Paparella: Volume I: Basic Sciences and Related Principles

Section 1: Embryology and Anatomy

Part 1: Ear

Chapter 1: Embryology of the Ear

Developmental Anatomy of the Ear

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Evolution of the Ear

The phylogeny of the three parts of the mammalian ear, recapitulated in abbreviated form during individual embryologic development, provides insight into the significance and relationship of the parts. In the cartilaginous or elasmobranch fishes, which include the sharks and rays, the inner ear is contained within the cartilaginous otic capsule, which protects it from injury. There are three semicircular canal, each provided with ampullae and otolith organs for the detection of angular changes in the position of the head. The utricle and saccule, each containing otolith organs, respond to the gravitational forces acting upon the head. In addition, there is a short diverticulum of the saccule, the lagena, which may be the forerunner of the cochlea in mammals. In the cartilaginous fishes it contains sensory receptors that appear to show maximum electrical activity in the normal or neutral position of the head. Hearing may also be present over limited frequencies. These fishes have no middle ear. Behind the ear is a pit, the spiracular cleft, which communicates deeply with the pharynx, and in some forms there is a dorsal diverticulum of the spiracular canal that makes contact with ventrolateral surface of the otic capsule near the horizontal semicircular canal; it may transmit vibrations in the water. A specialized sensory or neuromast organ in the spiracular canal leaves no doubt that the spiracular canal is formed by an invagination of the surface skin in the region of the so-called lateral line. The lateral line runs along the lateral side of the fish on either side and contains depressed pits with sensory neuromast receptors; these are supplied from cranial to caudal ends by the facial, glossopharyngeal, and vagus nerves. The labyrinth of the inner ear is derived embryologically by an invagination of the surface ectoderm, forming first a placode, then a pit, and finally a vesicle, cut off from the surface, which establishes neural relationships with the acoustic or eight cranial nerve. The composition of the upper and lower jaws with their articulations in the cartilaginous fishes furnishes evidence for the origin of the mammalian ossicles. The upper jaw, the palatoquadrate bar, articulates with the articular, which is part of the lower jaw or meckelian cartilage. There is evidence that the malleus is derived from the articular, the incus from the quadrate, and the stapes from a part of the second or hyoid arch.

In the bony fishes or teleosts, the skull is ossified as dermal or membrane bones around the primitive chondrocranium, which includes the now ossified periotic capsule lodging the inner ear structures. The inner ear resembles that of the cartilaginous fishes, although the saccule, the utricle, and a diverticulum of the latter (the lagena) are conspicuous. The lagena contains hair cells with a gelatinous capsule, as do the utricle and saccule; it may be sensitive to vibrations and be a forerunner of the cochlea of mammals. In some teleosts, there is a series of three weberian ossicles extending from the perilymphatic space to the swim bladder. These may be homologous to the malleus, incus, and stapes and perhaps transmit vibrations. The relationship between the swim bladder and inner ear affects auditory sensitivity and range. In some fishes, hearing may be well developed.

In the amphibians, a middle ear and tympanic membrane are present, although the former is degenerate in certain burrowing forms. In addition to the semicircular canals, the inner ear comprises a saccule, utricle, and lagena as in the fishes. The middle ear is funnel-like and is closed externally by the tympanic membrane. Sound is transmitted to the inner ear by a rod of bone, the columella, which consists of an outer segment, derived from the hyoid arch and homologous to the quadrate, and an inner expanded part, the otostapes, which is lodged in the fenestra ovalis. Specializations of the columella, some of the processes of which may be homologous with the mammalian ossicles, are beyond the scope of this discussion. Some of the amphibians, particularly the nontailed anurans, are capable of excellent hearing. Some burrowing, tailed amphibians have connections between the columella or related structures and the scapula, which may transmit vibrations from the forelimbs.

In the reptiles, a sunken tympanic membrane is usually found behind the jaw. The columellar system, with many specializations, is also found, and hearing is excellent, especially in the crocodiles and certain lizards. In the birds, which have acute hearing, the cochlea appears as a short, tubular, noncoiled structure, the basilar papilla. The lagena is carried on its tip. The basilar papilla is sensitive to a wide range of frequencies, usually between 100 and 500 Hz but in some species up to 12 kHz. The lagena may be responsive to very low frequencies. Vibrations are again carried from a tympanic membrane to the fenestra ovalis by a columella derived from the hyoid arch; it is expanded medially as a stapes. A secondary tympanic membrane compensates for internal pressures in the endolymph.

In all mammals, the three ossicles are present. The incudomalleal joint is considered to be a modified articulation between the quadrate and the articular of the meckelian cartilage. From the mesenchymal condensation posterior to the first gill pouch are developed a dorsal columella and a ventral portion, which is part of the hyoid suspensory apparatus. A proximal part of the columella is differentiated as the stapes. In the adult stages of some mammals and in the embryonic stages in humans, a branch of the second or hyoid arch artery passes through the stapedial condensation, termed the stapedial artery. This may persist in the adult and give rise to bleeding during surgery in the region of the stapes. The middle ear is clearly a diverticulum of the pharynx, involving at least the first pharyngeal pouch, and in the human part of the second pouch also. The origin of the tympanic membrane is unclear. It is certainly not homologous with the spiracular area os fishes but is developed ontogenetically as a placodal thickening of the upper end of the first external branchial or gill cleft. Although there is a progressive increase in complexity of the cochlear area culminating in the coiled structure of higher vertebrates, the inner ear is a highly conservative organ phylogenetically. The semicircular canals, the utricle, and the saccule, along with their surrounding periotic capsule of cartilage or bone (petrous bone), are present in all vertebrates and reflect the importance to the organism of obtaining information from the environment to establish position and to make appropriate adjustments for the apprehension of prey. The auricular branch of the vagus in the human (Arnold's nerve), which issues from the tympanomastoid fissure and supplies purely somatic structures such as the drum and the external ear canal, may be a relic of the lateral line system of aquatic vertebrates. The chorda tympani, although presenting some difficulties in relation to its position with respect to the middle ear, is generally considered a pretrematic (anterior to the gill slit) branch of the nerve of the second branchial arch (facial); its involvement in taste in mammals is of interest.

Development of the Ear

The arrangement of the pharyngeal (branchial) arches in the floor of the mouth in young embryos of about 4 mm is shown in Figure 15, Chapter 3. At a somewhat later stage (Fig. 1) the tubotympanic recess is demarcated from the midline structures by the lateral expansion of the pharyngeal lumen opposite the first, second and third arches. The tubotympanic recess is partially constricted medially by the forward migration of the third arch into the base of the tongue (see arrows in Fig. 1).

The tubotympanic recess forms an expanded cavity that contains the lateral extensions of the first, second, and third arches as well as the intervening endodermal pouches (first and second). The lateral part of the tubotympanic recess becomes the middle ear, and the connecting passage between it and the midline structures of the pharynx becomes the pharyngotympanic or eustachian tube. Since the third arch bounds the eustachian tube posteriorly, the artery of this arch (the internal carotid) comes to lie posterior to the tube in the adult. The artery then passes forward above the tube as the forward continuation of the dorsal aorta (see Chap. 3, Fig. 8).

The external auditory meatus develops as a thickening of the ectoderm at the upper end of the first external pharyngeal cleft (see Chap. 3, Fig. 5). The floor of the groove sinks into the underlying mesoderm as a cylindric meatal plug (Fig. 1), which becomes applied to the lateral wall and floor of the expanded end of the tubotympanic recess. Contact with the tubotympanic recess is made in such a way that when the drum is formed at the interface between the ectodermal and endodermal surfaces it lies obliquely, and such that the roof and anterior wall of the external auditory canal are shorter than the floor and posterior wall. The ectodermal meatal plug then hollows out to form a canal in which hair follicles and ceruminous glands develop. The "drum area" or tympanic membrane is the circular area of the contact between the meatal plug and the endoderm of the tubotympanic recess.

Further Development of the Tubotympanic Recess, Otic Capsule, and Cartilages of the First Two Arches

The otic capsule is the cartilaginous mass that encloses the inner ear and that later forms the petrous temporal bone. It lies above the lateral extremity of the tubotympanic recess, as shown in Figure 2A. The cartilage of the first arch (Meckel's cartilage) lies anterior to the tubotympanic recess; the cartilage of the second arch (Reichert's cartilage) lies behind it. The two cartilages soon become joined by fibrous, later cartilaginous, condensations or roof processes above the tubotympanic recess, between it and the overlying otic capsule (Fig. 2A). The roof processes differentiate into the body of the malleus and incus. Later, processes of the two ossicles form the long and short processes of the incus and also the anterior and inferior processes (handle) of the malleus. The handle of the malleus projects downwards, later to the tubotympanic recess, and is later trapped between it and the meatal plug (Fig. 1).

The tegmen tympani is formed as a flange growing out from the otic capsule and passing above and anterior to the tubotympanic recess (Fig. 2B). It forms the roof and anterior bony wall of the tubotympanic recess. The mandibular cartilage escapes under the free edge of the tegmen tympani (Fig. 2B) to enter the lower jaw. In a later stage (Fig. 2C), the otic capsule and the tegmen tympani become overlaid laterally by a sheet of membrane or dermal bone, the squamous temporal bone. The squamous temporal bone eventually overgrows the petrous temporal bone except for the mastoid process and free edge of the tegmen tympani in relation to the floor of the temporomandibular fossa (Fig. 2C and D). The upper part of Meckel's cartilage, as mentioned earlier, forms the malleus and the incus, with their various bony processes. The rest of Meckel's cartilage becomes transformed into the anterior ligament of the malleus and the sphenomandibular ligament (Fig. 2D). The further development of the ossicles is illustrated in Figures 3 and 4.

The tympanic ring is formed in membrane around the drum where the meatal plug and the tubotympanic recess are in contact. At birth (Fig. 2C), the ring is present but has not as yet become elongated into a definite bony meatus. As a result, the drum is very superficial in a baby and is easily injured by forceps or instrumental examination. The mastoid process is also absent at birth so that the facial nerve emerging from the stylomastoid canal is superficial and easily injured by the use of obstetric forceps. The tympanic ring extends after birth by further intramembranous ossification. The new bone is added laterally so that a bony meatus is developed, the drum being at its medial or deep end (Fig. 2D). As the bony external auditory meatus is established, the formation of the temporomandibular fossa and its complex fissures is also complete (Figs. 5 and 6). The fissure (gasserian fissure), which lies in the floor of the temporomandibular fossa, is compound. Laterally, it lies between the squamous temporal and the tympanic bone (squamotympanic fissure). Medially the squamotympanic fissure is subdivided by the interpolation of the free edge of the tegmen tympani (now a portion of the petrous temporal bone)(Figure 7). The fissure thus becomes the petrosquamous fissure anteriorly and the petrotympanic fissure posteriorly. From the fact of the development of the tegmen tympani, it can be seen that any structure escaping from the middle ear (eg Meckel's cartilage, chorda tympani nerve) must leave under cover of the tegmen tympani, that is, through the petrotympanic fissure (Fig. 5). The capsule of the temporomandibular joint is attached along the gasserian fissure. The fossa posterior to this is occupied by a process of the parotid gland and also contains the auriculotemporal nerve in close apposition to the capsule of the joint (Chap. 3, Fig. 23).

The second arch cartilage (Reichert's) gives rise to the styloid process, the stylohyoid ligament, the lesser cornu bone and the upper part of the body of the hyoid bone (Fig. 3). The stapes may be derived from the condensation at the upper end of Reichert's cartilage. There is evidence that the stapes ossifies in connection with the otic capsule. The form of the stapes is determined by the passage of the stapedial artery through the preosseous condensation of the ossicle. This vessel may represent the upper end of the second pharyngeal arch artery (Chap. 3, fig. 8).

Development of the Drum

The tympanic membrane or drum develops at the area of contact between the ectodermal meatal plug and the endodermal tubotympanic recess (Figs. 1 and 8A). The contact is oblique, so that the drum lies obliquely with respect to the axis of the external meatus. The chorda tympani nerve, the handle of the stapes, and a layer of mesoderm are trapped between the meatal plug and the tubotympanic recess (Fig. 8A). Thus, the drum consists of three layers: an outer ectodermal layer continuous with the skin of the external auditory meatus, an intermediate mesodermal layer containing the handle of the malleus and the chorda tympani nerve, and an inner endodermal layer continuous with the mucous membrane of the middle ear. The nerve supply of the drum reflects its origin. The ectodermal (outer) surface is supplied by the auriculotemporal branch of the trigeminal nerve and by the auricular branch of the vagus (Arnold's nerve) posteriorly. The last nerve is of interest in that it is the only somatic afferent branch of the vagus nerve. It may represent the last remnant of a once extensive system in lower vertebrates, including the lateral line system of fishes. The same nerves that supply the drum also supply the external auditory meatus. Irritation of the auricular branch of the vagus nerve may cause reflex coughing or vomiting; hence, its former name, the "alderman's nerve". Foreign bodies in the ear may, therefore, simulate thoracic conditions, and syringing of the external ear in elderly patients may cause fatal syncope. The afferent connections of the auricular branch of the vagus are uncertain; there is evidence that they pass to the nucleus of the spinal tract of the trigeminal nerve.

Postnatal Developments in the Ear

The four elements of the temporal bone at birth are easily distinguished: the petrous (including the tegmen tympani), the squamous temporal bone, the tympanic ring, and the styloid process. The mastoid antrum is present as a posterior extension of the middle ear, but there is no mastoid process. The mastoid process does not form a definite prominence until the end of the second year, and the mastoid air cells follow soon after. The tympanic ring extends laterally after birth, forming the bony canal. The temporomandibular fossa is small and faces more laterally at birth; thereafter it becomes deeper and faces more ventrally. Ossification of the petrous temporal bone is complex and is derived from multiple centers. Being phylogenetically ancient, the petrous bone (otic capsule) rarely shows developmental abnormalities. At birth, the middle ear cavity does not extend beyond about the origin of the handle of malleus from the body. Above this level the epitympanic recess or attic is occupied by gelatinous mesenchymatous material or epitympanic tissue. This tissue is very susceptible to infection and may also impede the movement of the ossicles at first. There is a progressive extension of the middle ear cavity during the first year at the expense of this epitympanic tissue. This extension takes place by a process of cavitation and differentiation so that the cavity extends dorsally to envelop the ossicles completely. When this extension is complete, the attic region forms a complicated labyrinth of mucosal spaces and recesses (i.e., pouches of Troltsch, pouch of Prussak). The ossicles develop outside the tympanic cavity. They are extramucosal but are secondarily incorporated into the tympanic cavity by the formation of the attic recesses. The superior ligaments of the malleus and the incus are the remnants of the original epitympanic tissue in which the ossicles were once embedded. The secondary mucosal extension also takes place around the stapes, the tendons of the stapedius and of the tensor tympani muscles, and all other intratympanic structures so that these also are extramucosal, though technically they are within the middle ear cavity (Fig. 10).

Development of the Inner Ear

The inner ear is developed as a thickening or placode of the ectoderm on the lateral surface of the head at the level of the fourth ventricle in embryos of 4 mm (Fig. 11A). The placode then sinks in, forming first a pit, then a vesicle cut off from the surface (Fig. 11B and C). The dorsal otocyst produces the semicircular canals and cristae. The ventral portion differentiates into cochlear structures. The endolymphatic duct originates from the dorsal surface in embryos of 6 mm (Fig. 11C and D). The semicircular canals appear in embryos of 15 mm and 37 days (Fig. 11D) as flanges protruding from the surface of the otocyst. The walls of the flanges then come into contact centrally where they break down, giving rise to canals that are well developed by the 30 mm stage (Fig. 11E). The anterolateral and posterior canals originate from the dorsoanterior, dorsolateral, and dorsoposterior portions of the otocyst respectively. The cochlea appears in the 15 mm stage (Fig. 11D) as a diverticulum at the lower pole of the otocyst. It coils progressively, finally attaining two and three quarter turns by the end of the embryonic period (end of third month). The coiling is time dependent and is probably a result of epidermal-mesenchymal interaction. The otocyst becomes constricted at its middle between the part bearing the semicircular canals and that bearing the cochlea. The saccule is derived from the middle anterior part of the otocyst and the utricle from the middle of the otocyst (Fig. 11F). The endolymphatic duct becomes shifted down by differential growth onto the connection between the utricle and the saccule, so that it is ultimately attached to the utriculosaccular duct. More details of the development of the labyrinth are shown in Figure 12.

Macculae and Otolithic Membrane

The medial and lateral walls of the ectodermal epithelium of the otocyst contribute to the sensory structures of the vestibular labyrinth. The maculae of utricle and sacculae originate from the anterior middle third of the otocyst.

Epithelial differentiation occurs in areas where the nerves enter the wall of the saccule and utricle (Fig. 13). In these zones, the epithelium becomes modified into a complex pseudostratified layer. Two types of cells are present. Sensory cells possess stereocilia, which differentiate them from the supporting cells, which bear microvilli. The supporting cells secrete a gelatinous substance that forms a cushion-like otolithic membrane. The membrane overlies the modified epithelium and bears superficial calcareous deposits, the otoconia.

Differentiation begins between the seventh and eight weeks of fetal life. The formation of the gelatinous layers follows that of the otoconia. By the 10th to 12 the week, the distinctive types of cells are apparent and the otolithic membrane is being formed. In fetuses of 14 to 16 weeks of age, the individual parts of the maculae appear to be well formed and are similar to those seen in the adult.

Cristae and Cupula

The sensory epithelium of the cristae is modified from primitive epithelial precursors similar to macular differentiation. The cristae are distinguishable in a fetus of 8 weeks as a mound-like elevation (Fig. 14A). The cristae attain virtually adult structure and size in the fetus of 23 weeks. Maturation of the cupula parallels that of the sensory stereocilia. In the adult, ciliary bundles insert into cupular tubules. At 26 weeks, each sensory hair cell bundle appears to be within a cupular tubule.

Otic Capsule

Concurrently with the differentiation of the maculae and cristae, the surrounding mesenchymal tissue of the fetus of 10 weeks (Fig. 14B) becomes the cartilaginous labyrinthine wall and periotic tissue of the 15-week stage (Fig. 14C). The dependency of the periotic mesenchyme on the otocyst for its formation into the otic capsule is well established. The experimental ablation of the otocyst during development results in the absence of the otic capsule. In some mammals, the otocyst acts as an inductor of stria capsule formation as early as 11.5 to 13 embryonic days. Thereafter, the capsule undergoes chondrogenesis in the absence of the otocyst's inductive influences.

Organ of Corti

The sensory end-organ in the cochlear duct develops from the epithelium along the posterior wall where the cochlear nerve fibers enter it (Fig. 15). Like the maculae and cristae, the spiral organ appears in early fetal life and attains adult proportions by midterm. Already in the placodal state, and also in the vesicle stage, the epithelium is stratified. This stratification is still a well-defined feature in the 8th-week-old fetus; in the anterior wall of the duct, however, it is much thinner than in the posterior and lateral walls. The other parts of the cochlea begin to differentiate at the beginning of the eight week; these elements are the surrounding otic capsule, the centrally placed modiolus, and the tympanic and vestibular scalae. The diameter of these scalae is greater than that of the cochlear duct. The interval is crossed by a spiral shelf *(lamina spiralis ossea)*, which extends from the modiolus between the scalae to the posterior wall of the scala media. As the structures increase in size, the cross-sectional form of the cochlear duct changes from rounded (Fig. 15A and B) to oval (Fig. 15B), then finally to triangular. As a result, it comes to have three walls - anterior, posterior, and outer (Fig. 15D). The anterior wall fuses with that of the scala vestibuli to form Reissner's membrane. The posterior wall merges with the wall of the scala tympani to form the basilar membrane; the outer wall rests on the spiral ligament; the inner angle of the cochlear duct is attached to the anterior surface of the osseous spiral lamina near the free margin of the latter.

With further growth of these structures, the epithelial duct becomes gradually modified. Along the anterior wall, in the area of the future Reissner's membrane, it loses its stratification and becomes a simple columnar epithelium in the 11-week fetus. At 14 weeks, this epithelium is cuboidal. Soon thereafter it flattens into a simple squamous type and continues so throughout the life. The epithelium along the outer wall becomes modified in such a way as to resemble a glandular epithelium. The epithelial layer covers a vascular connective tissue, the *stria vascularis*, which in turn rests on the spiral ligament. The epithelium of the posterior wall (which is the basilar membrane) becomes highly modified into the spiral organ of Corti and the tectorial membrane.

Much of what is known regarding proliferation of cells in the organ of Corti has been determined by observation of animal models. In the mammal, the majority of cell types undergo proliferation synchronously. Thus the sensory cells, spiral ganglion cells, pillar cells, Deiters' cells, Hensen's cells, Claudius' cells, internal supporting cells, and internal sulcus cells share either a common origin or are regulated by the same inductive process. The exact nature of this process has not been characterized; however, it is known that the presence of nerve fibers from the ganglion cells is necessary for complete differentiation of the hair cells. Differentiation is arrested in the absence of these fibers.

The first cells to complete their terminal mitosis are found near the apex, whereas later dividing cells are distributed at progressively basal locations. Final differentiation of the organ of Corti, however, begins in the basal portion and proceeds apically. Upon close examination, this gradient is not unidirectional; it begins near the middle of the basal turn rather than at the extreme basal end. A developmental precedence of inner hair cell differentiation over that of the outer hair cell is present. Innervation of the inner hair cells also occurs before innervation of the outer hair cells. This period of maximum histologic differentiation also coincides with the onset of auditory function. The developmental synchrony of functionally related cell groups noted above suggests that a functional ontogeny may also be shared.

The epithelium of the organ of Corti does not differentiate into its definitive parts in all cochlear turns until after midterm. The epithelium of the apical turn in a fetus of 11 weeks is a thickened, pseudostratified layer (Fig. 15A). Along the free surface of this epithelium in the apical turn is an ill-defined gelatinous membrane, the tectorial membrane (Fig. 15B). In the basal turn, the epithelium already shows a bulging and loosening of its cells in the region of the outer hair cells. In the 16-week fetus, this condition in the basal turn is more marked, but in the apical turn differentiation has not yet taken place (Fig. 15C). In the same stage, the tunnel of Corti is beginning to appear in the basal turn (Fig. 15D) but not in the apical turn (Fig. 15C). During the succeeding month the organ progressively completes its development toward its apical end, so that in a fetus of 21 weeks, the tunnel of Corti is present in all turns. At about this age or shortly thereafter, the internal ear attains its maximum size and becomes completely encased in its bony capsule. In the fetus of 25 weeks, the spiral organ closely resembles that of the adult. The disposition of the parts of the ear at birth are shown in Figure 16.

Development of the Nerve Supply

Classical opinion held that the cochleovestibular ganglion is of neural crest origin. A second theory that cites the ectoderm of the otic placode as the primordium in mammals is supported by conclusive evidence that such a relationship exists in amphibians. A similar view that the cochlea and vestibular ganglion in the human are also of placodal origin is not generally accepted.

Nerve fibers, presumably distal processes of ganglion cells, are present in the otic vesical as early as 4.5 weeks of gestation. On the other hand, synaptic terminals are not present until just prior to cochlear function at 6 to 7 months. It appears, therefore, that the peripheral processes of ganglion cells play a role in cochlear differentiation before the synapses develop. Nerve fibers are necessary for hair cell differentiation, and where the fibers are absent, organ of Corti development is arrested. The pattern of organ of Corti innervation parallels the order of differentiation; the development proceeds from basal to apical and the inner hair cells are innervated before the outer hair cells. It appears that the ganglion cells play an important regulatory or determinative role in the differentiation of the organ of Corti. It is equally likely that the differentiating sensory cells influence or direct the pattern of neuronal development. A chemotactic gradient generated by the sensory cells may in theory explain the outgrowth of nerve elements from the cochlear ganglion to the organ of Corti.

Auditory Development

The final morphologic event that establishes the onset of cochlear function has not been clearly identified. Formation of the inner sulcus that establishes the shearing force between the tectorial membrane and the hair cell cilia is an important final step but is probably not uniquely responsible for the onset of hearing. It is more likely that some form of autoregulation that synchronizes growth and development of single or multiple elements is responsible for the rapid maturation of the cochlea. The onset of function is paralleled by a maturation of functionally related tissue, both temporally and with respect to pattern of development. The time of onset and sequence of maturation of cochlear function is subject to species variability.

Regardless of the species considered, the development of hearing begins with low or low-to-moderate frequencies. More specifically in humans, hearing begins in the low-to-mid range frequencies. It follows that if the pattern of hearing development predicts the pattern of receptor organ development, then the apical turn should mature first and the basal turn last. However, as noted above, the gradient of cochlear development is generally from base to apex. It has been hypothesized that this apparent dissociation between ontogeny and function is due to a mismatch in vascular development or retained mesenchymal tissue in the immature ear, resulting in attenuation of high-frequency stimulation. A theory that is perhaps more attractive proposes that the transduction properties of the developing cochlea change as the organism matures, and this becomes manifest in a shift of place code. To this extent, evidence exists that the immature basilar portion of the cochlea responds maximally to low frequencies early in its development and then becomes increasingly responsive to higher frequencies as differentiation proceeds in the basal to apical pattern. A corresponding pattern of response characteristics may also exist more centrally in the auditory neurons.

The morphologic events responsible for the functional changes that occur in the auditory pathways are poorly understood. However, evoked potentials can be recorded concurrently with the onset of cochlear and nerve potentials. In the human, click stimuli evoke cortical potentials at 23 weeks and brain stem potentials at 34 weeks. As the cochlea continues to mature, the evoked increase in amplitude and stimulation thresholds decreases.

Chronology of the Development of the Ear

At Birth

The petrous bone is porous and open in texture. The subarcuate fossa is wide and lodges the paraflocculus of the cerebellum. The hiatus canalis facialis is unclosed and funnel-like and, since the mastoid process is undeveloped, the nerve is very near the surface and vulnerable to injury. The tympanic cavity is filled with gelatinous "epitympanic tissue" resembling mesenchyme. The jugular fossa is shallow. The tympanic annulus is incomplete superiorly, and the external meatus, which consists only of the cartilaginous portion, is shallow.

Summary of the Ossification of the Temporal Bone

The squamous temporal bone arises in membrane from a center about the eight week of fetal life. It then extends into the zygomatic arch. The glenoid fossa is shallow. A platelike extension of the squamous bone overlaps the tympanic antrum.

The periotic capsule (later becoming the petrous bone) ossifies in cartilage from four centers, beginning about the fifth month of fetal life. It consists of porous bone by the sixth month. The four centers are the opisthotic, the pro-otic, the pterotic, and epiotic. The opisthotic begins on the promontory, extends partly around the fenestra ovalis, into part of the internal acoustic meatus, invests the cochlea, and forms a platelike extension around the carotid artery, which makes up the floor of the tympanum. The pro-otic begins behind the internal acoustic meatus, covers part of the cochlea and the remaining circumference of the fenestra ovalis, and invests the superior semicircular canal. The pterotic ossifies the roof of the tympanum (tegmen tympani) and invests the lateral semicircular canal. The epiotic is the last to appear and is frequently double. It begins near the posterior end of the posterior semicircular canal.

After birth, the tympanic ring begins to grow, beginning at the tubercles at the superior end of the incomplete annulus. The two tubercles first fuse laterally, enclosing a foramen between them and the adjacent petrous bone. This foramen may persist in the adult; it remains normally in the adult as a slitlike tympanomastoid fissure through which passes the auricular branch of the vagus. The lateral extension of the tympanic ring forms the tympanic plate in the floor and posterior wall (nonarticular) of the glenoid fossa. Here, it is in relation to a process of the parotid gland interpolated between the tympanic plate and the articular capsule of the temporomandibular joint. The fissure between the tympanic plate and the glenoidal portion of the squamous temporal bone is the squamotympanic fissure. Medially, the tegmen tympani (petrous bone) is interpolated between the squamous bone and the tympanic plate, thus dividing it into an anterior petrosquamous and a posterior petrotympanic fissure. Through the latter passes the chorda tympani. A further extension of the tympanic plate extends onto the lateral wall of the carotid canal and forms a sheathlike (vaginal) process on the base of the styloid process. The mastoid appears in the first year after birth, and the petrosquamous suture is obliterated. Pneumatization of the mastoid, once thought not to occur until puberty, takes place much earlier and is very variable. The antrum is relatively large at birth and is bounded laterally by the squamous bone in the area of the suprameatal triangle (Macewen's). It becomes deeper as the external acoustic canal is deepened and the mastoid process forms, also becoming relatively smaller. Pneumatization extends from the mastoid antrum into the epitympanum and hypotympanum, and in some cases, toward the apex of the petrous temporal bone. The styloid process, which is derivative of the second or hyoid arch, ossifies in cartilage in four parts: the tympanohyal, the stylohyal, the ceratohyal, and the basihyal, these parts being primitively found in lower vertebrates. Ossification begins at the base in the tympanohyal before birth and joins the main temporal bone in the second year. The stylohyal center appears in the second year. It may fuse with the tympanohyal, or cartilaginous joint may persist between them. In some cases, the stylohyoid ligament may be partially or completely ossified all the way to the lesser cornu of the hyoid bone, causing difficulties in swallowing. The subarcuate fossa in the posterior surface of the pterygoid pyramid becomes shallow with advancing age, and the paraflocculus is withdrawn; it permits egress to a small subarcuate vein.

Table 1. Development of the Ear

Stage		Age	Developmental Events (Those Relating to the Ear are Italicized)
IX	1.5-2.0 mm	20-22 days	Formation of the neural fold
X	1.5-2.0 mm	20+/-1 days	*Optic placode forming* Primite heart tube laid down Optic sulcus forming in diencephalon
XI	2.0-3.0 mm	24+/-1 days	*Shallow otic pit* Cranial nerve ganglia forming Heart begins to beat Lungs appear Rathke's pouch appears
XII	3.5 mm	26+/-1 days	*Deep otic pit* Optic vesicle contacts ectoderm Heart shows unidirectional flow Thyroid appears Liver appears Arm buds appear
XIII	4.0-5.0 mm	28+/-1 days	*Otocyst cut off from surface*

			Endolymphatic duct appears Heart: partitioning of the atrium Primary lung buds appear. Leg buds appear
XIV	6.0-7.0 mm	28-30 days	*Otic vesicle present* *Well-demarcated endolymphatic duct* *Differential thickening of walls of otic capsule at sites of future cochlea and semicircular ducts* *Acousticofacial ganglion foreshadowed as thickening of anterior wall of otic vesicle* Olfactory placodes appear Heart: interventricular septum appears Urorectal septum appears Glandular outgrowths from gut Fin-like arm and leg buds
XV	7.0-8.0 mm	31-32 days	*Endolymphatic duct elongated and demarcated by groove from sac* *Meatal plug and auricular hillocks forming around first external groove* Cervical sinus of His forming Cerebellum and pineal appear Maxillary, mandibular, and frontonasal growth centers in face Gut extruded into exocoelom Secondary lung buds appear Lens vesicle cut off from surface Ureteric bud simple, no branching Urorectal septum Suprarenal cortex appears
XVI	8.0-11.0 mm	33+/-1 days	*Elongated endolymphatic duct* *Semicircular canals foreshadowed as flanges from otic vesicle* Retina: inner layer becomes three layered, pigment appears Lens vesicle surrounded by tunica vasculosa lentis Olfactory pits deepen Trachea separated from esophagus Omental bursa appears Ureter shows primary branching Indifferent gonad appears
XVII		35+/-1 days	*Walls of semicircular canal flanges fusing*

		preparatory to breakdown
		Cochlear duct appears at lower end of otic vesicle
		Olfactory pit approaches root of mouth
		Müllerian ducts appear
		Ureter shows temporary branching
		Finger rays appear in forelimb
XVIII 14.0-16.0 mm	37+/-1 days	*Pinna is well formed*
		Flanges of semicircular canal show impending central lysis
		Cochlear duct elongated and set off from utriculosaccular portion
		Nerve fibers present in relation to statoacusticus ganglion and labyrinth
		Choroid fissure of optic cup closes
		Optic fibers present but fail to reach diencephalon
		Upper lip forming; eyes face anteriorly
		Secondary and tertiary bronchi present
		Sex determinable
		Chondrification begins in base of skull, limbs and axial skeleton
XIX-XXIII	38-40 days	*Cochlea advances from three quarters turn to full two and three quarters turn*
		Cartilage appears in pinna
		Palatal process of maxilla appears
		Ossification begins in long bones, base of skull, and axial skeleton
		Membranous bone formation begins in dermal bones of face and cranial vault
	7-8 weeks	*Otic capsule becomes cartilaginous*
		Maculae differentiating
	9 weeks	*Tympanic ring beginning to ossify in membrane*
	10 weeks	*Tubotympanic recess forming "drum" with meatal plug*
		Sensory epithelium of inner ear differentiating
		Otoliths present
	15 weeks	*Ossicles become cartilaginous but have reached almost full size*
	16-19 weeks	*Bone appears in malleus and incus (16 weeks), in stapes (19 weeks)*
	22 weeks	*Tympanic ring ossified (incomplete*

	superiorly, not fused with otic capsule)
24 weeks	*Antrum appears*
	Perilymphatic spaces appear
28 weeks	*Mucoid "epitympanic" tissue becoming absorbed with extension of tympanic mucosa*
34 weeks	*Tympanic ring fused with capsule.*