thresholds are those reported by Robinson and Dadson (20), Berger (21), and Corso and Levine (22). Although this figure should not be interpreted literally, it indicates general differences between fetal, newborn, and adult hearing.

FREQUENCY DISCRIMINATION. Shahidullah and Hepper presented pure tones and spoken syllables to fetuses at 27 and 35 weeks PMA. (23) The fetus was presented the same sound until it became habituated to it by showing no motor response. A different sound was then presented. If the fetus responded (or dishabituated), it was concluded that the fetus could discriminate between the two sounds. This paradigm demonstrates rudimentary learning and short-term memory capabilities as well as frequency discrimination. All fetuses habituated to the first sound, with more stimulus presentations necessary for habituation at 27 weeks than at 35 weeks. Fetuses at 35 weeks responded to the dishabituating stimulus. The data are less convincing that fetuses can make the same discriminations at 27 weeks PMA.

LEARNING AND SPEECH. Research supports (with some negative results) the belief that the uterine sound environment preconditions newborns to familiar stimuli such as heartbeats. (19) Fifer and colleagues (24)(25) conducted a series of studies demonstrating that newborns prefer their mother's voices to that of another female. Furthermore, they prefer a "uterine" version to an airborne version. (26) Apparently, this parental preference does not extend to the father's voice. (27) Newborns respond differently to languages, musical sequences, television theme songs, and airport noises if exposed to those noises in utero. (19) These studies suggest that experience with external as well as internal sounds affect the fetus. Although prenatal sound exposures may predispose newborns to their social environments, other studies suggest that newborns are also genetically pretuned to process important stimuli. One example is the lateralization of speech stimuli to the left cerebral hemisphere in newborns. (28)

INTENSE NOISE. Few epidemiologic studies have investigated the relationship between fetal noise exposure and hearing loss in humans. Several studies report small but consistent effects, although these investigations have been criticized on methodologic grounds, especially for the failure to include adequate control groups. (29) It seems likely that the uterine environment buffers the fetus from insult, but if noise is excessively loud and of a long duration, damage to the cochlea results. Exposing pregnant ewes multiple times to 16-hour 120-dB SPL broadband noise resulted in modest IHC and OHC damage in the middle (mid frequency) and apical (low frequency) turns of the cochleae of the exposed fetuses. (30) Postnatally, damage is more extensive, targeting the basal (high frequency) turn of the cochlea. These results highlight differences between uterine and terrestrial hearing. High-frequency sounds that are emphasized postnatally by the resonance characteristics of the outer and middle ears are attenuated by maternal tissue in utero.

Preterm Newborn Auditory Capabilities

THE OUTER AND MIDDLE EAR SYSTEMS. Few measurements of middle and outer ear function have been conducted in newborns, and almost no data on preterm newborns exist. In adults, the contribution of the outer ear to the sound input to the cochlea can be considerable (20 dB or more). (31) The resonance frequency of the external auditory meatus is much higher in term newborns (5.1 to 7.2 kHz) than in adults (2.7 kHz). (32) Furthermore, low-frequency sound energy is absorbed by the compliant canal walls of the newborn rather than being transmitted to the middle ear. (33) High-frequency emphasis and low-frequency attenuation increase in smaller and younger newborns.

Middle ear sound power transmission is less in 1-month-olds than adults (4 dB less at 1 kHz and 11 dB less at 4 kHz). (34) Middle ear compliance is approximately half that of the adult at 1 kHz, possibly due to smaller middle ear cavities. Middle ear resistance is also higher in infants, which is consistent with known immaturities in coupling of the ossicular chain to the oval window. These results help explain threshold elevations reported for newborns.

RESPONSE TO SOUND. The first reports of scalp-recorded electrical activity in response to sound are at approximately 25 weeks PMA in preterm newborns. (35) Those responses (across all sensory modalities) are long latency negative potentials, consistent with transmission along the auditory pathway depolarizing large pyramidal cells in the primary auditory cortex. Over the last trimester, this long latency evoked response develops multiple biphasic components consistent with the maturation of dendritic and somatic excitatory/inhibitory connections.

REFINEMENT OF THE AUDITORY RESPONSE. Amin and colleagues (36) recorded auditory brainstem evoked responses (ABRs) in 173 preterm (<32 wk at birth) newborns. After 28 weeks, waves III (generated from the cochlear nucleus) and V (generated from the lateral lemniscus) were identified reliably in most of the newborns. Prior to 28 weeks PMA, about half of the recordings were scored as "no responses," and virtually none were scored as having adultlike waves. Other researchers also have reported a marked transition in the robustness of ABR recordings around 28 to 30 weeks PMA. (37)(38)(39) Before 30 weeks, ABR thresholds (to clicks) are more than 50 dB (nHL) above adult thresholds. By term, newborn thresholds are about 20 dB (nHL), still about 10 dB higher than adult ABR thresholds. (40)(41) Moore and colleagues (42) attribute the onset of a reliable ABR to the appearance of myelin sheaths on trapezoid body and lateral lemniscus axons. As suggested previously, the threshold elevation at term may result from middle ear immaturities.

The latencies of the ABR waves decrease with development, while their amplitudes increase, especially between 30 and 37 weeks PMA. (38) The more rostrally generated the wave, the longer the development. Mature latencies are achieved postnatally. In newborns of all PMAs, later waves are relatively more delayed and smaller in amplitude than the earlier waves. Axonal conduction velocities triple from the onset of the ABR to term, when adult values are achieved, paralleling marked increases in myelin density. (42) Synaptic transmission is the other major contributor to brainstem transmission times, which continue to shorten postnatally until 3 years of age. (43) The rate of stimulus presentation likely affects synaptic transmission. (44) Rate effects are large in preterm newborns and reduced but still substantial in term newborns. (45)(46)(47)(48)

From about 31 weeks PMA on, the cochlea, as assessed by otoacoustic emissions, is mature, although subtle differences have been reported. (49)(50)(51) There are virtually no emission data reported from preterm newborns (<31 wk PMA). By term, the cochlea is anatomically and functionally adultlike. (49)(50)(51)(52)(53) Other basic auditory capabilities that allow the newborn to engage its environment also seem functional at term. (54)

LEARNING AND SPEECH. The acoustic variations in speech sounds are nearly infinite, yet infants must break the speech stream into the limited number of building blocks combined to generate the words we say and understand to acquire language. By a few months post-

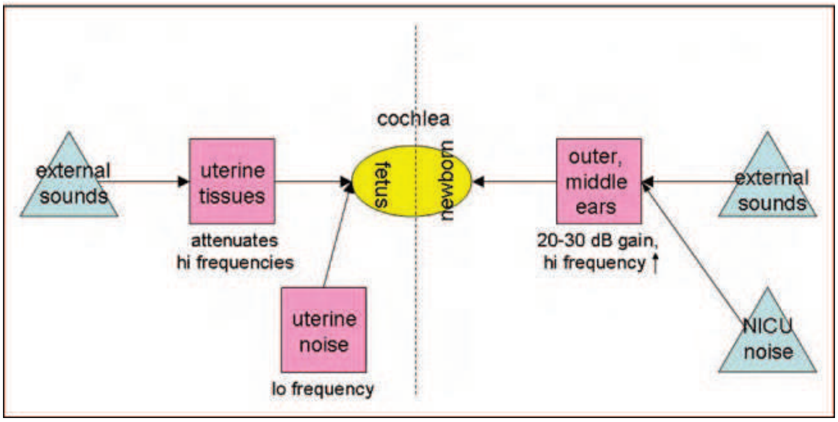

Figure 5. Contrasting sound environments of the fetus and newborn. Although fetal and preterm newborn cochleae and higher auditory pathways may be identical, the sound input they experience is significantly different.

natally (and at birth for some fundamental contrasts), infants are capable of responding to phonemic contrasts necessary for speech perception. (55) The work of DeCasper (27) and others indicates that the predisposition to respond preferentially to speech may be learned in the womb. Other data indicate humans also probably are prewired to process language. (28)(56) Nature and nurture cooperate to permit humans to begin the daunting task of becoming language users from birth.

Comparing the Uterine and NICU Environments

Prior to birth, the fetus and mother are a functional unit. After birth, the newborn must progress alone in a new environment with the help of well-intentioned caregivers. The plight of the preterm newborn is even more formidable. The environments (eg, sounds, light, temperature, oxygen, electrolytes, nutrients, waste products, pathogens, immune responses, hormones) to which preterm newborns are exposed contrast with the fetal environments at a critical time for the development of many systems, including the auditory system. Availability of adequate oxygenation is a good example. Preterm newborns are susceptible to an inadequate exchange of vital gases because of problematic deliveries and immature and diseased lungs. Newborns who survive after assisted ventilation are at a significantly increased risk for hearing impairment, and risks increase with increasing severity of pulmonary disease. (13) Providing too high concentrations of oxygen to the preterm newborn also may be problematic. (57) High oxygen saturation levels may affect the developing cochlea adversely, a hypothesis that seems plausible because the normal fetus has low oxygen tensions in utero. (58) Sohmer and colleagues (59) demonstrated that fetal thresholds to vibroacoustic stimulation are enhanced by having the mother breath oxygen instead of room air. One implication is that the preterm newborn is likely to be more sensitive to sound than the same age fetus because of greater oxygenation of the cochlea. The fetus may be buffered from intense sound and susceptibility to insult by maternal tissues and reduced oxygen levels.

The Uterine Sound Environment

In the absence of external sounds, the uterine sound environment is dominated by low-frequency noises from the mother's respiratory, cardiovascular, and gastrointestinal systems; body movements; and speech. (60) Heartbeat sounds are not as pervasive in the uterine sound environment as once believed; maternal speech is among the more prominent uterine sounds. (61)

The abdominal wall, uterus, and fluids surrounding the fetus act as a low-pass filter, attenuating higher-frequency sounds from the environment to a greater extent than low-frequency sounds (Fig. 5). For frequencies lower than 200 Hz, the attenuation is less than 5 dB. Some studies have noted an enhancement of external noises at these frequencies. (62) The attenuation increases with higher frequencies, reaching 20 to 30 dB at 2 kHz. (60)(63)

The fetus's response to sound is a function of both the uterine filter and the fetal auditory system. It seems likely that the fetus is relatively unresponsive to sounds (at least externally generated sounds) for a variety of reasons. Background noises in utero mask low (and high) external frequencies, high-frequency external sounds are attenuated by maternal tissues, the fetus does not benefit from the amplification of sounds by the middle and outer ears, and their cochlear responses may be limited by cochlear immaturities and low oxygen levels. The most direct assessment of cochlear functioning in utero is a study by Gerhardt and associates (64) in which they recorded cochlear responses from six fetal lambs. Compared with fetal cochlear thresholds, newborn thresholds were reduced by 11 dB at 125 Hz, 38 dB at 1,000 Hz, and 45 dB at 2,000 Hz. One newborn lamb was tested a second time 24 hours after the initial assessment, and thresholds were reduced further by 4 to 22 dB over the frequency range assessed. Thresholds are elevated for a short time after birth because of vernix and fluids in the outer and middle ears and possibly oxygen reduction concomitant with the birth process. (46). Thus, the reduced fetal response to sound may be even more dramatic than reported by Gerhardt and associates.

Speech in Utero

Researchers have been particularly interested in the transmission of speech to the fetus. Richards and colleagues (61) presented recordings of a word list to eight pregnant women during the early stage of labor. The women recited the same word list. The researchers positioned a hydrophone between the anterior cervical lip and the fetal head and verified the hydrophone's position by ultrasonography. External male voices were attenuated less than female voices. Speech sounds below 250 Hz were enhanced with increasing attenuation above 250 Hz to about 10 dB at 4,000 Hz. Maternal voices actually were enhanced.

Griffiths and coworkers (65) presented word lists to pregnant ewes and recorded from the necks of fetal lambs. The intelligibility of speech was significantly reduced by transmission through the mother. The prosodic information, such as the intonation and rhythmic aspects of normal conversation directed to the mother, seems to be available in the uterine environment, but higher frequency information responsible for the perception of consonants is attenuated. The Griffiths study did not consider the fetus's reduced response to sound. A study by Smith and associates (66) did. They recorded the cochlear microphonic (alternating current generated by sound-induced mechanical deformation of the hair cells that mimic the sound stimulus) from sheep fetuses presented speech sounds both in utero and ex utero. The average intelligibility score of these recordings ex utero was 73%, as judged by a panel of adults, compared with 41% in utero. The 32% reduction represents the loss in intelligibility of speech processed by the fetal cochlea in utero.

The NICU Sound Environment

For decades there has been concern that excessive noise levels in NICUs adversely affect long-term outcomes in high-risk infants. (67) Infants frequently are exposed to noise levels of 55 and 75 dB(A) SPL, comparable to the noise produced by a vacuum cleaner. Impulsive noises in the NICU reach well over 100 dB(A), (68) comparable to the noise produced by a power mower.

Although NICU noise levels are greater than recommended by the American Academy of Pediatrics (AAP) and greater than in intrauterine or home environments, they are below those known to induce hearing loss in adults. (69) However, it is unlikely that noise thresholds that induce hearing loss in adults apply to newborns for at least three reasons: 1) there are striking developmental differences in the sound energy transmitted into the cochlea due to growth and development of the outer and middle ears, as reviewed previously; 2) the cochlea (the site of lesion for noise-induced hearing loss) is maturing structurally and functionally while the preterm infant is in the NICU; and 3) the preterm infant experiences a variety of ototoxic exposures in the NICU. At this time, definitive research that addresses whether NICU noise levels result in hearing impairment is lacking.

Noisy environments cause stress responses in laboratory animals and humans by stimulating the autonomic nervous system. (70)(71) The AAP (67) has expressed concern that noise levels in the NICU elicit stress reactions, including arousal and crying (possibly leading to hypoxia), autonomic changes, and alterations in corticosteroid levels. Reduced room noise has been reported to result in decreased heart rate, less fussiness and crying, and more sleep. (72)(73)

Summary

Results of investigations of auditory development in fetuses and infants suggest that:

- Prior to 20 weeks GA, the cochlear partition does not seem capable of the sound-induced movements that are later responsible for the transduction of sound into neural impulses.
- The first responses to sound are recorded between 20 and 25 weeks PMA in the fetus.
- By approximately 30 weeks GA, the peripheral auditory system is mature enough that the sensitivity and frequency resolution of auditory function is relatively adultlike. By term, newborn sensitivity and frequency resolution is nearly indistinguishable from the adult.
- Small outer ear canals and immaturities in the middle ear in newborns (particularly small, preterm newborns) emphasize high frequencies and attenuate low frequencies.
- Although the neural pathway to the auditory cortex is functional when the cochlea becomes capable of responding to sound, myelination and synaptogenesis continue postnatally.
- The uterine environment is dominated by low-frequency sounds generated internally and externally. High frequencies are filtered by maternal tissue.
- The mother's voice is among the more prominent uterine sounds.

- Because fetuses develop in a fluid environment, their outer and middle ears are not prominently involved in hearing.
- Oxygenation is higher and more variable in the preterm newborn than the fetus. Consequences of increased oxygenation are an increased auditory sensitivity as well as concerns about toxicity to rapidly developing systems.
- Based on few data, nursery policies have shifted to reducing environmental stimulation to preterm newborns more consistent with the fetal experience. (74)(75)(76)

Suggested Link for Background on Sound and Anatomy of the Ear: http://hyperphysics.phy-astr.gsu.edu/hbase/sound/ear.html#c1. This Web site was developed by C.R. Nave, the Department of Physics and Astronomy, Georgia State University.

References

1. Pujol R, Uziel A. Auditory development: peripheral aspects. In: Meisami E, Timiras PS, eds. *Handbook of Human Growth and Developmental Biology, Vol IB*. Boca Raton, Fla: CRC Press, Inc; 1988:109–130

2. Romand R, ed. *Development of Auditory and Vestibular Systems 2*. Amsterdam, New York: Elsevier; 1992

3. Canlon B, Anniko M. The postnatal development of stimulated deoxyglucose uptake into the mouse cochlea and the inferior colliculus. *Arch Otorhinolaryngol*. 1987;244:273–277

4. Pujol R, Calier E, Lenoir M. Ontogenetic approach to inner and outer hair cell functions. *Hear Res*. 1980;2:423–430

5. Rubel EW, Ryals BM. Development of the place principle: acoustic trauma. *Science*. 1983;219:514–516

6. Keefe DH. Effect of external and middle ear characteristics on otoacoustic emissions. *International Symposium on Otoacoustic Emissions*. May 9–11, 1991

7. Kostovic I, Rakic P. Cytology and time of origin of interstitial neurons in the white matter in infant and adult human and monkey telecephalon. *J Neurocytol*. 1980;9:219–242

8. Chi JG, Dooling EC. Gyral development of the human brain. *Ann Neurol*. 1977;1:86–93

9. Yakovlev PI, Lecours A-R. The myelogenetic cycles of regional maturation of the brain. In: Minkowski A, ed. *Regional Development of the Brain Early in Life*. Oxford, England: Blackwell Scientific Publishers; 1967:3–64

10. American Academy of Pediatrics Committee on Environmental Health. Noise: a hazard for the fetus and newborn. *Pediatrics*. 1997;100:724–727

11. Erenberg A, Lemons J, Sia C, Trunkel D, Ziring P. Newborn and infant hearing loss: detection and intervention. American Academy of Pediatrics Task Force on Newborn and Infant Hearing, 1998–1999. *Pediatrics*. 1999;103:527–530

12. Hack M, Wilson-Costello D, Friedman H, Taylor GH, Schluchter M, Fanaroff AA. Neurodevelopment and predictors of outcomes of children with birth weights of less than 1000 g: 1992–1995. *Arch Pediatr Adolesc Med*. 2000;154:725–731

13. Vohr BR, Wright LL, Dusick AM, et al. Neurodevelopmental and functional outcomes of extremely low birth weight infants in the National Institute of Child Health and Human Development Neonatal Research Network, 1993–1994. *Pediatrics*. 2000;105:1216–1226

14. Doyle LW, Keir W, Kitchen WH, Ford GW, Rickards AL, Kelly EA. Audiologic assessment of extremely low birth weight infants: a preliminary report. *Pediatrics*. 1992;90:744–749

15. Hollien H, Feinstein S. Contribution of the external auditory meatus to auditory sensitivity underwater. *J Acoust Soc Am*. 1975;57:1488–1492

16. Gerhardt KJ, Huang X, Arrington KE, Meixner K, Abrams RM, Antonelli PJ. Fetal sheep in utero hear through bone conduction. *Am J Otolaryngol*. 1996;17:374–379

17. Birnholtz JC, Benacerraf BR. The development of human fetal hearing. *Science*. 1983;222:516–518

18. Hepper PG, Shahidullah BS. Development of fetal hearing. *Arch Dis Child Fetal Neonatal Ed*. 1994;71:F81–F87

19. Lecanuet JP, Schaal B. Fetal sensory competencies. *Eur J Obstet Gynecol Reprod Biol*. 1996;68:1–23

20. Robinson DW, Dadson RS. A re-determination of the equal loudness relations for pure tones. *Br J Appl Phys*. 1956;7:166–181

21. Berger H. Re-examination of the low-frequency (50–1000 Hz) normal threshold of hearing in free and diffuse sound fields. *J Acoust Soc Am*. 1981;70:1635–1645

22. Corso JF, Levine M. Pitch-discrimination at high frequencies by air- and bone-conduction. *Am J Psychol*. 1965;78:557–566

23. Shahidullah S, Hepper PG. Frequency discrimination by the fetus. *Early Human Dev*. 1994;36:13–26

24. DeCasper AJ, Fifer WP. Of human bonding: newborns prefer their mothers' voices. *Science*. 1980;208:1174–1176

25. Moon CM, Fifer WP. Evidence of transnatal auditory learning. *J Perinatol*. 2000;20:S36–S43

26. Fifer WP, Moon CM. The effects of fetal experience with sound. In: Lecanuet J-P, Krasnegor NA, Fifer WP, Smotherman WP, eds. *Fetal Development: A Psychobiological Perspective*. New York, NY: Erlbaum; 1995:351–366

27. DeCasper AJ, Prescott PA. Human newborns' perception of male voices: preference, discrimination, and reinforcing value. *Dev Psychobiol*. 1984;17:481–491

28. Molfese DL, Freeman RB Jr, Palermo DS. The ontogeny of brain lateralization for speech and nonspeech stimuli. *Brain Lang*. 1975;2:356–368

29. Henderson D, Subramaniam M, Boettcher FA. Individual susceptibility to noise-induced hearing loss: an old topic revisited. *Ear Hear*. 1993;14:152–168

30. Gerhardt KJ, Pierson LL, Huang X, Abrams RM, Rarey KE. Effects of intense noise exposure on fetal sheep auditory brain stem response and inner ear histology. *Ear Hear*. 1999;20:21–32

31. Shaw EAG. Transformation of sound pressure level from the free field to the eardrum in the horizontal plane. *J Acoust Soc Am*. 1974;65:1848–1861

32. Kruger B, Rubin RJ. The acoustic properties of the infant ear. A preliminary report. *Acta Otolaryngol*. 1987;103:578–585

33. Keefe DH, Folsom RC, Gorga MP, Vohr BR, Bulen JC, Norton SJ. Identification of neonatal hearing impairment: ear-canal measurements of acoustic admittance and reflectance in neonates. *Ear Hear*. 2000;21:443–461

34. Keefe DH, Bulen JC, Hoberg Arehart K, Burns EM. Ear-canal impedance and reflection coefficient in human infants and adults. *J Acoust Soc Am*. 1993;94:2617–2638

35. Weitzman ED, Graziani LJ. Maturation and topography of the auditory evoked response in premature infants. *Dev Psychobiol*. 1968;1:79–89

36. Amin SB, Orlando MS, Dalzell LE, Merle KS, Guillet R. Morphological changes in serial auditory brain stem responses in 24 to 32 weeks' gestational age infants during the first week of life. *Ear Hear*. 1999;20:410–418

37. Starr A, Amlie RN, Martin WH, Sanders S. Development of auditory brainstem potentials. *Pediatr*. 1977;60:831–839

38. Pasman JW, Rotteveel JJ, de Graaf R, Stegeman DF, Visco YM. The effect of preterm birth on brainstem, middle latency and cortical auditory evoked responses (BMC AERs). *Early Hum Dev*. 1992;31:113–129

39. Ponton CW, Eggermont JJ, Coupland SG, Winkelaar R. Frequency-specific maturation of the eighth nerve and brain-stem auditory pathway: evidence from derived auditory brain-stem responses (ABRs). *J Acoust Soc Am*. 1992;91:1576–1586

40. Lasky RE, Yang E. Methods for determining auditory evoked brainstem response thresholds in human newborns. *Electroencephalogr Clin Neurophysiol*. 1986;65:276–281

41. Lasky RE. The effects of rate and forward masking on human adult and newborn auditory evoked brainstem response thresholds. *Dev Psychobiol*. 1991;24:51–64

42. Moore JK, Perazzo LM, Braun A. Time course of axonal myelination in the human brainstem auditory pathway. *Hear Res*. 1995;87:21–31

43. Ponton CW, Moore JK, Eggermont JJ. Auditory brain stem response generation by parallel pathways: differential maturation of axonal conduction time and synaptic transmission. *Ear Hear*. 1996; 17:402–410

44. Pratt H, Ben-David Y, Peled R, Podoshin L, Scharf B. Auditory brain stem evoked potentials: clinical promise of increasing stimulus rate. *Electroencephalogr Clin Neurophysiol*. 1981;51:80–90

45. Lasky RE. A developmental study on the effect of stimulus rate on the auditory evoked brain-stem response. *Electroencephalogr Clin Neurophysiol*. 1984;59:411–419

46. Lasky RE, Rupert A, Waller M. Reproducibility of auditory brainstem evoked responses as a function of the stimulus, scorer, and subject. *Electroencephalogr Clinl Neurophysiol*. 1987;68:45–57

47. Lasky RE, Perlman J, Hecox K. Maximum length sequence auditory evoked brainstem responses in human newborns and adults. *J Am Acad Audio*. 1992;3:383–389

48. Jiang ZD, Brosi DM, Wilkinson AR. Immaturity of electrophysiological response of the neonatal auditory brainstem to high repetition rates of click stimulation. *Early Hum Dev*. 1998;52:133–143

49. Abdala C. A developmental study of distortion product otoacoustic emission (2f1 – f2) suppression in humans. *Hearing Res*. 1998;121:125–138

50. Lasky RE. Distortion product otoacoustic emissions in human newborns and adults: I. Frequency effects. *J Acoust Soc Am*. 1998a; 103:981–991

51. Lasky RE. Distortion product otoacoustic emissions in human newborns and adults: II. Level effects. *J Acoust Soc Am*. 1998b;103: 992–1000

52. Abdala C, Sininger YS. The development of cochlear frequency resolution in the human auditory system. *Ear Hear*. 1996;17: 374–385

53. Eggermont JJ, Brown DK, Ponton CW, Kimberley BP. Comparison of distortion product otoacoustic emission (DPOAE) and auditory brain stem response (ABR) traveling wave delay measurements suggests frequency-specific synapse maturation. *Ear Hear*. 1996;17:386–394

54. Furst M, Bresloff I, Levine RA, Merlob PL, Attias JJ. Interaural time coincidence detectors are present at birth: evidence from binaural interaction. *Hearing Res*. 2004;187:63–72

55. Kuhl PK. A new view of language acquisition. *Proc Natl Acad Sci USA*. 2000;97:11850–11857

56. Simos PG, Molfese DL. Electrophysiological responses from a temporal order continuum in the newborn infant. *Neuropsychologia*. 1997;35:89–98

57. Tin W, Wariyar U. Giving small babies oxygen: 50 years of uncertainty. *Semin Neonatol*. 2002;7:361–367

58. Metcalfe J, Bartels H, Moll W. Gas exchange in the pregnant uterus. *Physiol Rev*. 1967;47:782–838

59. Sohmer H, Geal-Dor M, Weinstein D. Human fetal auditory threshold improvement during maternal oxygen respiration. *Hear Res*. 1994;75:145–150

60. Querleu D, Renard X, Versyp F, Paris-Delrue L, Crepin G. Fetal hearing. *Eur J Obstet Gynecol Reprod Biol*. 1988;28:191–212

61. Richards DS, Frentzen B, Gerhardt KJ, McCann ME, Abrams RM. Sound levels in the human uterus. *Obstet Gynecol*. 1992;80: 186–190

62. Gerhardt KJ, Abrams RM. Fetal exposure to sound and vibroacoustic stimulation. *J Perinatol*. 2000;20;S20–S29

63. Peters AJ, Gerhardt KJ, Abrams RM, Longmate JA. Three-dimensional intraabdominal sound pressures in sheep produced by airborne stimuli. *Am J Obstet Gynecol*. 1993;169:1304–1315

64. Gerhardt KJ, Otto R, Abrams R, Colle JJ, Burchfield DJ, Peters A. Cochlear microphonics recorded from fetal and newborn sheep. *Am J Otolaryngol*. 1992;13:226–233

65. Griffiths SK, Brown WS, Gerhardt K, Abrams R, Morris RJ. The perception of speech sounds recorded within the uterus of a pregnant sheep. *J Acoust Soc Am*. 1994;96:2055–2063

66. Smith SL, Gerhardt KJ, Griffiths SK, Huang X, Abrams RM. Intelligibility of sentences recorded from the uterus of a pregnant ewe and from the fetal inner ear. *Audiol Neurootol*. 2003;8:347–353

67. American Academy of Pediatrics, Committee on Environmental Hazards. Noise pollution: neonatal aspects. *Pediatrics*. 1974;54: 476–479

68. Bess FH, Peek BF, Chapman JJ. Further observations on noise levels in infant incubators. *Pediatrics*. 1979;63:100–106

69. Kryter KD. *The Effects of Noise on Man*. New York, NY: Academic Press, Inc; 1970

70. Cantrell RW. Physiological effects of noise. *Otolaryngol Clin North Am*. 1979;12:537–549

71. Kam PC, Jam AC, Thompson JF. Noise pollution in the anaesthetic and intensive care environments. *Anaesthesia*. 1994;49: 982–986

72. Fajardo B, Browning M, Fisher D, Paton J. Effect of nursery environment on state regulation in very low-birth infants. *Infant Behav Dev*. 1990;13:287–303

73. Strauch C, Brandt S, Edwards-Beckett J. Implementation of a quiet hour: effect on noise levels and infant sleep states. *Neonatal Network*. 1993;12:31–35

74. Symington A, Pinelli J. Developmental care for promoting development and preventing morbidity in preterm infants (Cochrane review). *The Cochrane Library*. Issue 2, 2001. Oxford, England: Update Software.

75. Als H, Lawhon G, Brown E, et al. Individualized behavioral and environmental care for the very low birth weight preterm infant at high risk for bronchopulmonary dysplasia: neonatal intensive care unit and developmental outcome. *Pediatrics.* 1986;78:1123–1132

76. Als H, Gilkerson L, Duffy FH, McAnulty GB, et al. A three-center, randomized, controlled trial of individualized developmental care for very low birth weight preterm infants: medical, neurodevelopmental, parenting, and caregiving effects. *J Dev Behav Pediatr.* 2003;24:399–408

NeoReviews Quiz

6. Compared to adults, fetuses only hear environmental sounds that are relatively loud. They are especially insensitive to high-frequency sounds. Of the following, the *best* description of newborn hearing is that:

   A. Preterm newborns are much less responsive to external sounds than fetuses of the same age.
   B. Newborns respond to external sounds similarly to fetuses of the same age.
   C. Newborn hearing is nearly as sensitive as adult hearing except the anatomy of newborn ears emphasizes high-frequency sounds.
   D. Newborn hearing is similar to that of the adult except for accentuation of low-frequency sounds.
   E. Newborn hearing is comparable to that of the adult.

7. In the absence of external sounds, the uterine sound environment is dominated by low-frequency maternal noises. Of the following, the *most* pervasive uterine sound is generated by maternal:

   A. Body movement.
   B. Heartbeat.
   C. Peristalsis.
   D. Respiration.
   E. Speech.

8. Human hearing ranges from 20 to 20,000 Hz, with the greatest sensitivity in the range of 1,000 to 4,000 Hz. The fetal response to external sounds in this frequency range has been examined by real-time ultrasonography to define the timeline for functional development of hearing during fetal life in humans. Of the following, the *earliest* gestational age at which the human fetus responds to tones in the frequency range of 1,000 to 4,000 Hz is:

   A. 15 weeks.
   B. 20 weeks.
   C. 25 weeks.
   D. 30 weeks.
   E. 35 weeks.

9. Auditory brainstem evoked response (ABR) has been studied in preterm neonates to characterize the generation of waves III (generated from the cochlear nucleus) and V (generated from the lateral lemniscus). Of the following, the *earliest* gestational age at which the waves III and V can be identified reliably by ABR in human preterm neonates is:

   A. 24 weeks.
   B. 26 weeks.
   C. 28 weeks.
   D. 30 weeks.
   E. 32 weeks.

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