31 Ear

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Introduction

The ear is often involved in intrauterine and neonatal diseases such as congenital anomalies, chromosomal and gene defects, amniotic fluid infection sequence, transplacental infections, maternal-placental and fetal-placental perfusion defects, other causes of fetal hypoxia, congenital tumors, and other diseases. Therefore, histologic examination of the ear should be an important part of the perinatal autopsy. However, because the anatomy of the ear is complex, because the removal and plane of sectioning of the petrous bone are often haphazard, and because the specimen is often fragmented or incomplete, interpretation of routine microscopic sections of the ear is often exasperating and unhelpful. As a consequence, histologic examination of the ear is often neglected in perinatal autopsies. Understanding the anatomy of the ear, standardizing the method of removal and sectioning of the petrous bone, and making examination of the ear a routine part of the perinatal autopsy will make histologic examination of the ear more satisfying and fruitful. The purpose of this chapter is not only to demonstrate the histology of the ear but also persuade the reader that histologic examination of the ear is a worthwhile part of perinatal autopsy.

Anatomy

In Situ Surface Anatomy of the Petrous Bone in the Neonate

The inner and middle ear and part of the external ear lie within the petrous bone. The surface anatomy of the neonatal petrous bone serves two functions for the perinatal pathologist. First, understanding the surface anatomy allows the pathologist to develop a mental picture of the position and relationships of the components of the inner, middle, and external ears within the petrous bone. Second, the surface landmarks provide guideposts for the placement of resection lines for the removal of the petrous bone during the perinatal autopsy. This section describes those surface landmarks.

The petrous bone is an oblong wedge obliquely oriented in the floor of the cranium. When viewed in situ from above in the opened cranium, it presents two surfaces. The superior horizontal surface is the roof of the petrous bone and forms much of the floor of the middle cranial fossa. The posterior vertical wall attaches to the posterior edge of the superior wall and drops vertically downward, forming a right angle with the superior wall. The posterior wall of the petrous bone forms the anterior wall of the posterior cranial fossa. The angle formed by the junction of the superior horizontal and posterior vertical walls is the ridge of the petrous bone. The petrous bone is oriented obliquely in an anteromedial to posterolateral direction. The anteromedial end, which is narrower, abuts against the lateral wall of the sella turcica. The posterolateral end, which is broader, abuts against the inside of the lateral wall of the cranium near the posterior end of the squamous portion of the temporal bone. The anteromedial end of the petrous ridge is sharp; the posterolateral end is more rounded. In the neonate, the boundaries of the cranial bones are sharply outlined by the wide-open sutures. The superior horizontal surface, the posterior vertical surface, the petrous ridge, and the open sutures are surface landmarks that aid in identification of the petrous bone at autopsy (Fig. 31.1) [1, 2].

The arcuate eminence and the subarcuate fossa are additional landmarks on the superior surface. The arcuate eminence is a curved ridge on the superior surface. It contains the superior semicircular canal and duct. The subarcuate fossa is a blind-ending depression that extends under the arcuate eminence. It is lined with dura, which transmits the subarcuate artery to the inner ear. The tegmen tympani,

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L. M. Ernst et al. (eds.), *Color Atlas of Human Fetal and Neonatal Histology*, https://doi.org/10.1007/978-3-030-11425-1_31

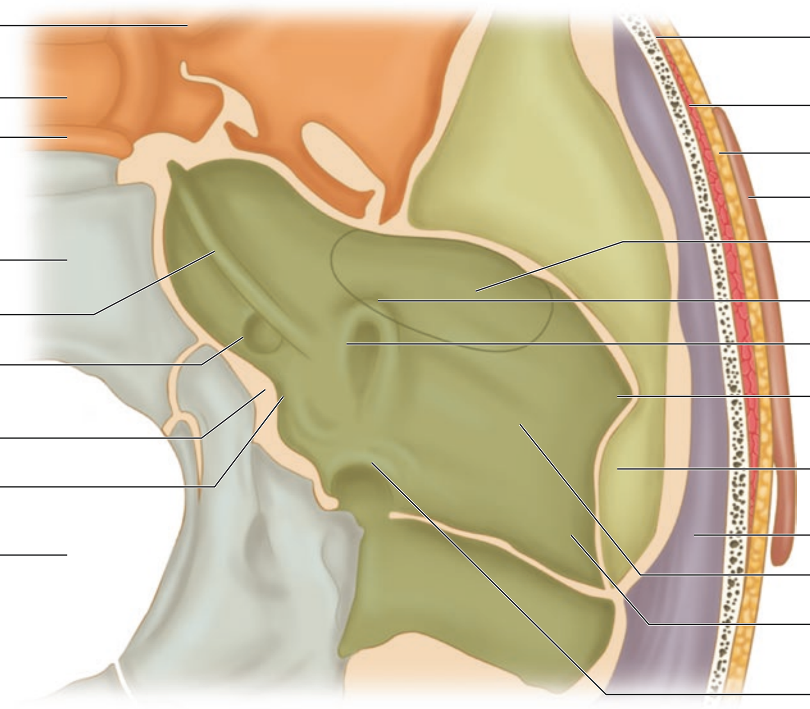

Fig. 31.1 In situ surface anatomy of the petrous bone of the neonate. This illustration views the right side of the cranium from above in the opened cranium. It focuses on the floor of the right middle fossa and the right petrous bone. The left edge is the midline. Dark green: petrous bone. Light green: squamous part of temporal bone. Orange: sphenoid bone. Blue: occipital bone. Violet: parietal bone. Tan areas and lines between bones: open sutures and minor fontanelles. The ostia of the cochlear and vestibular aqueducts are tucked under the edge of the petrous bone and are not visible on the surface. The indicated positions are approximate

though not delineated by surface landmarks, is an important area to visualize. It is a very thin area of the superior horizontal wall that forms the roof of the middle ear. Because it is so thin, it can easily be removed to unroof the middle ear and expose the epitympanic recess and the other structures within those cavities (Fig. 31.1).

The internal acoustic meatus, jugular fossa, ostium of the cochlear aqueduct, and the orifice of the vestibular aqueduct are additional landmarks located from anteromedial to posterolateral along the posterior wall. The internal acoustic meatus is the most anterior landmark. It is the orifice of the internal acoustic canal through which the eighth cranial nerve passes from the posterior fossa to the inner ear. The base of the cochlea lies adjacent to the internal end of the canal. The jugular fossa is important because it marks the site of the ostium of the cochlear aqueduct, which is tucked under the inferior edge of the petrous bone at the apex of the jugular fossa and is therefore not visible on the surface of the petrous bone. It contains the periotic duct. The orifice of the vestibular aqueduct is hidden in a depression in the posterior wall posterior to the jugular fossa. It contains the endolymphatic sac. The position of the cochlea can be estimated from the location of the internal acoustic meatus. The position of the saccular dilatation of the vestibule can be estimated from the location of the ostium of the cochlear aqueduct. The position of the utricular dilatation of the vestibule can be estimated from the location of the ostium of the vestibular aqueduct. The arcuate eminence marks the exact position of the superior semicircular canal and duct (Figs. 31.1 and 31.2).

Arrangement of the Inner, Middle, and External Ears Within the Petrous Bone

The spatial relationships between the petrous bone, inner ear, and middle ear are intricate (Figs. 31.2 and 31.3). They are parallel to each other, with the middle ear lateral to the inner ear. They are obliquely oriented from anteromedial to posterolateral. They extend from the lateral wall of the sella turcica anteromedially to the posterior end of the squamous portion of the temporal bone posterolaterally. The inner ear consists of an outer osseous labyrinth, which is also called the otic capsule, and the membranous labyrinth, which lies within the otic capsule (Figs. 31.3, 31.4, 31.5, 31.6, 31.7, and 31.8). The auditory and vestibular sensory end organs lie within the membranous labyrinth (Figs. 31.8, 31.9, 31.10, 31.11, 31.12, and 31.13). In addition, the otic capsule, membranous labyrinth, and middle ears are divided into three seg-

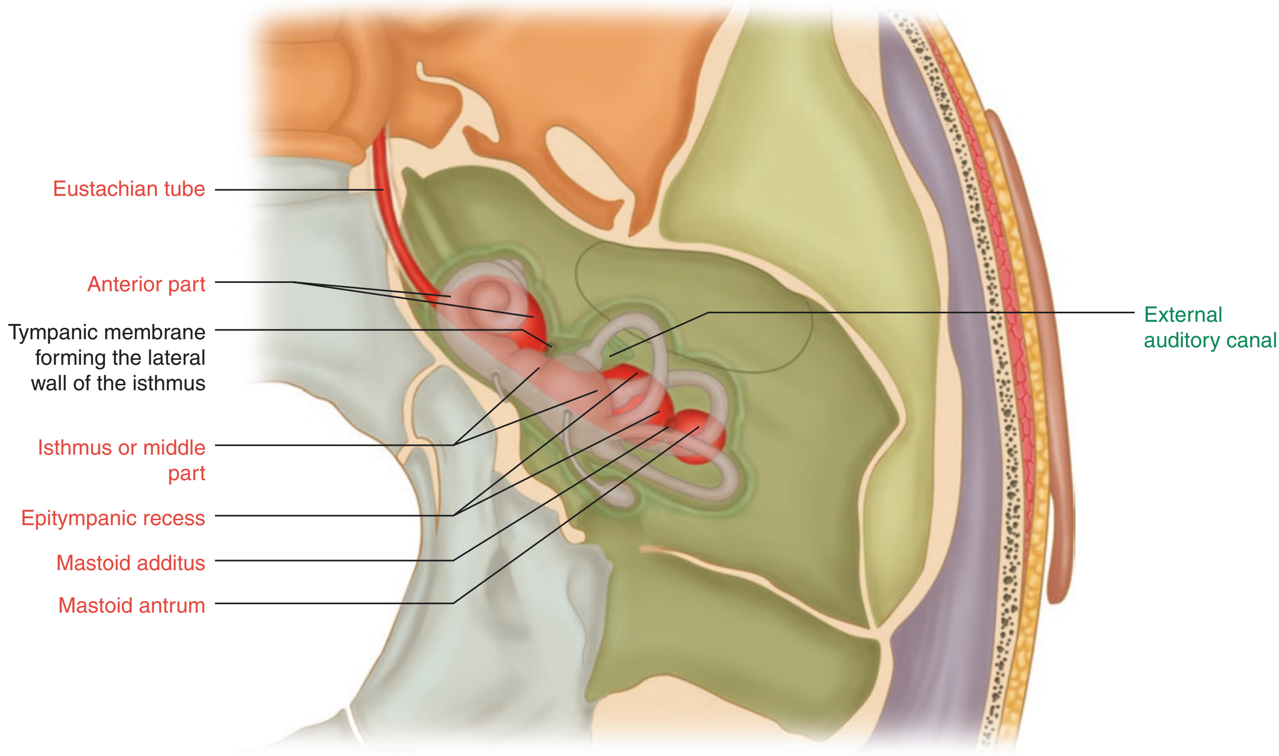

Fig. 31.2 Arrangement of inner, middle, and external ears. This is the same as Fig. 31.1 but with the inner ear, middle ear, and external auditory canal projected into the petrous bone. The osseous labyrinth is depicted in *blue*, the middle ear in *red*, and the external auditory canal in *green*. See Fig. 31.1 for the color code and labels of the bones and surface landmarks, and see the following figures (especially Figs. 31.4 and 31.6) for identification of the various components of the osseous labyrinth of the inner ear. From anteromedial to posterolateral, these components are the cochlea, the vestibule (with saccular and utricular dilatations), and the semicircular canals. The various components of the middle ear from anterolateral to posterior in the figure are as follows: Eustachian tube, anterior part, isthmus or middle part, tympanic membrane, forming the lateral wall of the isthmus. Note that the tympanic membrane is composed of an inner *red* layer (mucosa of middle ear) and an outer *green* layer (mucosa of the external auditory canal). Note the aditus, the small window at the waist between the epitympanic recess and the mastoid antrum. Note the unlabeled cochlear aqueduct and vestibular aqueduct. Finally, note the alignment of the anterior part of the middle ear with the cochlea, the isthmus with the vestibule, and the epitympanic recess and mastoid antrum with the semicircular canals

ments from anterior to posterior. The three segments of the otic capsule (osseous labyrinth) from anterior to posterior are the cochlea, vestibule, and semicircular canals. The vestibule is further divided from anterior to posterior into the saccular dilatation and the utricular dilatation (see Figs. 31.4 and 31.6). The analogous segments of the membranous labyrinth from anterior to posterior are the cochlear duct within the cochlea, the saccule within the saccular dilatation of the vestibule, the utricle within the utricular dilatation of the vestibule, and the semicircular ducts within the semicircular canals (see Figs. 31.5 and 31.7). The analogous segments of the middle ear are the anterior part, which is anterior to the tympanic membrane, lateral to the cochlea, and gives rise to the Eustachian tube from its anterior end; the middle part or isthmus, which is lateral to the vestibule and whose entire lateral wall is the tympanic membrane; and the posterior part, which is posterior and superior to the tympanic membrane, lies lateral to the semicircular canals, and is further subdivided from anterior to posterior into the epitympanic recess, the mastoid antrum, and the mastoid air cells. The inner and middle ears are so intimately pressed together that the basal spiral of the cochlear duct bulges into the tympanic isthmus anteriorly, forming the promontory on its medial wall. The isthmus of the tympanic cavity and the vestibule share a common boney wall. The lateral semicircular canal bulges into the epitympanic recess posteriorly (see Figs. 31.2 and 31.3).

The surface anatomy of the petrous bone of the neonate is different from that of the adult. As the bones mature, the surface landmarks change. For example, the sutures close, making the borders of the petrous bone less clear. The petrous ridge becomes sharper throughout its entire length. The arcuate eminence and subarcuate fossa are smoothed over and become barely visible. The orifice of the vestibular aqueduct becomes hidden in a linear crevice that is higher on the posterior wall in the adult than in the neonate. The changing

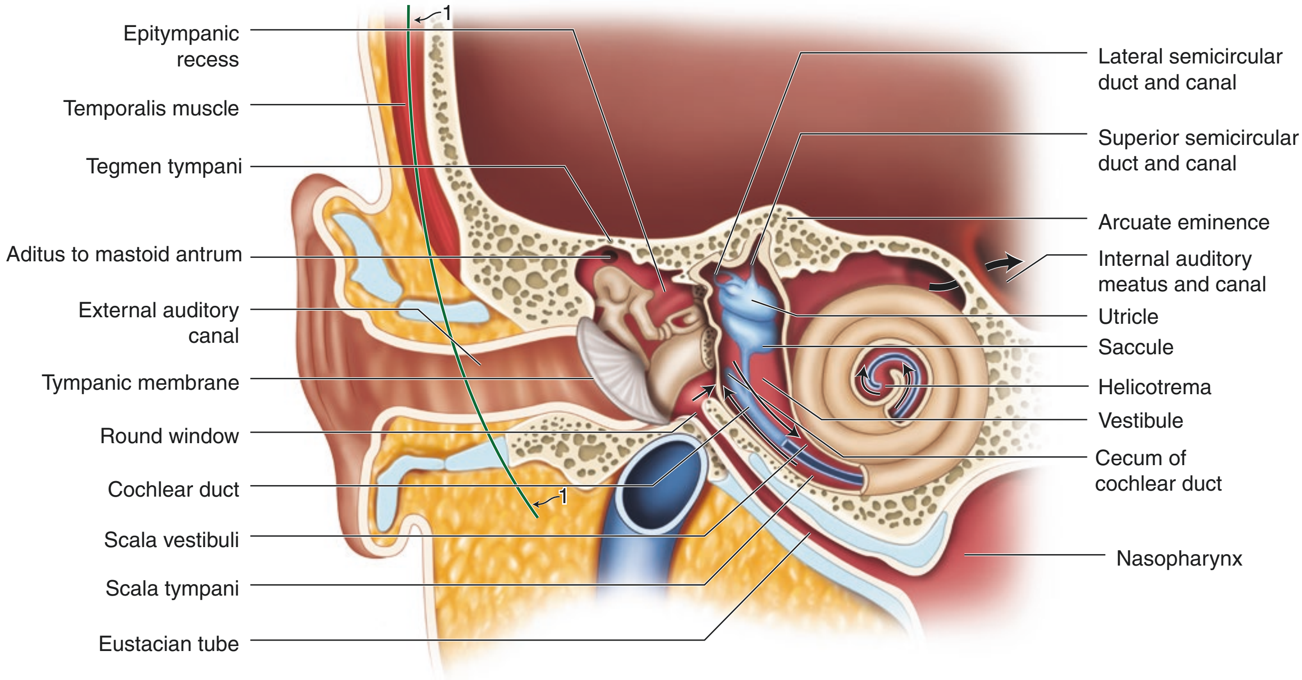

Fig. 31.3 Frontal section through the external, middle, and inner ears viewed from anterior to posterior, looking into the epitympanic recess and the aditus to the mastoid antrum. The tympanic membrane is tilted so that its inferior border is attached to the tympanic ring more medially than its superior border. As a result, the inferior wall of the external auditory canal is longer than its superior wall. Nearly the entire lateral wall of the tympanic cavity is formed by the tympanic membrane. The roof of the epitympanic recess is formed by the thin plate of bone called the tegmen tympani, which is an important surface landmark useful in the correct positioning of the incision lines for the removal of the petrous bone at autopsy. The aditus is a window in the posterior wall of the epitympanic recess, which opens into the mastoid antrum. The common boney wall between the tympanic cavity and the vestibule is perforated by two windows. The more superior is the oval window, which is closed by the footplate of the stapes and the radial ligament. The more inferior is the round window, which is closed by the secondary tympanic membrane. The scala vestibuli begins at the oval window, and the scala tympani ends blindly at the round window. The boney promontory, which is formed by the wall of the basal turn of the cochlea, lies between the oval and round windows. The opening of the Eustachian tube in the tympanic cavity is inferior and anterior to the round window. The Eustachian tube passes beneath the cochlea, and its course to the nasopharynx is nearly horizontal. The superior semicircular canal protrudes upward to form a raised linear prominence, the arcuate eminence, on the floor of the middle fossa. The lateral semicircular canal protrudes laterally to form a boney prominence on the medial wall of the epitympanic recess. The blind end, or cecum, of the cochlear duct abuts against the vestibular side of the promontory so that the scala tympani ends blindly at the round window. The duct connecting the cochlear duct to the saccule is the ductus reuniens. The *arrows* indicate that the pressure waves created by the stapes in the perilymphatic fluid travel through the scala vestibuli toward the cupola (apex) of the cochlea, through the helicotrema, into the scala tympani, back through the cochlea, and to the secondary tympanic membrane in the round window. Cranial nerves VII and VIII pass through the internal auditory canal and meatus in the posterior vertical wall of the petrous bone below the petrous ridge. Line "1" (the curved vertical line through the temporalis muscle and external auditory canal) is the frontal view of the first incision in removal of the petrous bone (see Fig. 31.64). Color code of the segments of the ear: green, external auditory canal; red, middle ear; blue, membranous labyrinth of the inner ear [4]

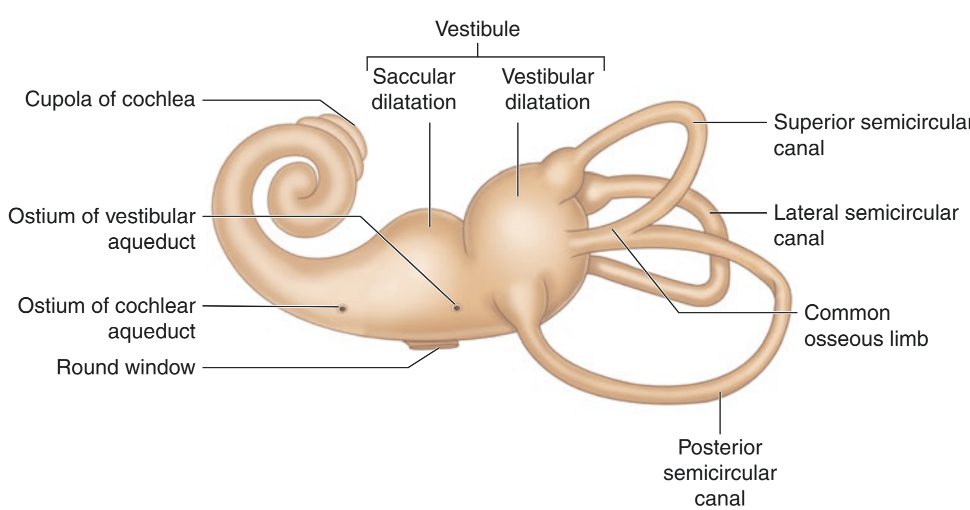

Fig. 31.4 Right osseous labyrinth (otic capsule) viewed from behind and medial, similar to the orientation in Fig. 31.2. The saccular and utricular dilatations of the vestibule contain the membranous saccule and utricle, respectively. The dilated ends of the three semicircular canals where they join the vestibules are the ampules of the semicircular canals. The sites of the ostia of the cochlear and vestibular aqueducts are approximate

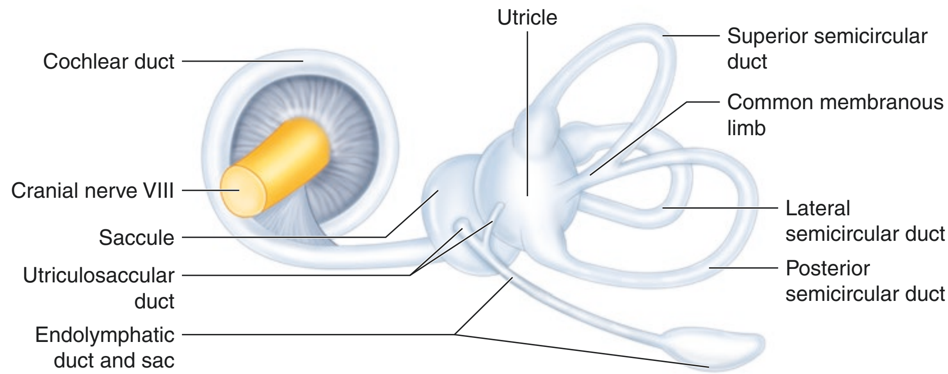

Fig. 31.5 Right membranous labyrinth viewed from behind and medial, similar to the orientation in Figs. 31.2 and 31.4. The membranous labyrinth fits within the osseous labyrinth. The vestibular and facial nerves have been omitted

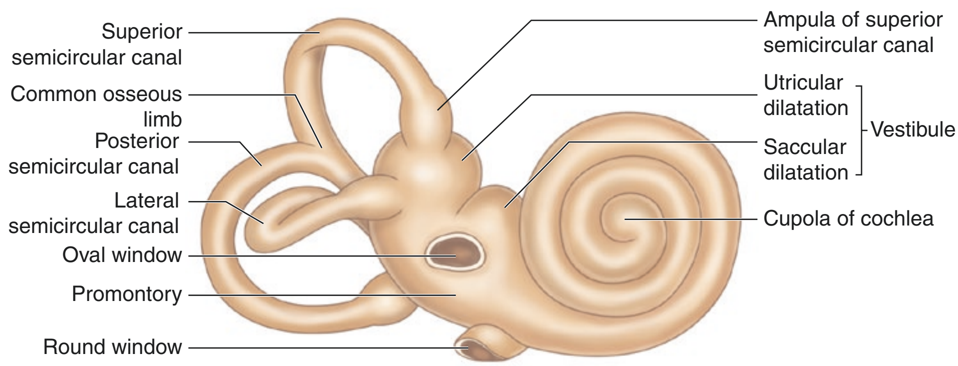

Fig. 31.6 Right otic capsule viewed from in front and laterally. The bony wall of the vestibule in this view is also the medial wall of the tympanic cavity, containing the oval and round windows separated by the promontory

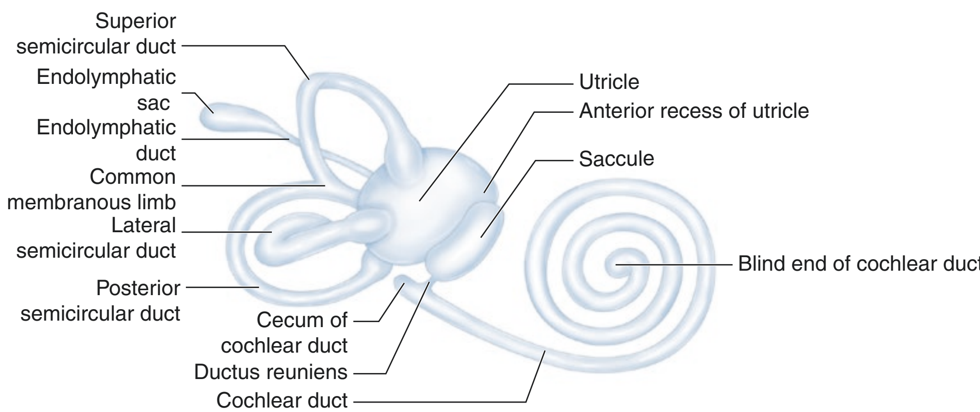

Fig. 31.7 Right membranous labyrinth from in front and laterally, similar to the orientation of the osseous labyrinth seen in Fig. 31.6. Note the anterior recess of the utricle overlying the saccule

anatomy of the petrous bone from the embryo to the adult has been described previously [2]. Compare the petrous bone of the neonate in Fig. 31.1 with that of the adult in any atlas of adult anatomy [3]. Knowledge of the changing anatomy of the fetal and neonatal petrous bone will aid the perinatal pathologist in its identification and removal at autopsy.

External Auditory Canal

The wall of the external two thirds of the external auditory canal is composed of soft tissue and cartilage. The wall of the inner one third passes through the temporal bone and is therefore composed of bone (see Fig. 31.3) [3, 4]. The bony tympanic ring surrounds the inner end of the bony canal. The tympanic membrane is attached to a groove in the tympanic ring.

Tympanic Membrane

The tympanic ring and the attachment of the tympanic membrane to it are tilted so that the posterior and inferior attachments are much deeper than the anterior and superior attachments. The tilt is so marked that the tympanic membrane is nearly parallel to the posterior-inferior wall of the

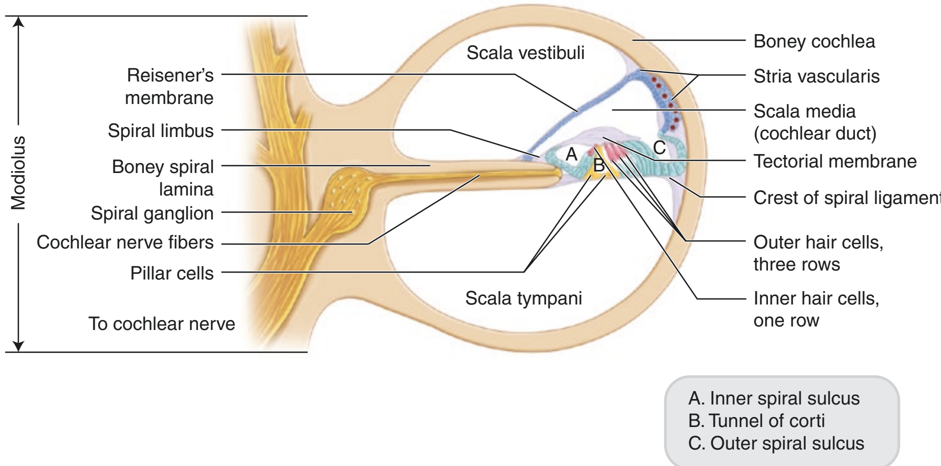

Fig. 31.8 Cross section of the bony cochlea, the membranous cochlear duct, and the organ of Corti. The bony cochlea encloses the membranous triangular cochlear duct (also called scala media) in the middle, the scala vestibuli above, and the scala tympani below. The bony central core of the cochlea, the modiolus, is at the left. The bilaminar bony spiral lamina extends from the area of the modiolus toward the center of the bony cochlear canal. The lateral wall of the cochlear duct is formed by a cushion of connective tissue, the spiral ligament, which lines the inner lateral surface of the bony cochlea. A sharp crest originates from the lower part of the spiral ligament and extends toward the center of the bony canal opposite to the bony spiral lamina. The basal membrane of the cochlear duct is attached to the bony spiral lamina medially and to the crest of the spiral ligament laterally, to form the floor or base of the cochlear duct. The roof of the cochlear duct is Reissner's membrane, which attaches to the spiral limbus medially and to the upper end of the spiral ligament laterally. Therefore, the lateral wall of the cochlear duct lies between the attachment of Reissner's membrane to the spiral ligament superiorly and the attachment of the basal membrane to the crest of the spiral ligament inferiorly. The organ of Corti lies on the basal membrane. The stria vascularis lies on the surface of the spiral ligament between Reissner's membrane and the basal membrane. The fine peripheral fibers of the cochlear nerves, which innervate the organ of Corti, pass through the middle of the bony spiral lamina and join with the spiral cochlear ganglion located in the area of the modiolus medially. Fibers from the spiral cochlear ganglion pass into the hollow center of the modiolus to form the cochlear nerve

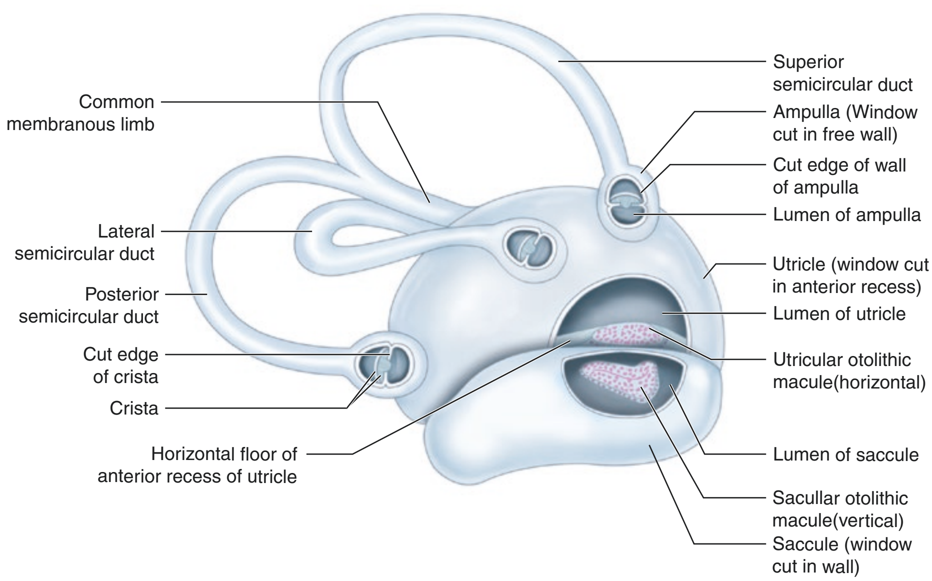

Fig. 31.9 The vestibular portion of the membranous labyrinth looking from anterior to posterior. Windows have been cut in the saccule, utricle, and each of the ampules of the three semicircular ducts to show the sensory organs of the vestibular system. The saccular otolithic macula is oriented vertically on a vertical wall of the saccule. This is an en face view of the saccular macula. The utricular otolithic macula is oriented horizontally on the horizontal floor of the anterior recess of the utricle, above the saccular otolithic macula. The two macules are therefore perpendicular to each other. This view of the utricular macula is slightly on edge. The three ampullary cristae are partially circumferential ridges on the inner surfaces of the ampullae, which partially occlude the ampullary lumens

external auditory canal. The tympanic membrane is the medial wall of the external auditory canal and the lateral wall of the tympanic cavity. It therefore is a common wall between the external auditory canal and the tympanic cavity. Because it is attached to the inner end of the bony external auditory canal, attempts to remove the middle and inner ears by an incision through the petrous portion of the temporal bone flush with the inner surface of the temporal bone often result in destruction of the tympanic ring, tympanic membrane, and the middle ear.

Middle Ear

The tympanic cavity is a long, narrow, rectangular cavity. It lies parallel to the full length of the lateral surface of the inner ear (see Figs. 31.2 and 31.3) [5]. The anterior end is anterior to the tympanic membrane. Part extends below the lower border of the tympanic membrane, especially anteriorly, and is called the hypotympanum. The anterior end is adjacent to the cochlea of the inner ear. The opening of the Eustachian tube is in the anterior-inferior aspect of the medial wall adjacent to the cochlea. The middle part is adjacent to the vestibule of the inner ear. It is the main chamber of the middle ear and is sometimes referred to as the *isthmus* because it is narrower than the anterior and posterior ends. Its lateral wall is the tympanic membrane. The tympanic membrane is therefore a common wall between the external auditory canal and the tympanic cavity. The isthmus contains the handle of the malleus attached to the tympanic membrane, the long process of the incus, and the stapes. The medial bony wall of the isthmus is the lateral wall of the vestibule. The lateral wall of the vestibule is therefore a common wall between the tympanic cavity and the vestibule. There are two windows in the medial wall: the round window, located anterior-inferiorly, and the oval window, located posterior-superiorly. The round window lies immediately behind the orifice of the Eustachian tube and is closed by a delicate membrane called the secondary tympanic membrane, which separates the tympanic cavity from the scala

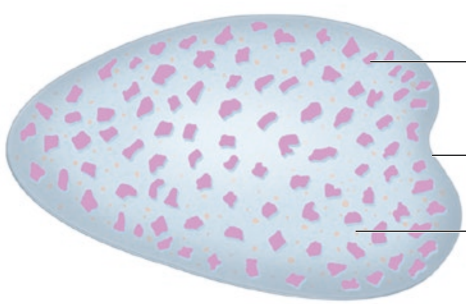

Fig. 31.10 En face view of the utricular macula. The *red otoliths* are embedded in the free surface of the gelatinous membrane that covers the top of the macula. The cilia of the hair cells are embedded in the deep surface of the membrane

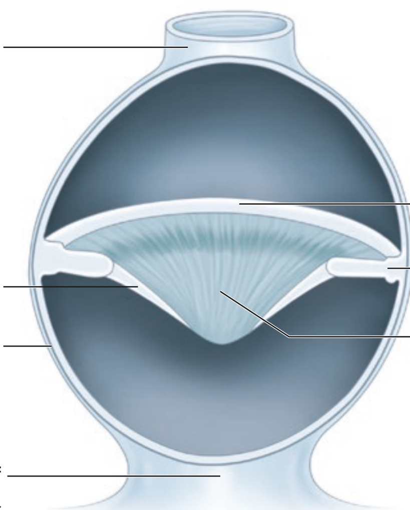

Fig. 31.12 A close-up view of the ampulla of a semicircular duct. A window has been cut in the ampulla to show the details of the crista inside. The cupola is a tongue-shaped, gelatinous membrane attached to the free edge of the crista. It extends partway across the lumen of the ampulla and does not contain otoliths

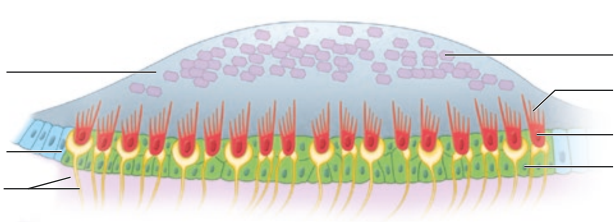

Fig. 31.11 Cross section of an otolithic macula. Cross sections of the saccular and utricular otolithic maculae are identical. They cannot be differentiated microscopically. The *red cells* are neurosensory hair cells. The cilia are embedded in the base of the gelatinous membrane that covers the top of the macula. The *green cells* are supportive cells. The *blue cells* are tall epithelial cells adjacent to the macula. They secrete the gelatinous membrane. The otoliths are embedded in the free surface of the gelatinous membrane. A thick pad of connective tissue containing peripheral fibers of the vestibular nerve lies beneath the epithelial macula

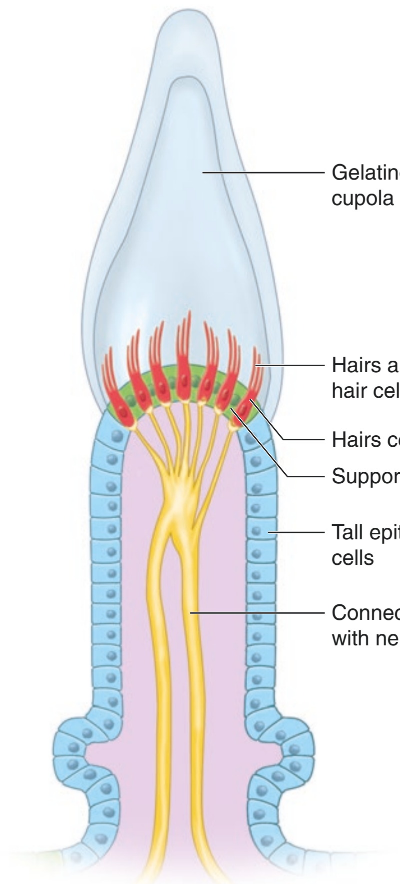

Fig. 31.13 Cross section of a crista. The *red cells* at the tip of the crista are neurosensory hair cells. The hairs and cilia of the hair cells are embedded in the base of the gelatinous cupola. Notice the absence of otoliths. The *green cells* at the tip are supportive epithelial cells. The *blue cells* along the edge of the stalk of the crista secrete the gelatinous cupola. The connective tissue core contains tiny peripheral branches of the vestibular nerve

tympani on the vestibular side of the window. The oval window is located posterior and superior to the round window. The foot plate of the stapes fills the oval window. The radial ligament attaches the edges of the foot plate to the edges of the oval window. The oval window separates the tympanic cavity from the scala vestibuli on the vestibular side. The base of the cochlea pushes the bony wall toward the tympanic cavity, producing a bulge in the wall between the round and oval windows, which is called the *promontory*. The posterior part is a recess in the posterior roof of the tympanic cavity, which forms an attic-like space superior and posterior to the upper rim of the tympanic membrane (see Figs. 31.2 and 31.3). This space is the epitympanic recess. It lies adjacent to the semicircular canals and contains the head of the malleus and the body and short process of the incus. The roof of the epitympanic recess is a thin region of the bony floor of the middle fossa called the *tegmen tympani* (see Figs. 31.1, 31.2, and 31.3). The tympanic cavity can easily be unroofed by removing the thin tegmen tympani. The wall of the lateral semicircular canal bulges into the epitympanic recess. An aperture in the posterior wall of the epitympanic recess, the mastoid aditus, leads posteriorly into the mastoid antrum and from there to the mastoid air cells, which are part of the middle ear. In most fetuses and neonates, the mastoid antrum is the most posterior part of the middle ear because the mastoid air cells, which are the most posterior part in adults, usually do not develop until late fetal or postnatal life (see Fig. 31.2).

The Eustachian tube exits from the anterior-inferior aspect of the medial wall of the tympanic cavity anterior to and below the round window, passes under the cochlea, and opens into the upper nasopharynx. In the fetus and infant, the tube is oriented horizontally (see Fig. 31.3). The tympanic cavity and mastoid air cells are in direct continuity with the outside environment through the Eustachian tube. Like the lung, before birth the middle ear contains amniotic fluid; after birth it contains air. The horizontal orientation of the Eustachian tube in the fetus and infant makes entry of amniotic fluid or nasopharyngeal fluid into the middle ear very easy. If those fluids are infected, intrauterine or neonatal otitis media and sepsis will likely follow. The spectrum of aspiration of amniotic fluid and the amniotic fluid infection sequence affects not only the lung but also the middle ear.

Inner Ear

Osseous Labyrinth

The inner ear is an irregular, oblong cavity in the petrous portion of the temporal bone. It is surrounded by an osseous capsule called the *osseous labyrinth*, *bony labyrinth*, or *otic capsule* (see Figs. 31.4 and 31.6) [6]. These three terms are used interchangeably. The osseous labyrinth has three interconnected parts (from anteromedial to posterolateral): the cochlea, which is a snail-shaped spiral tube joined to the anterior aspect of the vestibule; the vestibule, which is the central chamber; and the three semicircular canals, which are joined to the posterior aspect of the vestibule. The common cavity of the osseous labyrinth is the perilymphatic space, which is filled with fluid, the perilymph. The base of the snail-shaped cochlea faces posteriorly and slightly medially and lies at the inner opening of the internal auditory meatus. The apex or cupola of the “snail” points anteriorly and slightly laterally. The cochlea has a bony central core, the modiolus, which has been likened to a screw with the head of the screw at the base of the cochlea and its tip at the apex. The spiral lamina of the cochlea is analogous to the thread of the screw, and it projects like a shelf into the lumen of the cochlear canal along its equator. Its tip reaches the center of the canal. The spiral lamina forms part of the floor or base of the triangular cochlear duct. The vestibule presents two dilatations: the saccular dilatation anteriorly at the junction of the vestibule with the cochlea and the utricular dilatation posteriorly at the junction of the vestibule with the semicircular canals (see Figs. 31.4 and 31.6). The anatomy of the lateral wall of the vestibule, round window, promontory, and oval window is described above in the description of the middle ear. Three openings in the posterior wall of the vestibule lead to canals through the posterior wall of the petrous bone. The three canals are the internal auditory canal (also called the *internal acoustic canal*), the cochlear aqueduct (also called the *cochlear canaliculus*), and the vestibular aqueduct (also called the *vestibular canaliculus*) (see Figs. 31.1, 31.2, and 31.4). The most anterior is the internal auditory canal. Its opening in the osseous labyrinth is at the base of the spiral cochlea. Cranial nerves VII (facial) and VIII (vestibuloacoustic) pass through the canal and exit through its foramen, the internal auditory meatus (also called the *internal acoustic meatus*), in the posterior wall of the petrous bone. The opening of the cochlear aqueduct in the osseous labyrinth is in the wall of the scala tympani at the junction of the cochlea with the vestibule, and it exits the posterior inferior wall of the petrous bone into the subarachnoid space at the apex of the jugular foramen, creating a direct communication between the perilymphatic and subarachnoid spaces. It contains the periotic duct and a fluid that may be perilymph or subarachnoid fluid. It has no connection with the membranous labyrinth [7]. The most posterior is the vestibular aqueduct. Its opening in the osseous labyrinth is in the utricular dilatation of the vestibule, near its junction with the semicircular canals. It exits through a slit-shaped foramen in the posterior wall of the petrous portion of the temporal bone posterolateral to the jugular foramen (see Figs. 31.1 and 31.2). It contains the endolymphatic duct, which is a tube of membranous labyrinth that arises from the utriculosaccular duct and ends blindly in the dilated endolymphatic sac in the epidural space (see Figs. 31.1, 31.2, 31.5, and 31.7). It contains endolymph. The posterior segment of the osseous labyrinth is composed of the three semicircular canals: anterior (also called superior), posterior, and lateral. Both ends of each canal join the utricle. The three anterior ends are dilated; they are called the *ampullae* at their sites of union with the posterior-superior aspect of the vestibule. The posterior limbs of the anterior and posterior canals join to form the common crus. Therefore, there are only two openings into the posterior aspect of the utricle for the posterior limbs: one for the common crus and one for the lateral canal (see Figs. 31.4 and 31.6).

Membranous Labyrinth

The membranous labyrinth is a closed system of epithelial ducts and sacs derived from the ectodermal otic vesicle. It lies within the cavity of the osseous labyrinth (see Figs. 31.3, 31.5, and 31.7). It is composed of three major parts (from anteromedial to posterolateral): the cochlear duct within the bony cochlea; the saccule and utricle, which are two sacs within the saccular and utricular dilatations of the vestibule; and the three semicircular ducts within the bony semicircular canals. The cochlear duct begins as a blind end in the vestibule adjacent to the promontory and below the saccule. It follows the osseous cochlear spiral to its apex, the cupola, where it ends blindly. The cochlear duct therefore has two blind ends. One abuts the bony promontory in the vestibule below the saccule. The other lies at the apex of the spiral cochlea (see Figs. 31.3, 31.5, 31.7, and 31.8). The saccule is located anteriorly within the saccular dilatation of the vestibule, above the blind end of the cochlear duct and below and in front of the utricle. It is oval in shape and smaller than the utricle. The utricle is located posteriorly in the utricular dilatation of the vestibule, above and behind the saccule. A blind-ended recess of the utricle, the anterior recess, arises near the anterior opening of the lateral semicircular duct. This recess extends horizontally over the roof of the saccule (see Fig. 31.7) [8]. The three semicircular ducts empty into the posterior-superior aspect of the utricle. One end of each forms a dilated ampule at its site of insertion into the utricle. The three components of the membranous labyrinth are interconnected by small ducts. The ductus reuniens connects the cochlear duct to the saccule (see Figs. 31.3 and 31.7). The orifice of the ductus reuniens in the cochlear duct is some distance from its blind end. The segment of the cochlear duct between its blind end and the orifice of the ductus reuniens is called the *cecum of the cochlea* (see Figs. 31.3 and 31.7). The utriculosaccular duct connects the saccule with the utricle. The endolymphatic duct arises from the utriculosaccular duct (see Figs. 31.5 and 31.7). The posterior segment of the membranous labyrinth is composed of the three semicircular ducts inside the semicircular canals. Each has an ampulla, and each necessarily follows the course of its corresponding canal. Unlike the canals that join with the vestibule, the semicircular ducts connect to the utricle. The various parts of the entire membranous labyrinth are interconnected, from the cochlear duct anteromedially to the semicircular canals posterolaterally (see Figs. 31.3, 31.5, and 31.7).

Perilymphatic Space

The perilymphatic space completely surrounds the membranous labyrinth and separates the osseous labyrinth from the membranous labyrinth. Like the osseous labyrinth, membranous labyrinth, and middle ear, it can be divided into three parts, from anteromedial to posterolateral. The anterior part, in the cochlea, is composed of two parts: the scala vestibuli and the scala tympani. The membranous cochlear duct divides the spiral bony cochlear tube into three tubes: the triangular cochlear duct (scala media) in the middle; the scala vestibuli, above the cochlear duct adjacent to Reissner's membrane; and the scala tympani, below the cochlear duct adjacent to the basal membrane (see Figs. 31.3 and 31.8). The lumens of the scala vestibuli and scala tympani become continuous with each other at the apex of the spiral, through an aperture called the *helicotrema*. The scala tympani ends blindly at the round window. The scala vestibuli joins the perilymphatic space of the vestibule at the oval window. The perilymphatic space of the vestibule is the cisterna vestibuli. It surrounds the saccule and utricle and is continuous with those of the semicircular canals (see Fig. 31.3).

Periotic Duct

The periotic duct is a direct communication between the scala tympani part of the perilymphatic space and the subarachnoid space of the posterior fossa. The duct lies within the cochlear aqueduct, a bony canaliculus in the otic capsule and posterior wall of the petrous bone (see Figs. 31.1, 31.2, and 31.4). (The otic capsule is described above and in the Embryology and Histology sections below).

Auditory and Vestibular Sensory Organs

Two systems of sensory end organs are present in the inner ear: the cochlear system, which detects sound, and the vestibular system, which detects motion and gravity. The cochlear auditory sensory end organ is the organ of Corti, which is a strip of neurosensory epithelium located in the basal membrane (the floor) of the entire length of the spiral cochlear duct (see Fig. 31.8).

The vestibular system is composed of two groups of neurosensory epithelial end organs. The first group is composed of two otolithic maculae, the saccular macula and the utricular macula, which detect linear motion. The two otolithic maculae are an interrelated pair. The saccular otolithic macula is a thickened ellipsoid plaque of neurosensory epithelium in the epithelial lining of the vertical wall of the saccule, which lies below the anterior recess of the utricle. Its flat surface is oriented vertically, and its long axis is oriented anteroposteriorly (Fig. 31.9) [5, 9]. It detects vertical linear motion and gravity. The utricular otolithic macula is a thickened ellipsoid plaque of neurosensory epithelium in the epithelium of the horizontal floor of the anterior recess of the utricle. Its flat surface lies horizontally, and its long axis is oriented anteroposteriorly (Figs. 31.9, 31.10, and 31.11). It lies immediately above and perpendicular to the vertically oriented saccular macula [5, 10]. It detects horizontal linear motion.

The second group is the three ampullary cristae or ridges of sensory epithelium, one in each of the three ampullae of the semicircular ducts. The three ampullary cristae, an interrelated trio, are linear ridges of thickened neurosensory epithelium oriented transversely to the long axis of the ducts. They extend only partially around the inner circumference of the ampullae (see Figs. 31.9, 31.12, and 31.13). Each is oriented in a plane different from the others. The cristae detect angular motion.

Embryology

Both the epithelial and connective tissues of the ear are derived from two closely related embryologic primordia, both of which arise within the ectodermal ring [11, 12]. The inner ear is derived from the otic placode, which is an ectodermal thickening within the rostral segment of the ectodermal ring. The external and middle ears are derived from the first and second pharyngeal complexes, which arise from the pharyngeal segment of the ectodermal ring (Table 31.1).

Embryonic development of the ear begins early in the sixth postmenstrual week with the appearance first of the otic placode (the future membranous labyrinth of the inner ear), followed by the first and second pharyngeal arches (the future auricle), the first pharyngeal cleft (the future external auditory

Table 31.1 The embryological origins of the external, middle, and inner ears

First pharyngeal arch
Anterior part of auricle (from auricular hillocks 1, 2, and 3)
The head of malleus, body and short process of incus (from posterior end of Meckel's cartilage and mesoderm of first pharyngeal arch)
Second pharyngeal arch
Posterior part of auricle (from auricular hillocks 4, 5, and 6)
Handle of malleus, long process of incus, head and limbs of stapes (from Reichert's cartilage and mesoderm of second pharyngeal arch). Note: the foot plate of the stapes is from the otic capsule
First pharyngeal cleft
External auditory canal
External epidermal surface of tympanic membrane
First pharyngeal pouch
Eustachian tube
Tympanic cavity
Internal endodermal surface of tympanic membrane
Otic placode, pit, and vesicle
Membranous labyrinth: cochlear duct, ductus reuniens, saccule, utriculosaccular duct, endolymphatic duct and sac, utricle, and semicircular ducts
Periotic mesoderm
Osseous labyrinth (otic capsule): cochlea, vestibule, and semicircular canals
Foot plate of stapes

canal), and the first pharyngeal pouch, also referred to as the *tubotympanic recess* (the future tympanic cavity and Eustachian tube). All appear early in the sixth week. During the rest of the sixth week, the first pharyngeal cleft and first pharyngeal pouch grow toward each other, but their distal ends remain separated by a layer of mesenchyme from the arches. The distal ends of the cleft and pouch and the intervening mesenchyme are the first pharyngeal membrane, which will become the future tympanic membrane. The primordia of the ossicles condense within the mesenchyme of the first pharyngeal membrane and the mesenchyme adjacent to the first pouch: first the malleus, in the mesenchyme of the first pharyngeal arch, located in first pharyngeal membrane; followed by the incus, in the mesenchyme of the first arch, adjacent to the first pharyngeal pouch; then the stapes, in the mesenchyme of the second arch, adjacent to the first pouch. Meanwhile, the otic placode develops into the otic pit. A layer of mesenchyme condenses around the epithelial pit. The mouth of the pit becomes narrow, and the pit becomes the otic vesicle. The epithelium of the otic pit becomes the membranous labyrinth of the inner ear. The condensed mesenchyme surrounding the epithelial pit becomes the osseous labyrinth of the inner ear. These primordia of the auricle, external auditory canal, tympanic membrane, ossicles, tympanic cavity, Eustachian tube, and membranous and osseous labyrinths are established by the end of the sixth week.

From the beginning of the seventh week to the end of the tenth week (the end of the embryonic period), the final form of all of the organs develops from these primordia. The following events are occurring simultaneously during the last 4 weeks of the embryonic period.

The auricle is completely formed by the middle of the tenth week. The first pharyngeal cleft becomes the external auditory canal. In the tenth week, the lining epithelium of the canal proliferates and forms a plug, the meatal plug, which completely occludes the lumen of the distal third of the canal [5, 13].

The tympanic end of the tubotympanic recess enlarges to become the tympanic cavity, and its pharyngeal end becomes the Eustachian tube. The head of the malleus forms in the mesenchyme of the future tympanic membrane in association with the posterior end of the cartilage of the first arch, Meckel's cartilage. The body and short process of the incus form adjacent to the wall of the tympanic cavity, also in association with the cartilage of the first arch, Meckel's cartilage. The head of the malleus and the body and short process of the incus come to lie in the epitympanic recess. The handle of the malleus arises from the mesenchyme of the second arch in association with posterior end of the cartilage of the second arch, Reichert's cartilage, and remains attached to the tympanic membrane. The long process of the incus and the head and limbs of the stapes also form in association with the cartilage of the second arch, Reichert's cartilage, and come to lie within the main part of the tympanic cavity, the isthmus. The footplate of the stapes arises from the otic capsule and fills the oval window. The parts of the ossicles derived from the first arch are located in the epitympanic recess, whereas the parts derived from the second arch are located in the isthmus of the tympanic cavity. By the end of the tenth week, the mesenchymal ossicles have nearly attained their adult morphology and have begun to convert to cartilage. The diarthrodial synovial incudomalleolar and incudostapedial joints are formed, and the stapediovestibular joint is formed by the radial ligament. The enlarging tympanic cavity envelops the ossicles and the mesenchyme that surrounds them, so that they lie within the tympanic cavity, and the tympanic cavity is filled with the primitive mesenchyme.

The development of the inner ear is even more complex [11, 12]. The otic vesicle detaches from the surface ectoderm and comes to lie in its final position, medial to the developing tympanic cavity. The epithelium of the otic vesicle is thick, multilayered, and composed of small, oval, basophilic, undifferentiated cells with the appearance of pluripotent placodal cells. This histology remains unchanged until the epithelium begins to differentiate during the tenth week. During the seventh week, the round otic vesicle elongates in the ventral and dorsal directions. The ventral elongation will become the cochlear duct; the dorsal elongation, the endolymphatic duct. During the eighth week, the semicircular ducts appear as three hollow plates at the base of the endolymphatic duct. The epithelium in the center of the plates fuses, leaving the patent semicircular ducts at the periphery of the plates. By the end of the eighth week, the fused epithelium in the center of the plates disappears, and one end of each duct dilates at its point of insertion into the utricle, forming the ampullae of the semicircular ducts. The otic vesicle between the developing semicircular ducts and the cochlear duct forms two dilatations. One, the saccule, is located anteriorly, above the developing cochlear duct. The other, the utricle, is located above and behind the saccule. Both ends of each semicircular duct enter the utricle. The end of the endolymphatic duct enlarges into the endolymphatic sac. The elongating cochlear duct begins to spiral. The connection between the saccule and the cochlear duct becomes a narrow tube called the *ductus reuniens*. Its origin from the cochlear duct is some distance from the blind end of the cochlear duct, which is called the *cecum* of the cochlear duct. The connection between the utricle and saccule becomes a narrow tube called the *utriculosaccular duct*. The endolymphatic duct becomes a branch of the utriculosaccular duct. The cochlea elongates and spirals.

During the tenth week, the epithelium of the membranous labyrinth begins to differentiate [12, 14]. The primitive, multilayered epithelium becomes a single layer of flat epithelium, except in the sites of the future auditory and vestibular sensory end organs. In these sites, the ingrowing peripheral branches of the eighth cranial nerve induce the epithelium to differentiate into plaques of tall, ciliated neurosensory epithelium that are the rudiments of the neurosensory sensory end organs. The auditory organ is the organ of Corti, located in the basal membrane of the cochlear duct. It first appears in the vestibular end of the cochlear duct and then extends along the full length of the duct. The vestibular system of balance consists of the vertically oriented macula of the saccule, the horizontally oriented macula of the utricle, and the three radially oriented cristae of the ampullae of the semicircular ducts. Each of these six organs begins with the differentiation of tall, ciliated, neuroepithelial sensory cells.

The epithelium of the inner ear continues to induce the condensation of adjacent mesenchyme around itself to become an increasingly dense envelope of connective tissue, which abuts directly against the membranous labyrinth [12]. This is the precursor of the osseous labyrinth, also called the *bony labyrinth* or *otic capsule*. There is no space between the mesenchymal otic capsule and the membranous labyrinth. By the end of the tenth week, the elongation of the cochlear duct has reached nearly two and one-half spirals, the mesenchymal otic capsule has begun to convert into cartilage, and the auditory and vestibular sensory end organs are rapidly differentiating.

At the end of the embryonic period (tenth week), most of the major components of the ear are well-developed. However, a few important processes in the histologic maturation of the ear remain for the fetal period:

- In the external auditory canal, the canalization of the meatal plug and the concomitant final maturation of the tympanic membrane
- In the middle ear, the resorption of the embryonic mesenchyme, the establishment of the tympanic cavity, and the maturation of the secondary tympanic membrane covering the round window
- In the inner ear, the final elongation of the cochlear duct to two and three-quarter turns, the formation of the perilymphatic space, the final maturation of the sensory end organs, and the ossification of the ossicles and otic capsule

Histology

External Auditory Canal

The entire external auditory canal is lined by keratinizing, stratified squamous epithelium, which is continuous with the skin of the pinna. The development of the embryonic and fetal histology of the skin of the external auditory canal is similar to that of the skin elsewhere in the body. The skin of the outer cartilaginous segment of the canal differs from that of the inner osseous segment. Recanalization of the meatal plug begins during the 13th week and is complete by the 18th week [13]. In the outer cartilaginous segment, early keratinization and primitive hair follicles appear in the third month. Sebaceous glands, ceruminous glands, and extensive keratinization appear in the fifth or sixth month in utero. By the time of birth, the lining epithelium of the outer cartilaginous portion of the canal includes numerous hair follicles, sebaceous glands, and ceruminous glands, but no sweat glands (Fig. 31.14). The ceruminous glands are simple, coiled, tubular glands that are thought to be modified apocrine glands similar to those in the eyelids, axilla, areola, groin, and elsewhere. Their coiled secretory portions form large lobules deep to the hair follicles and sebaceous glands. Their ducts empty into the hair follicles above the mouths of the sebaceous glands and onto the epidermal surface. The epithelium of the ceruminous glands is composed of a luminal layer of large secretory cells with granular, acidophilic cytoplasm and apical secretory granules and an outer layer of myoepithelial cells (Fig. 31.15). The secretory cells may contain yellow-brown pigment.

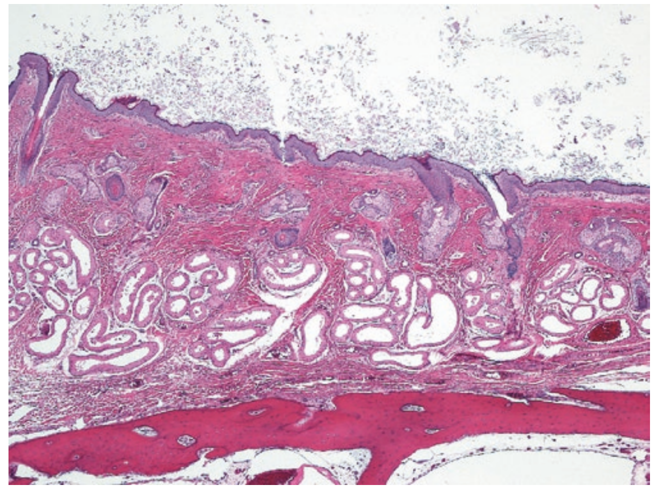

Fig. 31.14 Epidermal lining of the outer part of the external auditory canal at 6 months postnatal age. The surface is covered by keratinizing, stratified squamous epithelium. Hair follicles and sebaceous glands are confined to the upper half of the lining. Ceruminous glands occupy the lower half of the lining below the hair follicles and sebaceous glands. Lining with these histologic features is characteristic of the outer cartilaginous part of the canal but may extend a short distance into the bony inner part of the canal, as it does in this case. Sweat glands are not present in any part of the external auditory canal (H&E, 2×)

The ceruminous glands continue to mature into childhood and do not become fully functional until puberty or adolescence. Therefore, ceruminous waxy plugs in the external auditory canal are unusual before late childhood, although vernix caseosa may fill the canal in late fetuses and neonates.

The lining epithelium of the inner bony portion of the external auditory canal is different from that of the outer cartilaginous portion, in that it is thin and lacks dermal papillae and adnexa (Fig. 31.16) [15]. Adjacent to the tympanic membrane, its deep surface is undulating. Early in the fetal period, the stratified squamous epithelium is thin and not yet keratinized (Figs. 31.16 and 31.17). By mid-gestation it is keratinized and may be pigmented (Figs. 31.18, 31.19, 31.20, and 31.21).

Before birth, the external auditory canal is filled with amniotic fluid. After birth, it is filled with air. However, routine microscopic sections of the middle and inner ears often do not include the external auditory canal, so these features are usually not appreciated.

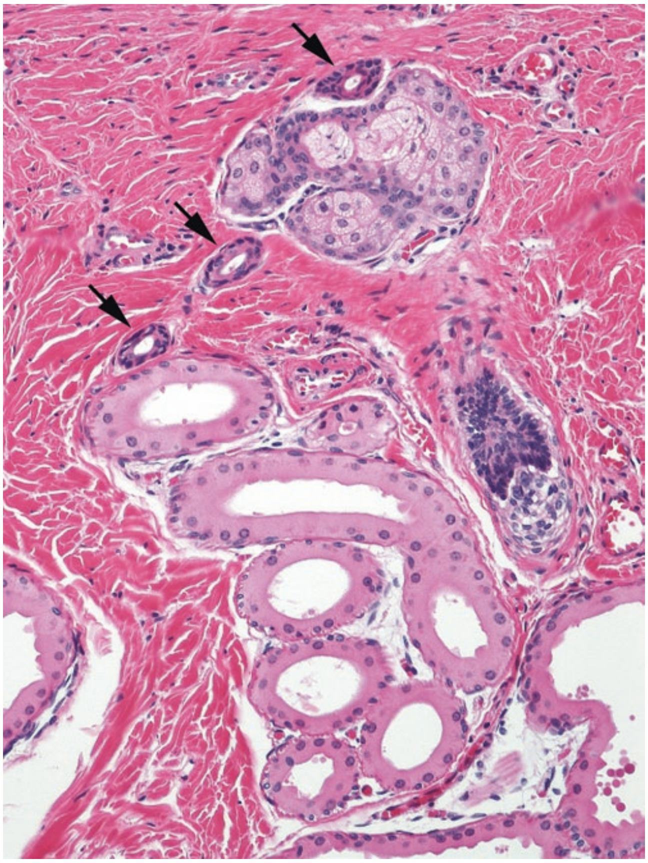

Fig. 31.15 Higher-power view of the ceruminous glands seen in Fig. 31.14. The ceruminous glands are located deep to the sebaceous glands. They are simple, coiled tubular glands with a single layer of tall, bright pink secretory cells and a single basal layer of myoepithelial cells. The three *arrows* point to the ceruminous duct, which empties either into the hair follicle above the ostium of the sebaceous gland or into the surface epithelium (H&E, 20×)

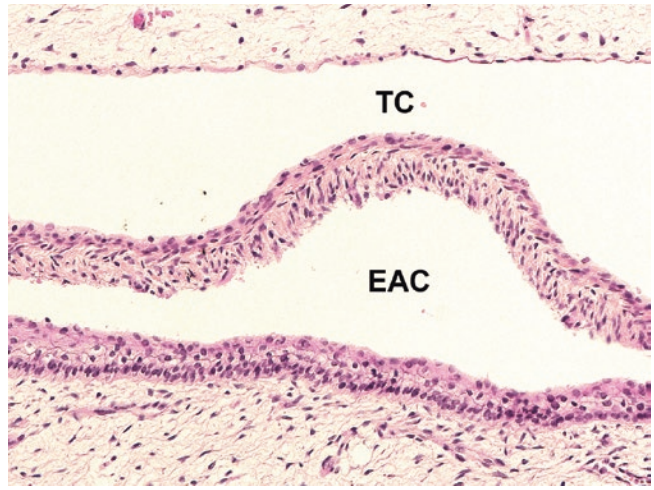

Fig. 31.16 Epidermal lining of the inner part of the external auditory canal near its junction with the tympanic membrane at 15 weeks gestation. The bilayered membrane between the lumen of the external auditory canal (EAC) and the tympanic cavity of the middle ear (TC) is the tympanic membrane. The epithelial membrane beneath the lumen of the external auditory canal is the epidermal lining of the inner part of the external auditory canal. It is a thin, nonkeratinizing, stratified squamous epithelium that lacks hair follicles, sebaceous glands, ceruminous glands, and rete ridges (H&E, 20×)

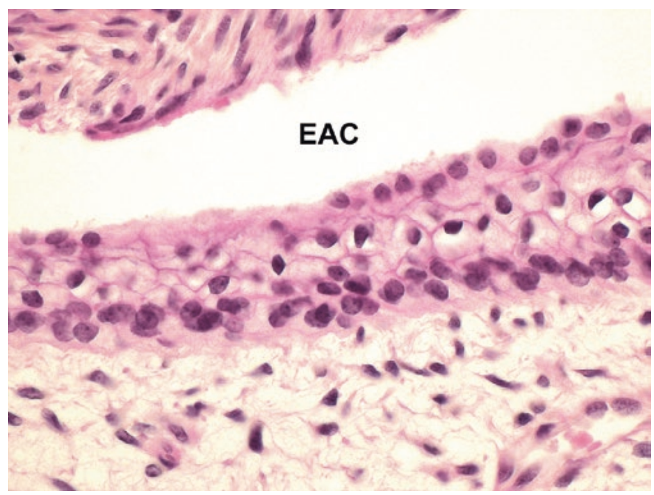

Fig. 31.17 Higher-power view of the lining of the inner part of the external auditory canal seen in Fig. 31.16. The thin, nonkeratinizing, stratified squamous epidermis lacks a granular layer (H&E, 60×). *EAC* the lumen of the external auditory canal

Tympanic Membrane

The mature histology of the tympanic membrane cannot be appreciated until the meatal plug is removed at 13–18 weeks gestational age. The mature tympanic membrane is composed of three layers, except in the pars flaccida [15]. The outer layer is extremely thin, stratified keratinizing squamous epithelium lacking dermal ridges and adnexa. It is continuous with the lining of the inner bony segment of the external auditory canal, which derives from the ectoderm of the first pharyngeal cleft. In the early fetal period, it is extremely thin and nonkeratinized (Fig. 31.22). By midgestation, it is thicker and well-keratinized (Fig. 31.23). By 6 months postnatal age, it remains heavily keratinized (Fig. 31.24). Through a process of "auditory epithelial migration," the keratin and outer layers of the epidermis migrate from the middle to the periphery of the tympanic membrane and then onto the surface of the inner bony segment of the external auditory canal, from which they are ultimately expelled. This process ensures that the epidermal surface of the tympanic membrane remains thin, devoid of keratin, and pliable [15]. The middle layer of the tympanic membrane is a connective tissue from the first pharyngeal cleft and pouch; it is composed of two layers, an outer layer of radial fibers and an inner layer of circular fibers, which are well-developed by 15 weeks gestation (Fig. 31.22). The inner surface of the tympanic membrane is continuous with the lining of the tympanic cavity. It is derived from the endoderm from the first pharyngeal pouch and consists of squamous epithelium (Figs. 31.23 and 31.24).

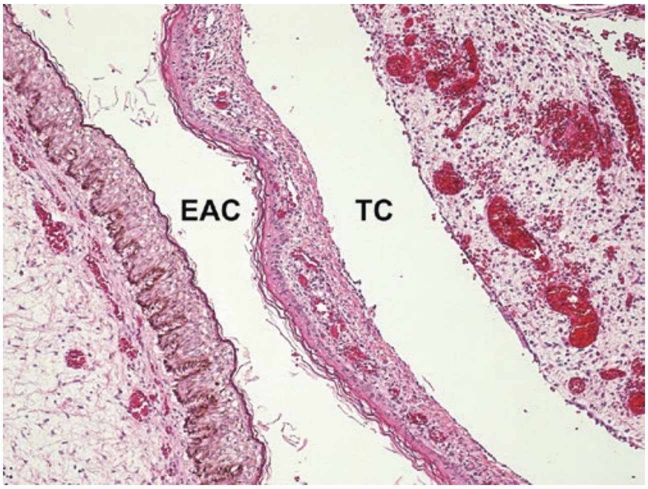

Fig. 31.18 Epidermal lining of the inner part of the external auditory canal near its junction with the tympanic membrane at 23 weeks gestation. The membrane between the lumen of the external auditory canal (EAC) and the tympanic cavity (TC) is the tympanic membrane. The wall of the tympanic cavity is to the right, and the epidermal lining of the external auditory canal is to the left. Unlike the epidermal lining at 15 weeks gestation (seen in Figs. 31.16 and 31.17), this epidermis is thicker, has granular and keratin layers, and has an undulating rather than a flat deep surface. Like the epidermis at 15 weeks gestation, it lacks hair follicles, sebaceous glands, and ceruminous glands. Sweat glands are not present (H&E, 10×)

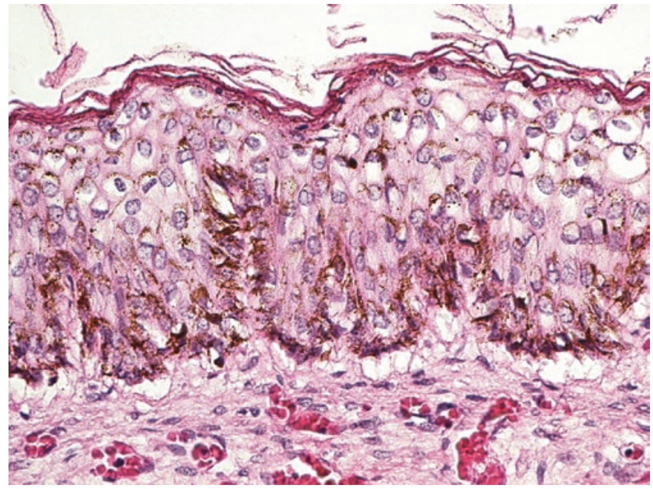

Fig. 31.19 Higher-power view of the keratinized epidermal lining of the external auditory canal seen in Fig. 31.18. The epidermis may be heavily pigmented, as in this case (H&E, 40×)

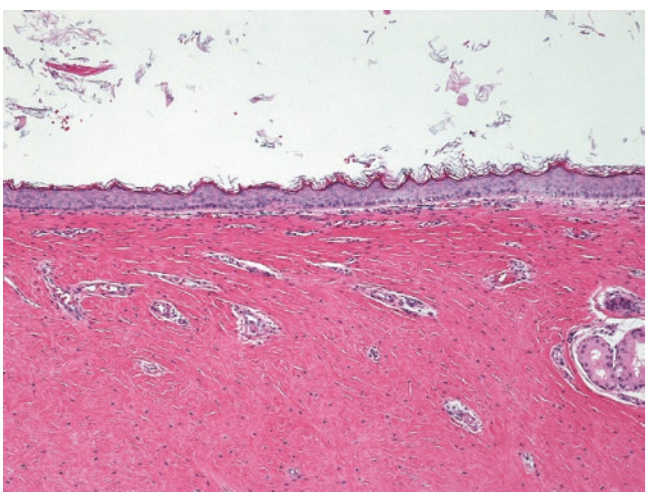

Fig. 31.20 Epidermal lining of the inner part of the external auditory canal at 6 months postnatal age, from the same patient depicted in Figs. 31.14 and 31.15. In contrast to the epidermal lining of the outer part of the external auditory canal, the epidermal lining of the inner part of the external auditory canal lacks hair follicles, sebaceous glands, ceruminous glands, and rete ridges. The right edge of the section demonstrates the abrupt change from the ceruminous-bearing epidermis of the outer part of the canal to the nonceruminous-bearing epidermis of the inner part of the canal (H&E, 40×)

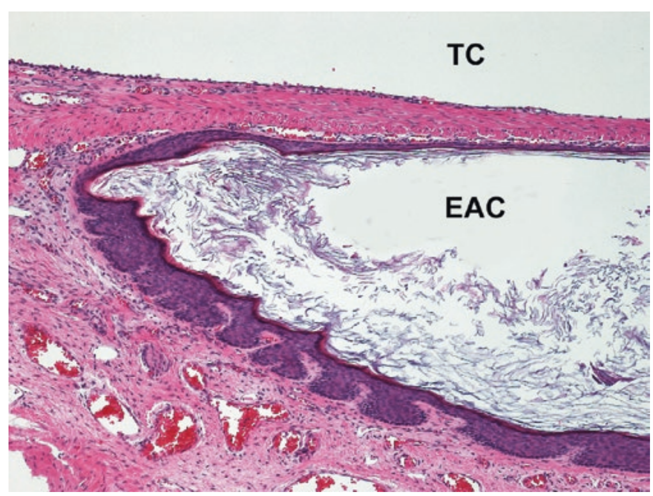

Fig. 31.21 Epidermal lining of the inner part of the external auditory canal at its junction with the tympanic membrane at 6 months postnatal age, from the same patient depicted in Figs. 31.14, 31.15, and 31.20. The tympanic membrane separates the lumen of the external auditory canal (EAC) from the tympanic cavity of the middle ear (TC). The deep surface of the epidermal lining near the tympanic membrane changes from flat to undulating. As the epidermis of the canal is reflected onto the inner surface of the tympanic membrane, it becomes thin, and its deep surface again becomes flat. The lumen of the external auditory canal may contain much keratin debris despite the auditory epithelial migration described in the text (H&E, 10×)

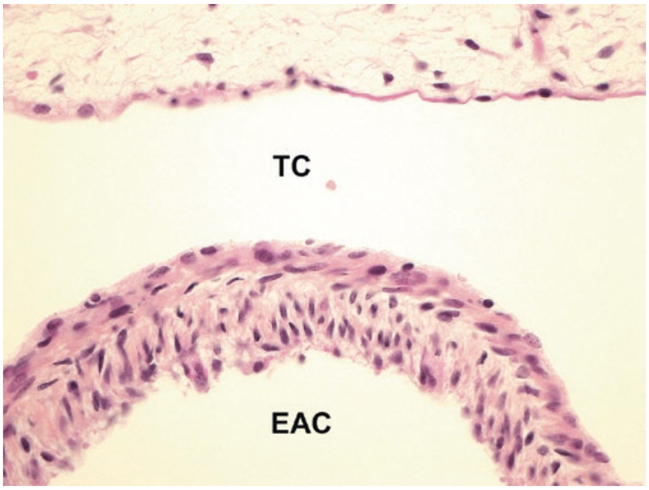

Fig. 31.22 Tympanic membrane at 15 weeks gestation (higher-power view of Fig. 31.16). The tympanic membrane is the upside-down "U" in the lower half of the field. The space below the membrane is the lumen of the external auditory canal (EAC). The space above the membrane is the tympanic cavity of the middle ear (TC). The tympanic membrane is composed of two layers of connective tissue: an outer layer of radial fibers (the side facing the EAC) and an inner layer of circular fibers (facing the TC). The extremely thin epidermis has fallen off the outer surface, and the single layer of endoderm has fallen off the inner surface (H&E, 40×)

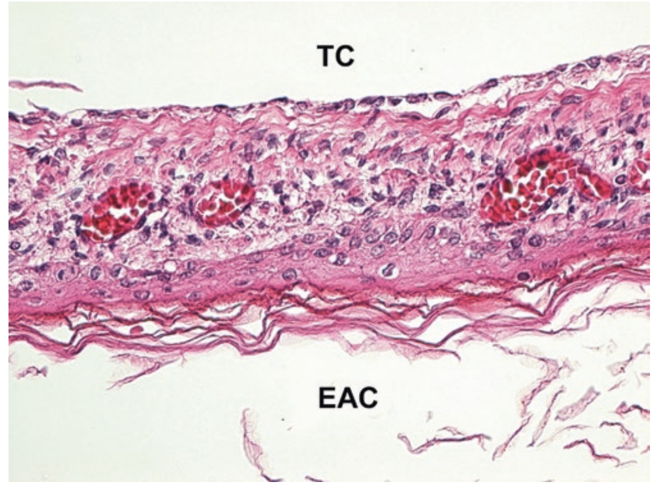

Fig. 31.23 Tympanic membrane at 23 weeks gestation (higher magnification of Fig. 31.18). In contrast to the tympanic membrane at 15 weeks gestation in Figs. 31.16 and 31.22, the epidermis of the tympanic membrane at 23 weeks gestation is thicker and is heavily keratinized. The inner surface is covered by a single layer of flat epithelium, which is an extension of the lining of the tympanic cavity. The two layers of connective tissue forming the middle layer of the membrane are not as distinct as those at 15 weeks gestation or as those seen at 6 months postnatal age, as in Fig. 31.24 (H&E, 40×). *EAC* lumen of external auditory canal, *TC* tympanic cavity of middle ear

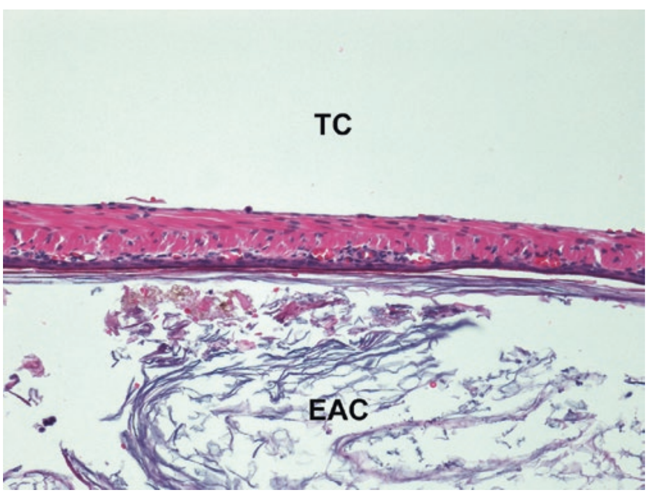

Fig. 31.24 Tympanic membrane at 6 months postnatal age (higher-power view of Fig. 31.21). The epidermis of the outer surface is thinner than that seen at 23 weeks. The two layers of connective tissue are distinct. The epithelial lining of the inner surface is similar to that seen at 23 weeks gestation (H&E, 40×). *EAC* lumen of external auditory canal, *TC* tympanic cavity of middle ear

Middle Ear

The histology of the middle ear changes significantly during the fetal period. Ossification of the ossicles begins at 16 weeks, first in the incus and followed sequentially by the malleus at 16–17 weeks and finally the stapes at 18 weeks. Ossification is complete by 24 weeks [2], and the ossicles are adult size by term. Beginning with the embryonic period and extending into the early fetal period, the tympanic cavity is almost completely filled with embryonic mesenchyme, which surrounds the ossicles and leaves very little lumen (Fig. 31.25). In the early fetal period, the epithelium lining the small cavity consists of simple or slightly stratified flat endoderm. It is thinnest over the inner surface of the tympanic membrane and the convex surfaces of the mounds of mesenchyme that fill the lumen. In these thin areas, it is a single layer of flat cells that lack cilia (Figs. 31.25 and 31.26). It is thickest in the corners and crevices of the cavity, where it becomes irregularly stratified and cuboidal to columnar, with patches of cilia (Figs. 31.25 and 31.27). With increasing gestational age, the subepithelial mesenchyme becomes thicker and more edematous. At mid-gestation, it continues to surround the ossicles and other structures that traverse the tympanic cavity, such as the tendon of the tensor tympani muscle (Figs. 31.28 and 31.29). The mesenchyme contains variable amounts of extramedullary hematopoietic tissue (Figs. 31.30 and 31.31). The epithelium remains thin and inconspicuous over the inner surface of the tympanic membrane, where it is a single layer of flat endothelium (see Fig. 31.23), and over the mounds of mesenchyme, where it is a single layer of flat or cuboidal endothelium (see Fig. 31.30). In the corners and crevices, it becomes irregularly pseudostratified, columnar, and cuboidal, with many patches of cilia (see Fig. 31.31). As pregnancy approaches term, the subepithelial embryonic mesenchyme is reabsorbed, and

Fig. 31.25 Tympanic cavity at 15 weeks gestation, from the same patient as depicted in Figs. 31.16, 31.17, and 31.22. The tympanic cavity (TC) is a narrow slit behind the tympanic membrane (to the left) and becomes slightly wider at its corner (to the right). The *asterisk* indicates the root of the tympanic membrane; the *double asterisks* mark the tympanic ring. The extremely thick layer of edematous and embryonic-appearing mesenchyme between the epithelial lining and the cartilage fills the space that would be tympanic cavity if not for the presence of the mesenchyme. The epithelium lining the thick mound of mesenchyme is thin; the epithelium lining the corner is thicker (H&E, 4×)

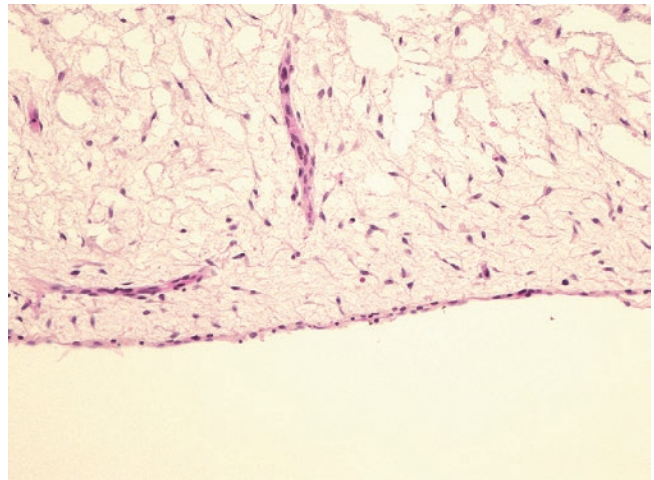

Fig. 31.26 Higher magnification of Fig. 31.25, depicting the thin epithelial lining of the tympanic cavity at 15 weeks gestation. The thin epithelial lining over the thick mesenchyme is a single layer of squamous cells (H&E, 20×)

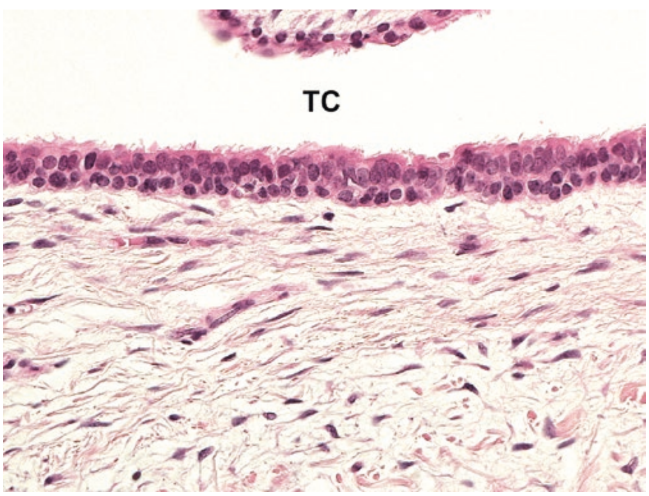

Fig. 31.27 Higher magnification of Fig. 31.25 depicting the thicker epithelial lining of the corner of the tympanic cavity (TC) at 15 weeks gestation. The epithelium is stratified cuboidal epithelium with patches of cilia (H&E, 60×)

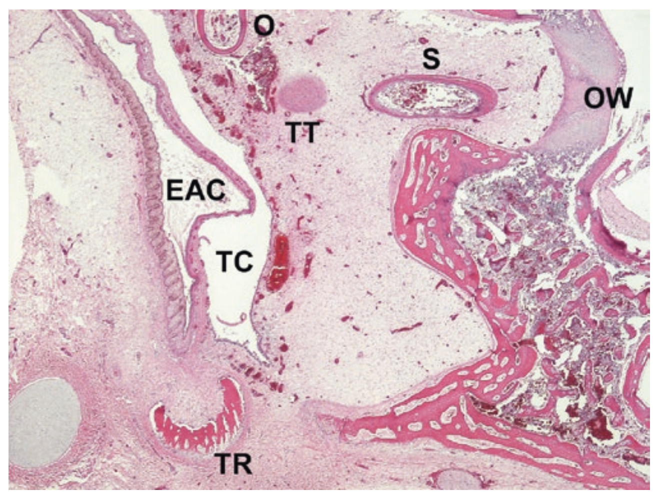

Fig. 31.28 Tympanic cavity at 23 weeks, from the same patient as depicted in Figs. 31.18, 31.19, and 31.23. Shown from top to bottom are an unidentified ossicle (O), stapes (S), edge of oval window (OW), tendon of the tensor tympani muscle (TT), lumen of the external auditory canal (EAC), tympanic cavity (TC), and tympanic ring (TR). The tympanic cavity remains a narrow slit behind the tympanic membrane but becomes slightly wider at the corner of the cavity. The unidentified ossicle, the tendon of the tensor tympani muscle, and the stapes are buried in the mass of mesenchyme that fills most of the tympanic cavity. The space to the right of the edge of the oval window is the periotic space (the cistern) of the vestibule. The connective tissue of the tympanic membrane inserts into the groove of the tympanic ring (H&E, 4×)

the lumen becomes larger. Less mesenchyme surrounds the ossicles and other structures (Figs. 31.32 and 31.33). The mesenchyme disappears from the tympanic side of the secondary tympanic membrane in the round window. The secondary tympanic membrane attains its adult appearance of a thin, trilayered membrane: a single layer of squamous epithelium derived from that of the tympanic cavity on the tympanic side, a middle layer composed of a thin sheet of connective tissue, and an inconspicuous single layer of periotic reticular squamous cells on the vestibular side (Figs. 31.32 and 31.34). Extramedullary hematopoiesis gradually diminishes from the embryonic mesenchyme. The epithelium continues to become thinner and less conspicuous (see Figs. 31.32 and 31.33). By the last week of pregnancy or the neonatal period, the mesenchyme com-

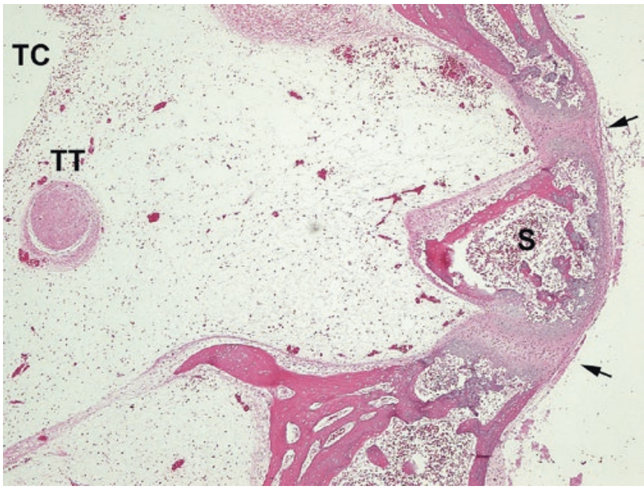

Fig. 31.29 Thick mesenchyme filling the tympanic cavity (TC) at 24 weeks gestation. Shown are the tendon of the tensor tympani muscle (TT), the foot plate of the stapes (S) in the oval window, and the radial ligament (*arrows*). The space to the right of the oval window is the periotic space (the cistern) of the vestibule (H&E, 4×)

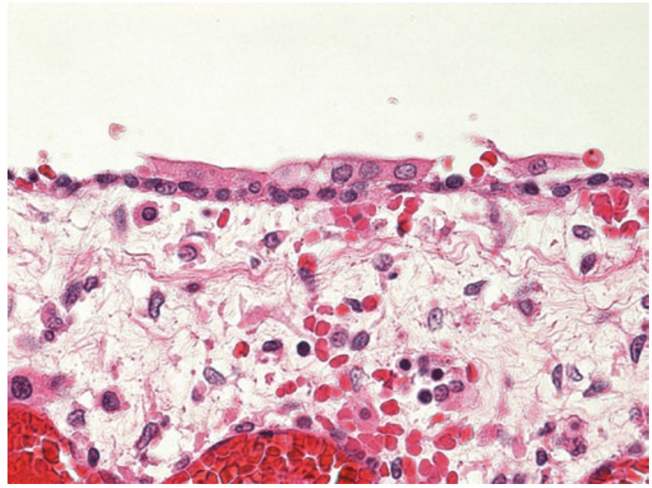

Fig. 31.30 Higher magnification of Fig. 31.28, depicting the thin epithelial lining of the tympanic cavity at 23 weeks gestation. The thin epithelial lining over the thick mesenchyme is simple cuboidal epithelium, which often falls off owing to mild autolysis, as seen in this section. Mild extramedullary hematopoiesis is present (H&E, 60×)

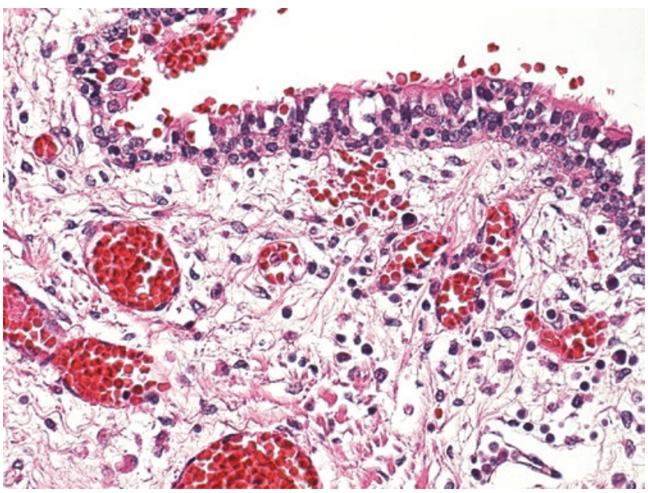

Fig. 31.31 Higher magnification of Fig. 31.28, depicting the thicker epithelial lining of the corner of the tympanic cavity at 23 weeks. Pseudostratified, ciliated columnar epithelium lines the corners and crevices of the tympanic cavity. Mild extramedullary hematopoiesis is present (H&E, 40×)

Fig. 31.32 Tympanic cavity at 38 weeks gestation. The membrane separating the lumen of the external auditory canal (EAC) from the tympanic cavity (TC) is the tympanic membrane. The handle of the malleus is attached to its inner surface. The irregular common bony wall between the tympanic cavity and the cavity of the vestibule is depicted. Toward the end of pregnancy, the masses of edematous mesenchyme that filled the tympanic cavity earlier in pregnancy have mostly disappeared, leaving a wide-open tympanic cavity. Only thin remnants of the mesenchyme remain covering the bony wall in the upper right and between the round and oval windows. The radial ligament at the bottom (*arrows*) attaches the edges of the head of the stapes to the inner edge of the oval window. Only a thin layer of mesenchyme surrounds the handle of the malleus, in contradistinction to the masses of mesenchyme in which the ossicles were buried earlier in pregnancy (H&E, 4×). *RW* round window enclosed by the secondary tympanic membrane, *ST* scala tympani, *SV* scala vestibuli

pletely disappears, including that surrounding the ossicles and the tendon of the tensor tympani muscle. The lining epithelium lies directly upon the underlying bone and the ossicles, and the mucosa becomes a mucoperiosteum (Figs. 31.35 and 31.36). The ossicles become fully mobile for the first time, allowing auditory signals, which previously could reach the inner ear only by bone conduction, to now reach the inner ear through the tympanic membrane and ossicles. The tall, pseudostratified, ciliated columnar endothelium in the corners and crevices may increase in thickness (Fig. 31.37). During the late fetal and neonatal periods, the mucosa around the opening of the Eustachian tube may form complex rugae. The normal epithelium in this area may contain a few mucus-producing cells (Fig. 31.38), but the presence of serous or mucous glands or large numbers of goblet cells anywhere in the mucosa of the tympanic cavity is abnormal and is probably a metaplastic response to excessive amniotic fluid or infection. Before birth, the tympanic cavity contains amniotic fluid and debris. After birth, it contains air.

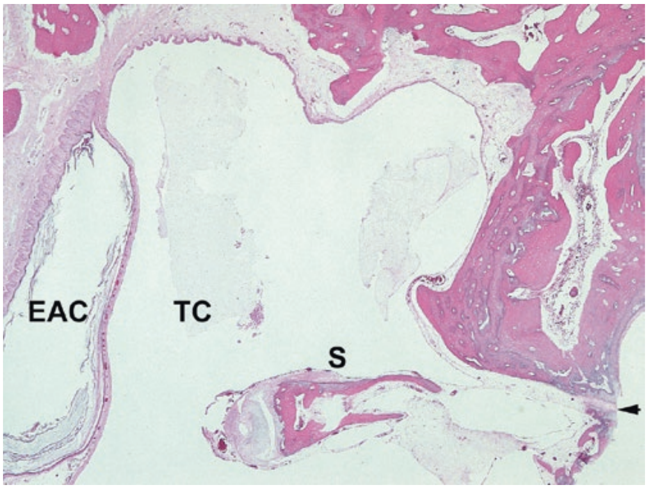

Fig. 31.33 Another view of the tympanic cavity (TC) at 38 weeks gestation, from the same patient depicted in Fig. 31.32. The membrane separating the lumen of the external auditory canal (EAC) from the tympanic cavity is the tympanic membrane. The cavity is wide open. A thin layer of edematous mesenchyme remains covering the bony wall only at the upper end of the cavity. The articular head and limbs of the stapes (S) are visible, along with the radial ligament (*arrow*), which anchors the foot plate of the stapes in the oval window. The mesenchyme covering the stapes is very thin. The incudostapedial diarthrodial joint is also visible (H&E, 2×)

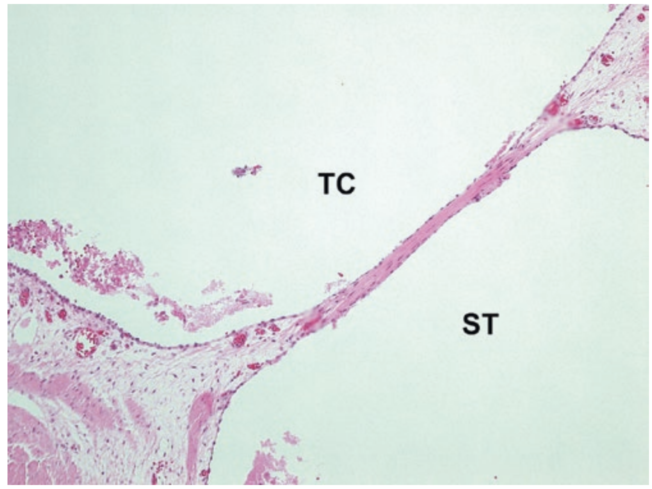

Fig. 31.34 The secondary tympanic membrane at 38 weeks gestation. The secondary tympanic membrane encloses the round window. The space above and to the left of the round window is the tympanic cavity (TC). The space below and to the right of the window is the scala tympani (ST), which ends blindly at the round window. The secondary tympanic membrane is a delicate, trilayered sandwich composed of a thin middle layer of connective tissue covered on its tympanic surface by a single layer of squamous epithelial cells (a continuation of the epithelial lining of the tympanic cavity) and covered on its vestibular side by a single layer of squamous periotic reticular cells (a continuation of the reticular lining of the scala tympani). Earlier in pregnancy, the tympanic surface of the secondary tympanic membrane is buried under a mass of edematous mesenchyme (H&E, 10×)

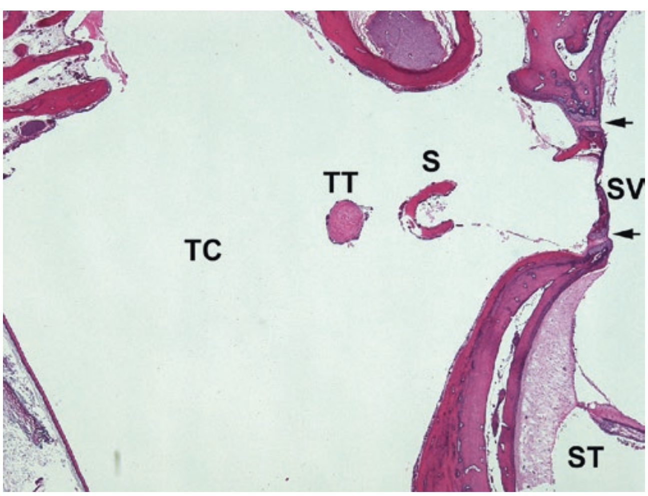

Fig. 31.35 The tympanic cavity (TC) at 6 months postnatal age. The lumen of the external auditory canal is in the lower left. The membrane in the lower left that separates the lumen of the external auditory canal from the tympanic cavity is the tympanic membrane. In the lower right, the structure separating the scala vestibuli (SV) from the scala tympani (ST) is the basal turn of the cochlear duct. The cavity is wide open. The edematous mesenchyme is completely absent. The stapes (S, with limbs tangentially cut) and the tendon of the tensor tympani muscle (TT) are devoid of a mesenchymal covering. The radial ligament (*arrows*) attaches the foot plate of the stapes in the oval window. Note the common bony wall between the tympanic cavity and the perilymphatic spaces of the inner ear (H&E, 2×)

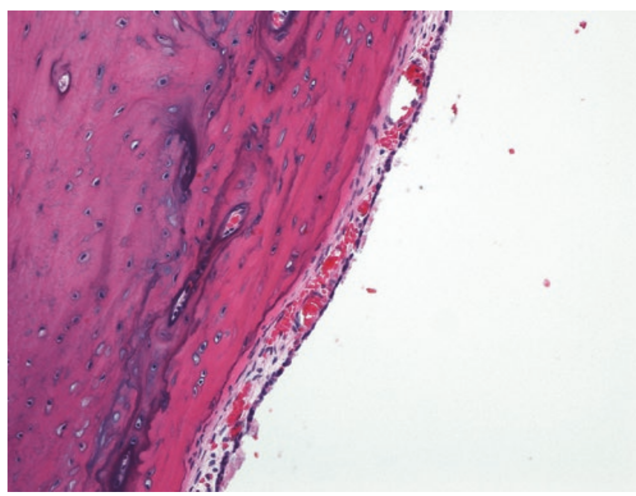

Fig. 31.36 The mucoperiosteum of the tympanic cavity at 6 months postnatal age. This is a higher magnification of Fig. 31.35, depicting the epithelial lining of the tympanic cavity. A single layer of squamous cells and a very thin layer of subepithelial connective tissue cover the bony wall of the tympanic cavity. This epithelial lining is called the *mucoperiosteum* (H&E, 20×)

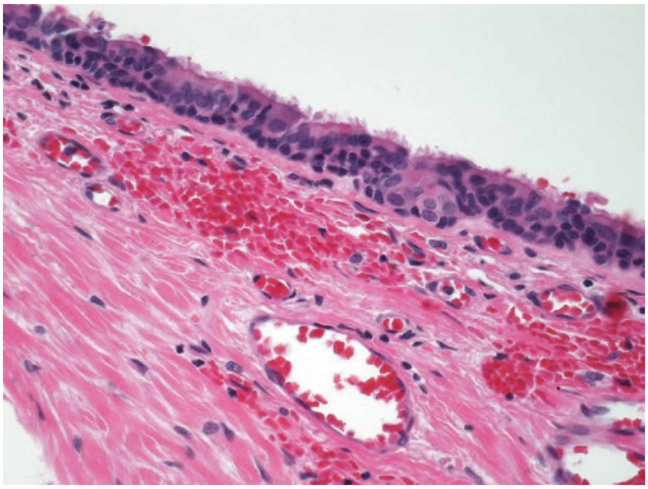

Fig. 31.37 The thicker epithelial lining of the corners and crevices of the tympanic cavity at 6 months postnatal age. This is a higher magnification of Fig. 31.35, showing the pseudostratified, ciliated cuboidal and columnar epithelium, which covers the recesses of the tympanic cavity (H&E, 40×)

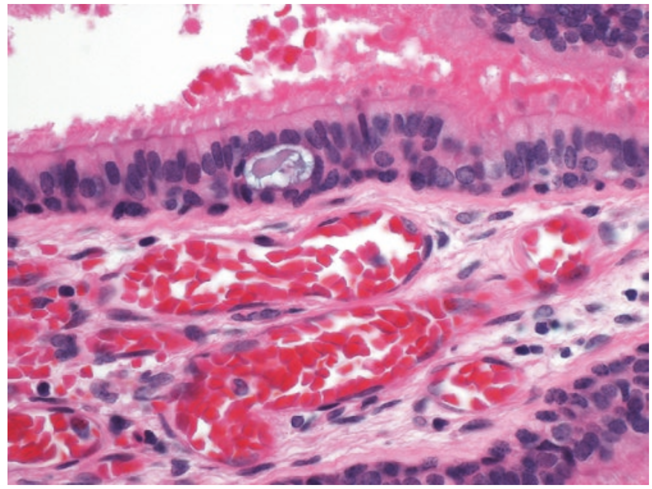

Fig. 31.38 The epithelial lining of the tympanic cavity near the opening of the Eustachian tube at 6 months postnatal age from the same patient as the previous three figures. The mucosal lining of the cavity near the opening of the Eustachian tube is rugated, and the pseudostratified, ciliated columnar epithelium may contain occasional mucus-producing cells. Mucus-producing cells should not be seen in other parts of the cavity (H&E, 60×)

Eustachian Tube

The short segment of the tympanic end of the Eustachian tube is supported by a bony wall. The remainder of the tube is supported by a wall of elastic cartilage. The entire length is lined by pseudostratified, ciliated columnar epithelium. Its pharyngeal cartilaginous end includes seromucous glands and lymphoid organs referred to as *Gerlach's tubal tonsils*. Like all lymphoid tissues, these do not develop germinal centers or mature plasma cells until 2–6 weeks postnatal age.

Inner Ear

Otic Capsule

Ossification of the otic capsule begins only after the cartilaginous capsule reaches adult size at 16 weeks. Multiple sites of ossification appear during the 16th week. Ossification of the otic capsule is complete by the 24th week [2]. The otic capsule is seen in many sections of the cochlea, vestibule, and semicircular canals. It is a thin rim of very dense, often basophilic, bone, which is distinct from the petrous bone in which it is embedded.

Perilymphatic Space

The formation of the perilymphatic space of the inner ear occurs during fetal life [11, 12, 14]. As early as the tenth week, the mesenchyme of the inner surface of the cartilaginous osseous labyrinth becomes vacuolated and is transformed into a reticulum called the *perilymphatic reticulum*. The reticulum is gradually resorbed, which results in the formation of a space, the perilymphatic space, between the osseous labyrinth and the membranous labyrinth. This space contains the perilymphatic fluid. This process begins in the scala tympani, then extends into the scala vestibuli, and finally spreads throughout the vestibule and into the semicircular canals. The scala tympani and scala vestibuli are completely devoid of reticulum by the end of the 12th postfertilization week (Figs. 31.39 and 31.40). The process may be completed in the vestibule and then in the semicircular canals at any gestational age from 20 weeks to term, but the perilymphatic reticulum may never be completely resorbed from parts of the vestibule and semicircular canals in some individuals. The periotic reticulum forms the perichondrium of the cartilaginous otic capsule and presumably the periosteum of the osseous otic capsule. Several of the figures of the vestibule and semicircular canal demonstrate various degrees of resorption of the perilymphatic reticulum.

Cochlear Aqueduct and Periotic Duct

The development of the periotic duct and cochlear aqueduct is related to the development of the perilymphatic space and the otic capsule and is completed during the fetal period. The primitive periotic duct develops in conjunction with the inferior cochlear vein and its bony canal and Hyrtl's fissure

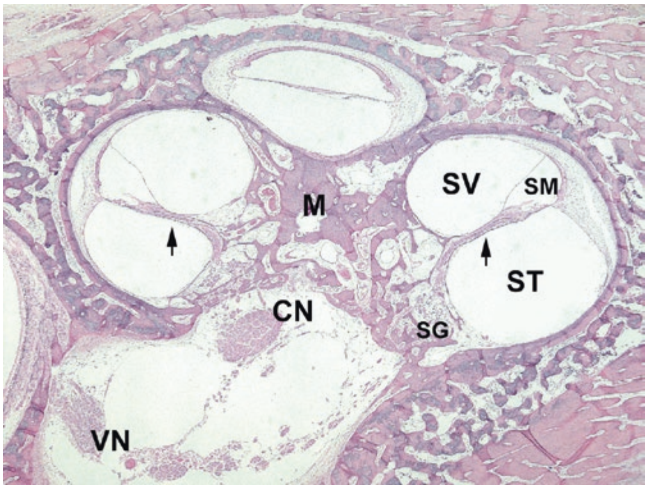

Fig. 31.39 Cross section of the cochlea at 27 weeks gestation. Three sections of the spiral bony cochlear canal are shown around the central bony core of the cochlea, the modiolus (M), like the leaves of a three-leaf clover. The two on either side of the modiolus in this image are nearly perfect cross sections, which are mirror images of each other. They are near the base of the cochlea. The one at the top of the modiolus is an oblique section. It is toward the apex (cupola) of the cochlea. The bony spiral laminae (*arrows*) extend like arms from the edge of the modiolus into the lumen of the cochlear canal. The modiolus is traversed by multiple channels to accommodate fibers of the cochlear nerve (CN). Lacunae at the edge of the modiolus contain the spiral cochlear ganglia (SG). At the bottom of the modiolus, the multiple channels and spaces empty into a large canal within the bone, the internal auditory canal. Small branches of the cochlear nerve stream through these fenestrae into the canal and join together to form larger branches of the cochlear nerve, one of which is seen in the canal (CN). The space at the bottom right edge is the saccule of the membranous labyrinth within the vestibule. Small fibers of the vestibular nerve (VN) stream from the saccular otolithic macula through fenestra in the bony wall of the vestibule to join together to form larger branches of the vestibular nerve within the internal auditory canal, one of which is seen in the canal (VN). Each of the three sections of the cochlear canal is surrounded by a thin rim of very dense bone, the otic capsule of the cochlea. Note its distinction from the surrounding petrous bone. The medial ends of the bony walls end in the modiolus. At the bottom of the modiolus, they end in the bony wall of the external auditory canal. The saccule is surrounded by a similar thin bony wall, the otic capsule of the vestibule. The bony cochlear canal is divided into three channels, which are clearly depicted in the two perfect cross sections. The central triangular channel is the cochlear duct (also called the *scala media*, SM) of the membranous labyrinth. It contains endolymph and ends blindly at both ends, one at the apex of the cochlea and the other in the vestibular cistern below the saccule. The channel above the cochlear duct is the scala vestibuli (SV), which ends in the vestibular cistern near the oval window. The channel below the cochlear duct is the scala tympani (ST), which ends blindly at the round window. The details of the cross section of the canal to the right of the modiolus are seen in the following four figures (H&E, 2×)

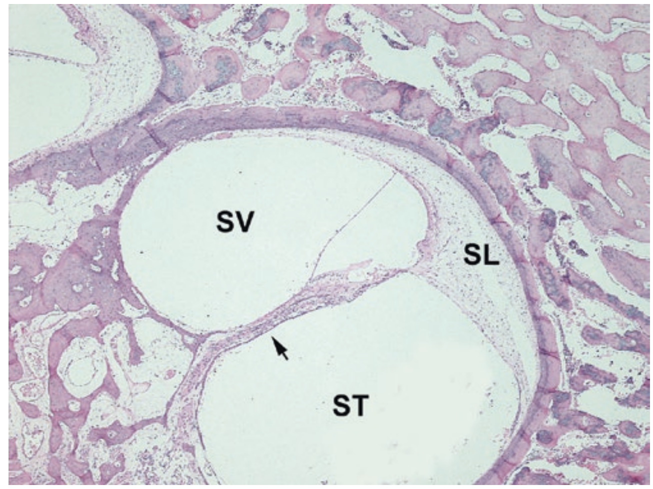

Fig. 31.40 Higher magnification from Fig. 31.39 depicting the bony cochlear canal and the membranous cochlear duct at 27 weeks gestation. The modiolus is to the left. The bony wall of the canal is the distinct, thin, blue rim of dense bone around the lateral wall of the canal. It curves over the top of the canal and then medially to join the modiolus. It curves around the bottom of the canal and off the bottom edge of the picture. In Fig. 31.39, it can be seen to fuse with the junction of the modiolus and the wall of the internal auditory canal. The bony spiral lamina (*arrow*) arises from the modiolus and extends like an arm halfway across the equator of the canal, bisecting its lumen. The periosteum along the inner surface of the lateral wall of the bony canal is thickened to form a pyramidal cushion of stroma. This cushion is the spiral ligament (SL). Its apex, the crest of the spiral ligament, extends into the lumen of the canal along its equatorial plane, opposite the spiral lamina. A membrane, the basal membrane, extends from the tip of the spiral lamina to the crest of the spiral ligament. This is the base or floor of the cochlear duct. A delicate membrane, Reissner's membrane, extends from the upper surface of the tip of the spiral lamina diagonally upward and inserts into the spiral ligament near its upper end. The triangular duct formed by the basal membrane, Reissner's membrane, and the spiral ligament is the cochlear duct (H&E, 4×). *ST* scala tympani, *SV* scala vestibuli

(the tympanomeningeal fissure). The periotic duct forms a direct communication between the scala tympani component of the perilymphatic space and the subarachnoid space. Hyrtl's fissure forms a direct continuation between the tympanic cavity and the subarachnoid space and is separate from the cochlear aqueduct and periotic duct. In early fetuses, subarachnoid hemorrhage in the posterior fossa commonly spreads into the perilymphatic space of the inner ear through the periotic duct and into the tympanic cavity through Hyrtl's fissure. By 24 weeks, Hyrtl's fissure is closed, and the direct communication between the subarachnoid space and the tympanic cavity is lost. The direct communication between the subarachnoid space and the perilymphatic space through the periotic duct becomes permanent. Therefore, after 24 weeks, subarachnoid hemorrhage in the posterior fossa may spread through the periotic duct into the inner ear but not into the tympanic cavity [2].

Cochlear Duct

During the 11th week, the cochlea and cochlear duct attain their final length, and their spirals consist of two and three-quarter turns [11, 14]. Growth and maturation of the organ of Corti begins at the base of the cochlear duct as a thickening in the epithelium in one side of the round cochlear duct. This side of the wall becomes flat and forms the basal membrane or floor of the mature cochlear duct. The tall, columnar epithelium covering the floor of the developing organ of Corti

Fig. 31.41 Higher magnification of Fig. 31.40 depicting the cochlear duct (also called the *scala media*, SM) at 27 weeks gestation. The two thin lamina of bone, upper and lower, that constitute the spiral lamina are apparent at this magnification. The basal membrane stretches from the tip of the spiral lamina to the crest of the spiral ligament (SL). The stria vascularis (StV) forms the surface of the spiral ligament between the insertion of Reissner's membrane (RM) above and the spiral prominence, the bump immediately above the crest of the spiral ligament below. Note the thin, dense otic capsule (H&E, 10×). *ST* scala tympani, *SV* scala vestibuli

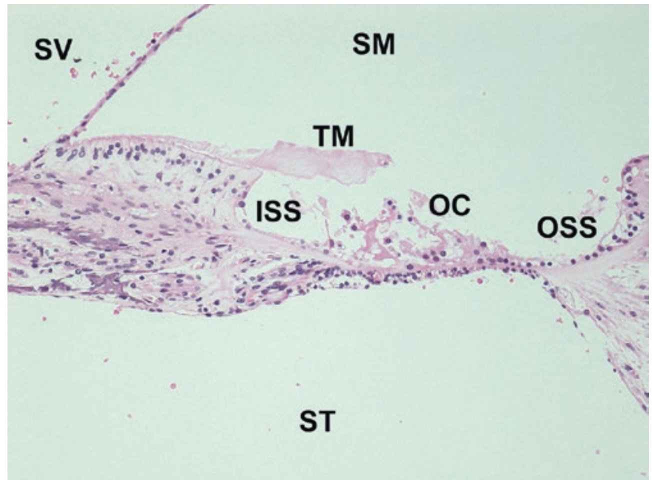

Fig. 31.42 Higher magnification of Fig. 31.41 depicting the organ of Corti (OC) at 27 weeks. In routine sections, the organ of Corti is typically severely fragmented. This is one of the best-preserved examples found among the many cases in our material. The tectorial membrane (TM) often survives. The two bony lamina of the spiral lamina are clearly depicted. Tiny nerves pass from the neurosensory cells of the organ of Corti through the spiral lamina between its two laminae to enter the spiral cochlear ganglia in the modiolus. See Fig. 31.8 for more details (H&E, 20×). *ISS* inner spiral sulcus, *OSS* outer spiral sulcus, *SM* scala media, *ST* scala tympani, *SV* scala vestibuli

continues to become thicker and develops two longitudinal ridges separated by a valley—a larger inner ridge nearer the center of the spiral and a smaller outer ridge nearer the lateral wall of the spiral. The tall epithelium of the larger, inner ridge secretes the gelatinous tectorial membrane that covers the top of the epithelium. The outer, smaller ridge will become the organ of Corti. By 14 weeks, the round cochlear duct has attained its mature triangular shape in cross section. The floor of the duct is the basal membrane containing the organ of Corti. The wall opposite the basal membrane is the vestibular or Reissner's membrane, which is the roof of the cochlear duct. Reissner's membrane and the basal membrane join to form an acute angle, the apex of the triangle, toward the center of the cochlear spiral. The lateral wall of the triangle is formed by the stria vascularis and the spiral ligament. The space above Reissner's membrane is the scala vestibuli. The space below the floor is the scala tympani. By 14 weeks, the inner and outer hair cells and the pillar cells are present. The inner margin of the tectorial membrane is attached to the spiral limbus, and the free outer edge is embedded in the cilia of the inner and outer hair cells. By 16 weeks, the epithelial cells of the inner ridge degenerate and disappear, forming the inner spiral sulcus. The tectorial membrane stretches across the inner spiral sulcus. Cells between the inner and outer hair cells degenerate and disappear, forming the tunnel of Corti. The development of the organ of Corti approaches completion as early as 20 weeks gestation [14], when primitive fetal response to auditory stimuli received through bone conduction is first detectable. The development of the organ of Corti may not be complete until 25 weeks or later in some fetuses. This discrepancy may be explained in part by the fact that maturation begins at the base of the cochlear duct and progresses toward the apex of the spiral, so that the time of complete maturation will depend upon where along the spiral the section is obtained (see Figs. 31.4 and 31.40). The sophistication with which the fetus responds to auditory stimuli increases simultaneously with the increasing maturation of the organ of Corti as gestational age advances. The organ of Corti is often autolyzed in routine sections even in otherwise well-preserved specimens (Figs. 31.41 and 31.42). Reissner's membrane is delicate and trilayered. Its inner cochlear surface is covered by simple squamous epithelium derived from the ectoderm of the otic vesicle. The inconspicuous middle layer is a wisp of connective tissue. The outer vestibular surface is covered by simple squamous epithelium derived from the periotic reticulum. The histology of all free walls of the membranous labyrinth in the saccule, utricle, and semicircular ducts is similar to that of Reissner's membrane (see Figs. 31.40, 31.41, and 31.42). The spiral ligament is a thick, curved, pyramidal pad of stroma on the inner surface of the lateral bony wall of the cochlea. It forms the lateral wall of the cochlear duct. It is thickened periosteum and may be a specialized remnant of the periotic reticulum (see Figs. 31.40 and 31.41). The stria vascularis is a unique vascularized, stratified epithelial membrane on the surface of the spiral ligament. Its surface is a single layer of dark, eosinophilic, cuboidal cells referred to as *dark cells* or *marginal cells*. Deep to the dark cells is a thick layer of haphazardly arranged, more lightly stained

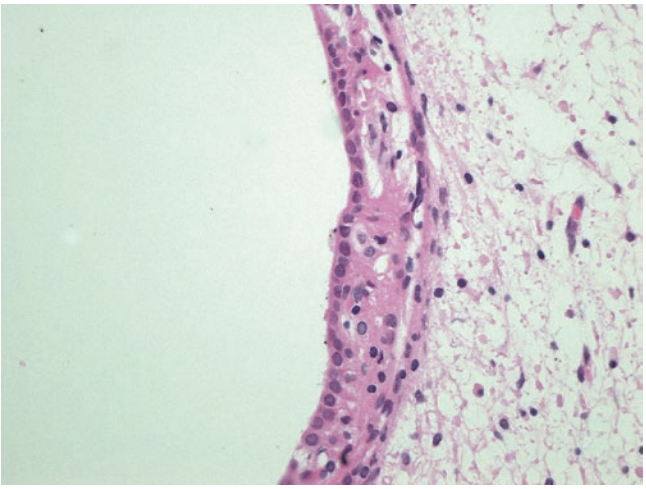

Fig. 31.43 The stria vascularis at 27 weeks gestation, from the same specimen shown in Figs. 31.39, 31.40, 31.41, and 31.42. The stria vascularis is a layer of vascularized, stratified epithelium. The surface is covered by a single layer of dark, eosinophilic cuboidal cells referred to as *dark cells* or *marginal cells*. Deep to the dark cells is a thick layer of haphazardly arranged, more lightly stained polygonal cells referred to as *light cells* or *basal cells*. There are numerous capillaries in the layer of light cells. The stroma of the spiral ligament lies beneath the stria vascularis (H&E, 60×)

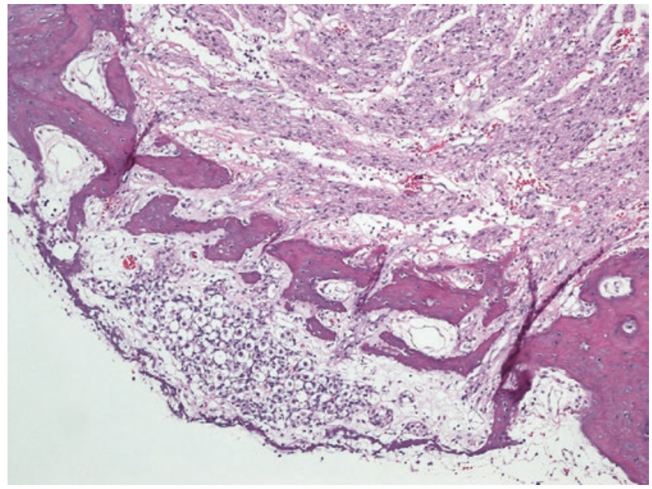

Fig. 31.44 The spiral cochlear ganglion at 27 weeks gestation. The ganglion is in the left lower corner. Nerve fibers pass through numerous fenestrae in the bone to join a branch of the cochlear nerve in the upper left corner (H&E, 10×)

polygonal cells referred to as *light cells* or *basal cells*. There are numerous capillaries in the layer of light cells. Epithelial membranes are characteristically not vascularized. The stria vascularis may be the only vascularized epithelial membrane in the human body and is thought to contribute to the maintenance of the volume and ionic makeup of the endolymph (Figs. 31.41 and 31.43). The nerves from the sensory hair cells pass through channels in the center of the spiral lamina (see Fig. 31.42) and join the spiral ganglion in the periphery of the modiolus. Nerves from the spiral ganglion pass through bony channels and join to form larger nerves in the modiolus (Fig. 31.44). Branches of the cochlear and vestibular nerve join to form the eighth cranial nerve in the internal auditory canal and exit the posterior wall of the petrous bone through the internal auditory meatus (Fig. 31.45).

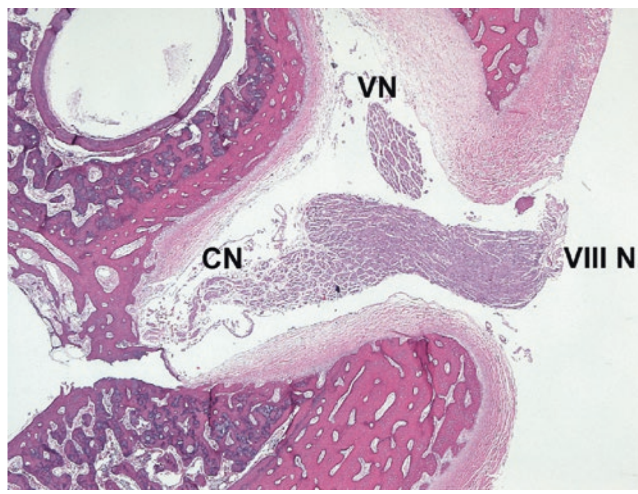

Fig. 31.45 The internal auditory meatus at 27 weeks, from the same specimen as Fig. 31.44. The vestibular nerve (VN) and the cochlear nerve (CN) join together in the internal auditory canal to form the eighth cranial nerve (VIII N.), which passes through the canal and exits through the internal auditory meatus in the posterior wall of the petrous bone (H&E, 2×)

Vestibular System

The delicate membranes of the saccule and utricle are usually destroyed in routine sections of even well-preserved specimens of the middle and inner ears (Fig. 31.46). Occasionally these structures are reasonably intact in routine sections (Figs. 31.47 and 31.48). The periotic reticulum of the saccule, utricle, and semicircular ducts may be incompletely resorbed in some fetuses of mid to late gestational ages (Figs. 31.47, 31.48, and 31.49).

The progression of maturation of the utricular and saccular maculae and the ampullary cristae is similar [11, 14]. They first appear at 10 weeks, and their maturation is complete by 14 weeks. They differ in that the maculae are ellipsoid plaques covered by gelatinous otolithic membranes (see Figs. 31.9, 31.10, 31.11, 31.50, 31.51, 31.52, 31.53, 31.54, and 31.55), whereas the cristae are narrow transverse ridges capped by gelatinous tongue-like membranes called the *cupola*, without otoliths (see Figs. 31.9, 31.12, 31.13, 31.53, and 31.56). At 10 weeks, the maculae and cristae are composed of a thick layer of two types of epithelial cells: ciliated neurosensory cells and supportive cells. The tall epithelial cells surrounding the sensory organs secrete a gelatinous membrane in which the cilia of neurosensory cells are embedded. In the maculae, this

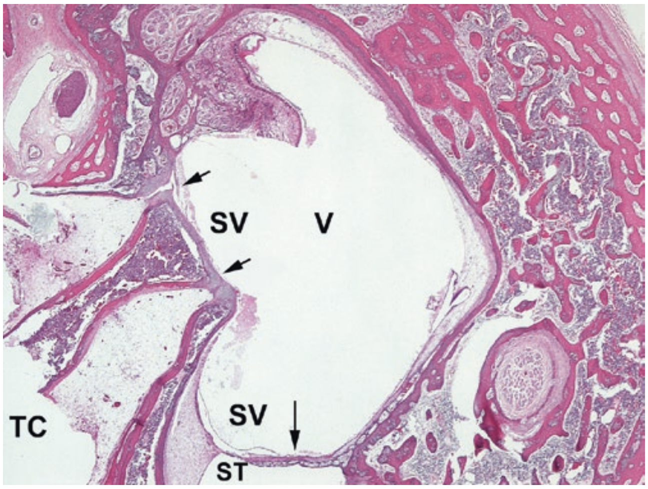

Fig. 31.46 The vestibule (V) and its junction with the cochlea at 24 weeks gestation. SV in the mid vestibule indicates the scala vestibuli adjacent to the oval window; SV in the lower end of the vestibule is the scala vestibuli at the junction of the basal turn of the cochlea with the vestibule, also the site of the scala tympani (ST). At the middle left is the footplate of the stapes, which is anchored in the oval window by the radial ligament (*short arrows*). The delicate membranes of the saccule and utricle of the membranous labyrinth, which should be seen in the vestibule, are not seen because they were destroyed during removal and sectioning of the specimen as almost always occurs. The membranous labyrinth is more well-preserved in the following figures. The thin bony otic capsule of the vestibule is distinct from the petrous bone. The junction of the cochlea with the vestibule is at the bottom of the vestibule, where the *long arrow* points to the spiral lamina and basal membrane of the cochlear duct. Reissner's membrane is almost completely collapsed. The crest of the spiral ligament is clearly seen (H&E, 2×)

Fig. 31.47 The vestibule and its junction with the lateral semicircular canal at 23 weeks gestation. In contrast to the previous figure, this membranous labyrinth is unusually well preserved. The otic capsule is distinct from the surrounding petrous bone. The periotic reticulum of the ampulla of the lateral semicircular duct (A) has not been completely resorbed. The *bidirectional arrow* marks the opening of the ampulla into the utricle (U). The walls of the utricle and the saccule (S) are partially disrupted. A fragmented membrane of unknown origin lies between the utricle and the saccule (H&E, 2×). *C* crista of the ampulla

Fig. 31.48 Vestibule at 27 weeks gestation. A partial cross section of the cochlear canal and duct are seen at the lower right. The otic capsule of the cochlea and vestibule is clearly visible. The saccule (S) is distinguished from the utricle (U) by its location closest to the cochlea. The otolithic macula of the utricle is the thickened plaque in its wall closest to the saccule. The otolithic macula of the saccule is the thickened area in its wall closest to the utricle. Nerve fibers from the two otolithic maculae pass through fenestra in the bone and join together to form the branch of the vestibular nerve (VN) seen here in a canal within the otic capsule of the vestibule (H&E, 2×). *ST* scala tympani, *StV* stria vascularis, *SV* scala vestibuli

membrane is flat and covers the entire surface of the ovoid organ. In the cristae, it is a tongue-shaped membrane called the *cupola*, which arises from the apex of the full length of the crista and extends like a valve flap into the lumen. A thick layer of stromal cells and nerves beneath the epithelium adds to the thickness of the organs. By the 14th week, the free surfaces of the membranes of the otolithic saccular and utricular maculae contain basophilic crystals of calcium carbonate and protein called otoliths, so that the maculae are referred to as *otolithic membranes* (see Figs. 31.11, 31.52, 31.54, and 31.55). The microscopic appearance of the otoliths varies. In some sections, they are nearly invisible (Fig. 31.52). In others, they are small and round, or in some others, they may be irregular and oblong (Fig. 31.54). In still others, the otolithic membranes may be fragmented and lie in the lumen of the labyrinth, in which case they are easily mistaken for infectious organisms (Fig. 31.55). In contrast, the membranes of the cristae, the cupola, are devoid of otoliths and lengthen to stretch across almost the entire lumen of the ampullae (see Figs. 31.12, 31.13, and 31.56).

The semicircular canals may be seen in perfect cross sections (Figs. 31.57 and 31.58) or in oblique sections of various degrees (not illustrated). The bony wall of the canal, the otic capsule, is distinct from the surrounding petrous bone. The duct is attached to the inner surface of the bony canal by perilymphatic reticulum. The canal is lined by the simple squamous epithelium that is derived from the perilymphatic reticulum and serves as peri-

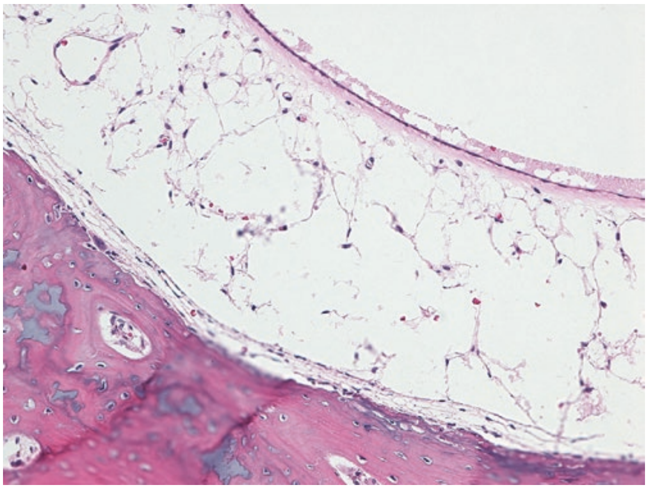

Fig. 31.49 Higher magnification of the left lower wall of the saccule in Fig. 31.48, depicting the periotic reticulum of the saccule at 27 weeks gestation. The lumen of the saccule is in the upper right. The otic capsule is in the lower left. The lining of the saccule is a single layer of flat epithelium common to the entire membranous labyrinth. The periotic reticulum fills the space between the epithelial lining of the saccule and the otic capsule (H&E, 20×)

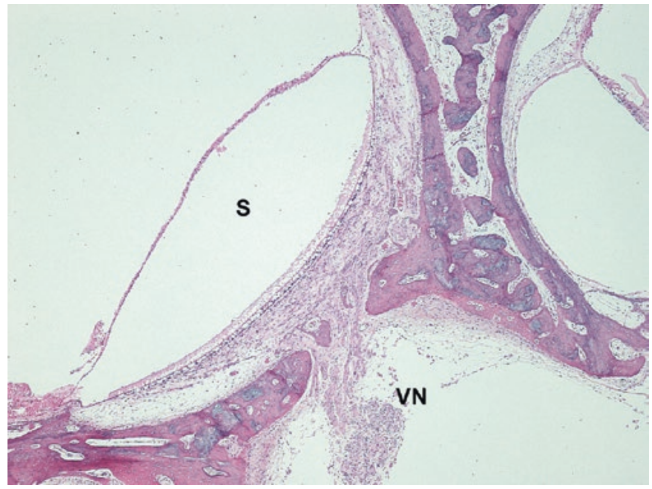

Fig. 31.50 An unusually well-preserved saccule (S) at 27 weeks gestation. The basal turn of the cochlear canal and duct appear in the upper right corner. The otic capsule of the vestibule and cochlea is unusually well delineated. The delicate free wall of the saccule, like Reissner's membrane, is trilayered: The middle layer is connective tissue. The inner surface is covered by simple squamous epithelium characteristic of the membranous labyrinth. The outer surface is covered by the simple squamous reticular epithelium of the periotic reticulum. The opposite wall is secured to the inner surface of the otic capsule by the thick saccular otolithic membrane. Fine peripheral nerve filaments from the neurosensory hair cells of the macula pass through the subepithelial stroma of the macula and then through multiple fenestra in the otic capsule to join together in the internal auditory canal to form the branch of the vestibular nerve (VN) seen here (H&E, 4×)

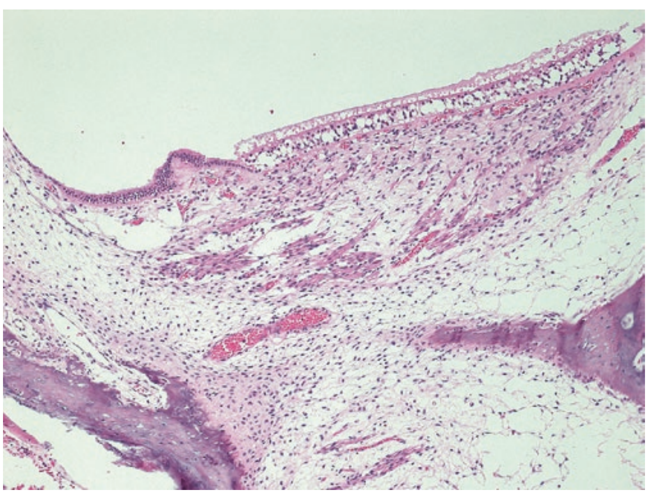

Fig. 31.51 Saccular otolithic macula at 27 weeks gestation. This is a higher-magnification view of the same specimen seen in Fig. 31.50. Nerve fibers from the macula pass through fenestra in the bony otic capsule (H&E, 10×)

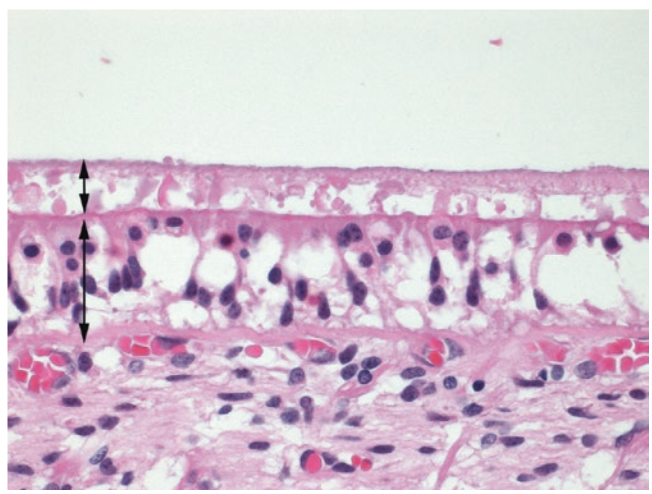

Fig. 31.52 Higher magnification of Fig. 31.51, depicting the saccular otolithic macula at 27 weeks gestation. A gelatinous membrane (*short arrow*) covers the surface of the epithelial layer of the macula, which consists of several layers of vertically oriented cells (*long arrow*). Even in this relatively well-preserved specimen, the epithelial cells are mildly autolyzed. Some of the hair cells can be recognized; their cilia are embedded in the deep surface of the gelatinous membrane. A basement membrane lies beneath the epithelium. The cells of the subepithelial stroma are predominantly horizontally oriented, and the stroma contains numerous tiny nerve fibers and capillaries. Coarse basophilic crystals, called *otoliths* or *otoconia*, are usually seen on the surface of the gelatinous membrane but are not visible here. See also Fig. 31.11 for details and compare with Fig. 31.54 (H&E, 60×)

Fig. 31.53 Higher magnification of Fig. 31.47, depicting the junction of the ampulla (A) of the lateral semicircular duct with the utricle (U) at 27 weeks gestation. The *arrow* marks the opening between the ampulla and the utricle. The utricular otolithic macula (M) is the thick blue lining of the utricle in the right lower corner (H&E, 4×). *C* crista of the ampulla

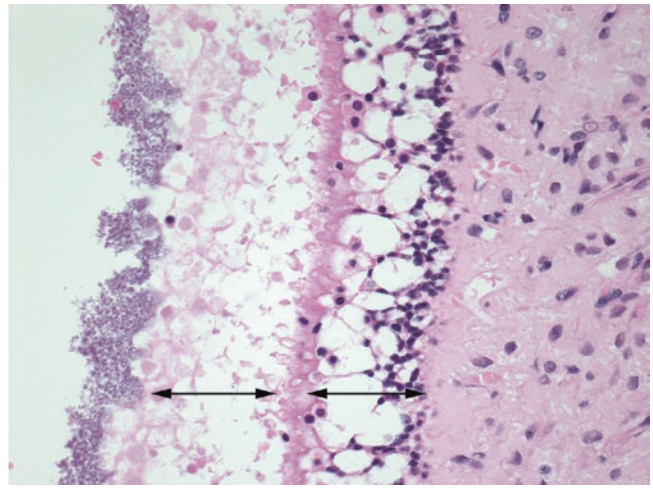

Fig. 31.54 Higher magnification of Fig. 31.53 depicting the utricular otolithic macula at 27 weeks gestation. The *arrow on the left* indicates the gelatinous membrane covering the surface of the epithelium. The *arrow on the right* indicates the sensory epithelial membrane. Numerous coarse basophilic crystals, the otoliths, are embedded in the surface of the gelatinous membrane, unlike the otolithic macula seen in Fig. 31.52. See also Fig. 31.11 for details and the text for a discussion of variability in the appearance of the otoliths (H&E, 40×)

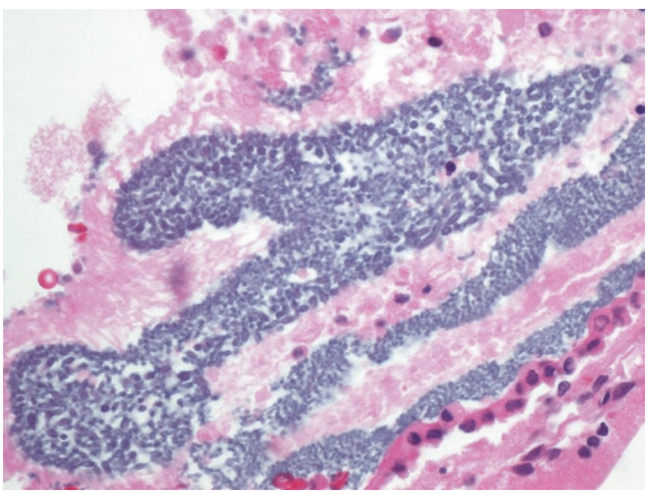

Fig. 31.55 Fragments of an otolithic membrane lying free in the vestibular cistern at 27 weeks gestation. The deeply basophilic otoliths in this section vary from coarse and elongate in the upper layer to small and round in the lower layer. These are easily mistaken for infectious organisms. Compare with the otoliths in Fig. 31.52, which are nearly invisible, and those in Fig. 31.54, which are smaller and rounder than those in this section. See Fig. 31.11 for more details (H&E, 40×)

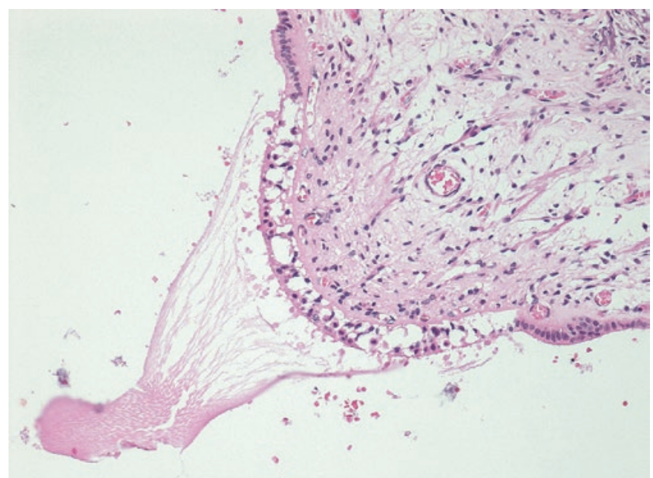

Fig. 31.56 Higher magnification of Fig. 31.53, depicting a cross section of the crista of the lateral semicircular ampulla at 27 weeks gestation. The stromal core of the crista, in the upper right corner, contains numerous small nerve fibers and capillaries. The strip of sensory epithelium forms a cap over the tip of the crista. It is mildly autolyzed. The gelatinous cupola is the eosinophilic, tongue-shaped flap that is attached to the sensory epithelium and extends toward the lower left. For details, see Fig. 31.13. Compare with the otolithic macula of the saccule and utricle in Figs. 31.11, 31.13, 31.52, and 31.54 (H&E, 20×)

osteum. The duct is lined by simple squamous epithelium derived from the ectodermal membranous labyrinth. Various amounts of perilymphatic reticulum may remain in the canal.

Endolymphatic Duct

The endolymphatic duct arises from the utriculosaccular duct and passes through the vestibular aqueduct of the vestibular otic capsule and into the dura. Its distal end is a large, dilated sac in the dura of the posterior wall of the petrous bone (see Figs. 31.1, 31.2, 31.4, 31.5, and 31.7). The narrow duct is lined by simple epithelium, which varies from squamous to cuboidal (Fig. 31.59). The large sac has a very irregular wall. The epithelial surface is thrown into numerous rugae and fjord-like inlets (Fig. 31.60). The epithelium ranges from simple low cuboidal to irregularly stratified cuboidal (Fig. 31.61).

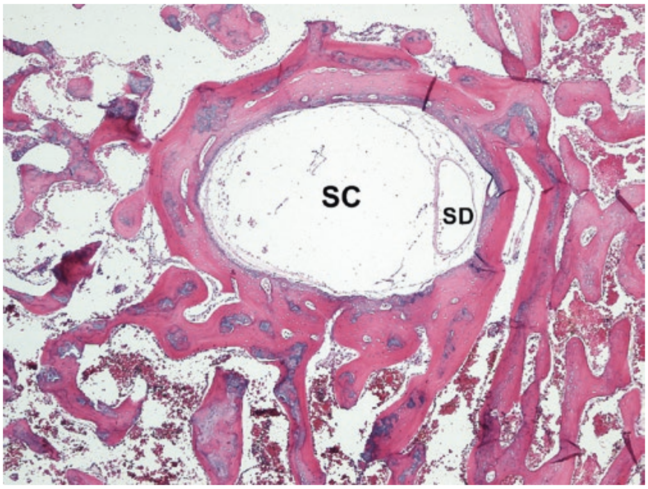

Fig. 31.57 Semicircular canal (SC) and semicircular duct (SD) at 27 weeks. The thin, bony otic capsule of the canal is distinct from the petrous bone in which it is embedded. Some periotic reticulum remains around the duct and the opposite side of the canal. The canal is lined by simple squamous periotic reticulum (H&E, 4×)

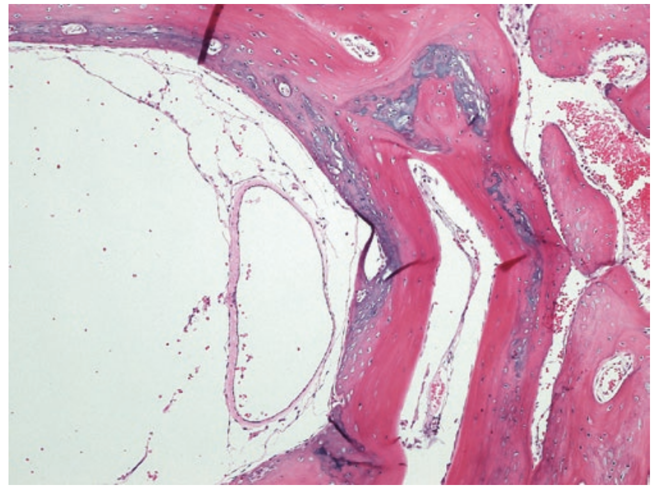

Fig. 31.58 Higher magnification of Fig. 31.57, depicting the semicircular duct at 27 weeks gestation. The duct is anchored to the wall of the canal by periotic reticulum. It is lined by simple squamous epithelium (H&E, 10×)

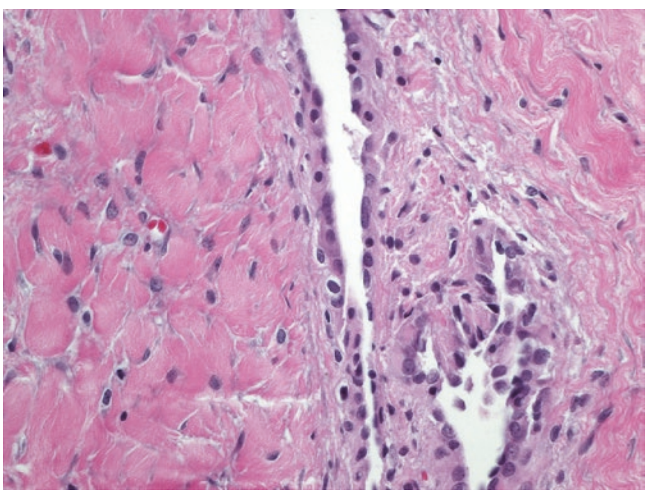

Fig. 31.59 Endolymphatic duct at 27 weeks. The duct in this section is located in the dura. It is lined by simple squamous and cuboidal epithelium. The irregular epithelial structure adjacent to the duct at the bottom right is the beginning of the endolymphatic sac (H&E, 40×)

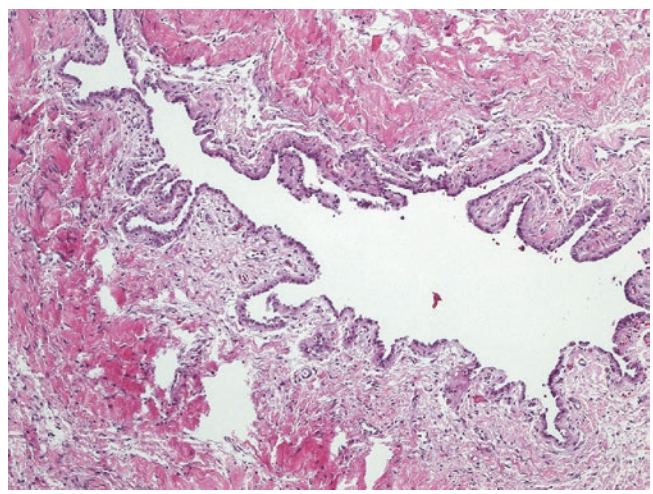

Fig. 31.60 Endolymphatic sac at 27 weeks gestation. The sac is a dilatation of the distal end of the duct. Its wall is extremely irregular, with numerous rugae and fjord-like inlets (H&E, 10×)

Special Considerations

Examination of the Ear in the Perinatal Period

Why should perinatal pathologists include the examination of the ears in perinatal autopsies? This question is frequently asked. At a time when perinatal autopsy pathology is forced to compete for resources with the increasing demands of pediatric surgical pathology, the tendency is to spend fewer resources on perinatal pathology, not more. Several factors challenge that tendency. First, most of us humans die before we are born. This is a difficult concept, but many studies show that between 60% and 80% of pregnancies end in embryonic or fetal death. Second, the ear is often involved in the major categories of causes of intrauterine diseases and deaths, such as congenital anomalies with or without chromosomal or gene defects, infections (either amniotic fluid infection sequence or transplacental infections), perfusion abnormalities (either maternal placental or fetal placental), and congenital tumors [16]. The intrauterine abnormalities of the ear often cause neonatal hearing loss in those who survive. Third, the rapidly advancing fields of fetal medicine, imaging, and surgery impart an increasing clinical relevance to perinatal pathology. If perinatal pathologists are to keep abreast of or lead our clinical colleagues in the study of perinatal diseases, we need to perform more perinatal autopsies, not fewer and, in more detail, not less—including the examination of the ears.

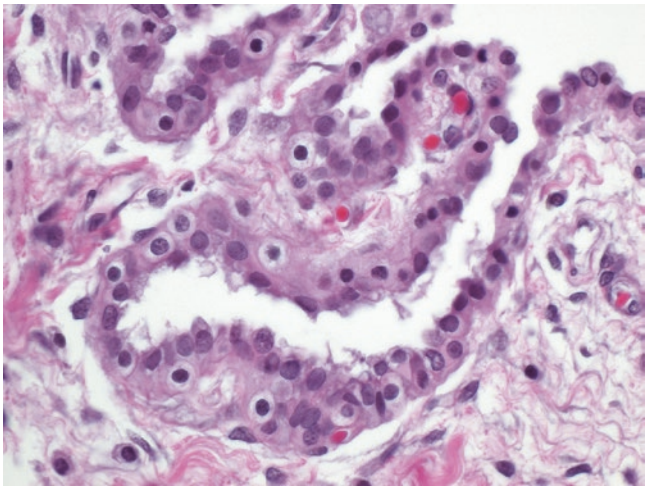

Fig. 31.61 Higher magnification of Fig. 31.60, depicting the epithelium of the endolymphatic sac at 27 weeks gestation. The sac is lined by simple and irregularly stratified cuboidal epithelium (H&E, 60×)

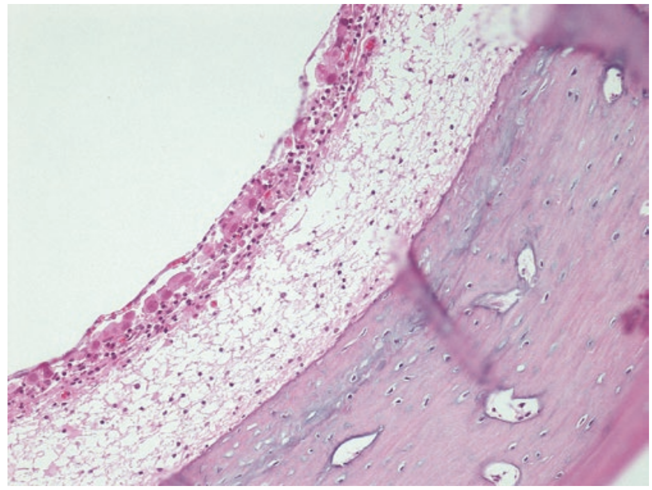

Fig. 31.62 Congenital cytomegalovirus infection of the cochlear duct at 37 days postnatal age in a baby born at 33 weeks gestation. The infected cells are in the stria vascularis overlying the stroma of the spiral ligament (H&E, 20×)

Examples of abnormalities of the ear that accompany perinatal death or threaten the hearing of those who survive are numerous [16–19]. The histologic continuum of normal aspiration of amniotic fluid, excessive aspiration of amniotic fluid, and amniotic fluid infection sequence is one of the most common findings in sections of the ear. Because the tympanic cavity is in direct continuity with the amniotic cavity through the Eustachian tube, and because the course of the Eustachian tube in fetuses and neonates is nearly horizontal, a small amount of amniotic debris is often seen in sections of the middle ear of fetuses and neonates. Normally, this small amount of amniotic debris is removed, as it is from the lung, but fetal distress may result in an excessive amount of amniotic debris in the tympanic cavity, similar to that occurring in the lung. Therefore, an excessive amount of amniotic debris in the tympanic cavity should suggest significant intrauterine fetal distress. In extreme situations, the amniotic debris may persist and incite a foreign-body inflammatory reaction resulting in polypoid nodules attached to the ossicles or the wall of the tympanic cavity. Glandular and squamous metaplasia of the lining epithelium may accompany retention of amniotic debris. This is more likely in neonates than in fetuses. In cases of amniotic fluid infection sequence, acute inflammatory debris and infectious agents—including cocci, bacilli, fungi, and spirochetes—may be found in the tympanic cavity. Acute inflammation of the embryonic mesenchyme of the tympanic cavity, the mucosa, or the subjacent bone indicates invasive otitis media. A normal amount of extramedullary hematopoiesis should not be mistaken for otitis media.

Blood-borne transplacental infections may affect the inner and middle ears of fetuses and newborns. Cytomegalovirus commonly involves the stria vascularis of the cochlear duct (Figs. 31.62 and 31.63) and the sensory organs of the saccule and utricle. Hearing loss is one of the most frequent clinical findings in congenital cytomegalovirus infection. Rubella, Herpes simplex infection, toxoplasmosis, and *Listeria* also may infect the middle or inner ears. H. simplex and *Listeria* infections can be either ascending or transplacental.

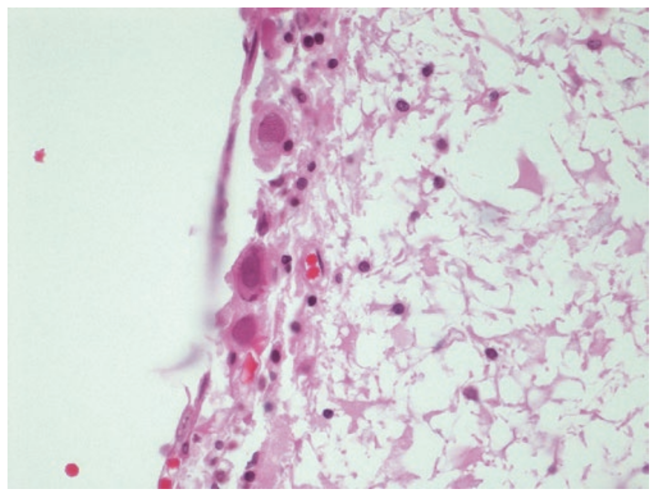

Fig. 31.63 Higher magnification of Fig. 31.62, depicting congenital cytomegalovirus infection of the cochlear duct at 37 days postnatal age. The infection has severely damaged the stria vascularis. Compare Fig. 31.43 (H&E, 60×)

Fetal distress may cause acute hemorrhage in the middle and inner ears, as it does in other organs. Acute abruptio placenta with subependymal, intraventricular, and subarachnoid hemorrhage is especially likely to be associated with severe hemorrhage of the middle and inner ears. One cause for the hemorrhage in the ears could be hypoxic-ischemic damage to the tissues of the middle and inner ears. Another reason could be the direct communication between the subarachnoid space and the inner ear through the periotic duct throughout fetal and neonatal life and the direct communication between the subarachnoid space and the tympanic cavity through Hyrtl's fissure prior to 24 weeks, when the fissure closes. These two communications allow subarachnoid hemorrhage in the posterior fossa to flow from the subarachnoid space into the inner and middle ears [7].

Rarely, congenital neuroblastoma, leukemia, teratoma, or Langerhans cell histiocytosis may involve the middle or inner ears. Many congenital anomalies affect the ears, but special care in removing and sectioning the temporal bone may be required to demonstrate many of these malformations.

Removing the Temporal Bone

The reliable demonstration of normal and pathologic histology depends upon the use of effective techniques in removal and sectioning of the temporal bone. Haphazard removal is likely to yield unsatisfactory results due to fragmentation, crushing, incomplete removal, and poor orientation. Several methods have been advocated, which vary from simple methods to complex methods that are labor-intensive and expensive. Each institution can choose a technique that best fits its goals and resources.

Four incision lines are needed to remove the petrous bone (Fig. 31.64). The first passes through the temporalis muscle, separates the soft tissue from the outside of the temporal bone, and transects the external auditory canal (see Fig. 31.3). The second separates the anteromedial end of the petrous bone from the side of the sella turcica and is nearly parallel to the first incision. It should be placed as close to the wall of the sella turcica as possible. The third cuts through the roof of the petrous bone anterior to the area of the tegmen tympani, as close to the anterior vertical wall of the middle fossa as possible. It is extended into the underlying bone. It is perpendicular to the first two. The fourth is a cut along the infe-

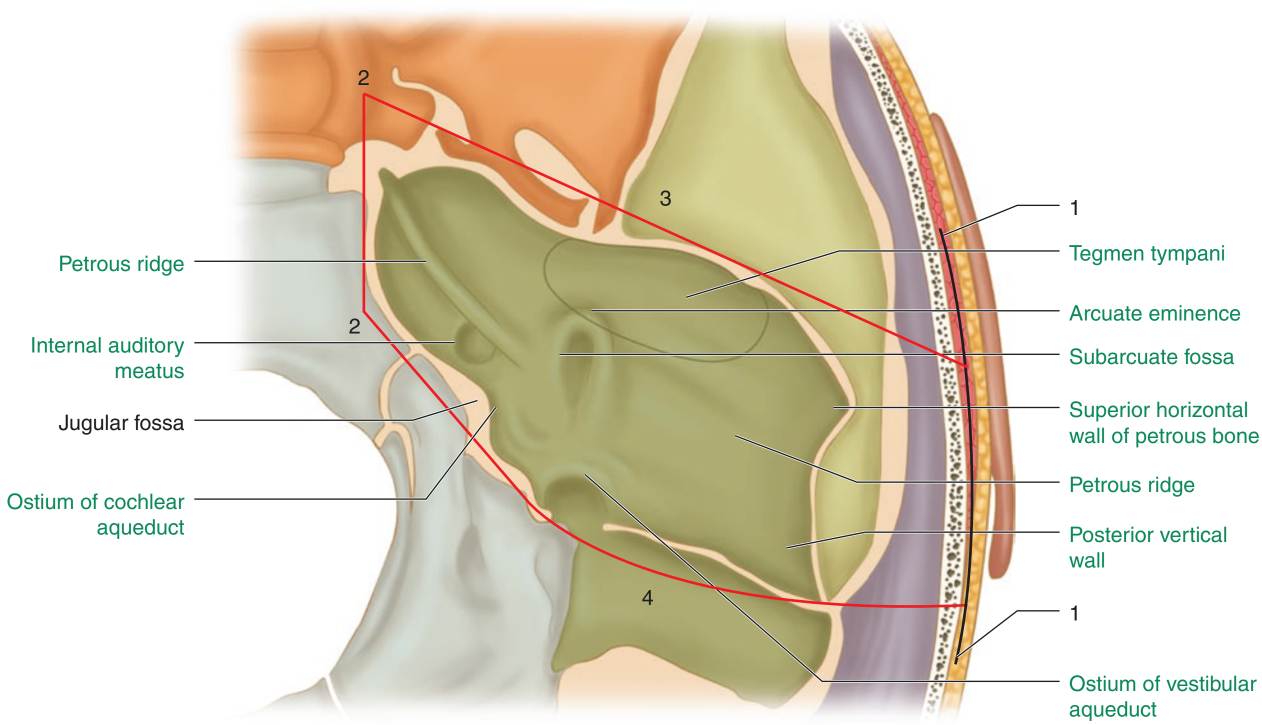

Fig. 31.64 Four incision lines for removal of the petrous bone. The first lateral incision does not pass through bone but rather through the soft tissue of the scalp. It is depicted by the black line through the temporalis muscle following the curve of the cranium and forms a flap of the scalp including the temporalis muscle, subcutaneous tissue, skin, and pinna, which can be folded laterally away from the cranium. The separation of this flap is extended downward and under the cranium anteriorly, where the external auditory canal is located and transected. See Fig. 31.3, which shows this first incision in the frontal plane, represented by the black line labeled "1," which passes through the temporalis muscle, curves under the cranium, and transects the outer cartilaginous portion of the external auditory canal, which is located on the anterior surface of the removed petrous bone near its lateral end. The second medial incision passes through bone and separates the anteromedial end of the petrous bone from the side of the sella turcica and clivus. It should be made flush against the side of the sella and clivus. The third anterior incision is through the boney floor of the middle cranial fossa as far anterior as possible. It should include all of the tegmen tympani. It extends through the lateral wall of the cranium, which was exposed by incision number "1." Incision number "3" connects incisions "1" and "2." The fourth posterior boney incision is along the inferior margin of the posterior vertical wall of the petrous bone. Laterally, incision number "4" also extends through the lateral wall of the cranium. All incisions are extended until the petrous bone is free and can be removed. Compare this figure with Figs. 31.1 and 31.2. Note that the incision lines in this figure include all the surface landmarks in Fig. 31.1 and all the components of the inner, middle, and external ears indicated in Fig. 31.2. Color code: dark green, petrous bone; light green, squamous portion of temporal bone; orange, sphenoid bone; blue, occipital bone; violet, parietal bone; tan areas, open sutures and minor fontanelles

rior edge of the posterior wall of the petrous bone to include the orifice of the cochlear aqueduct at the superior edge of the jugular fossa. This is extended anteriorly toward the third cut. The four cuts are extended until the bone is free. This method provides a complete petrous bone, including the distal external auditory canal, tympanic membrane, middle and inner ears, ostia of the external auditory meatus and cochlear and vestibular aqueducts, and a portion of the Eustachian tube. After removal, the specimen should be thoroughly fixed. After fixation, the amount of decalcification varies. Ossification begins in the third month and continues throughout fetal life and into infancy. Therefore, the amount of decalcification should be carefully monitored and tailored to each specimen. Specimens from first-trimester and early second-trimester fetuses may need no decalcification.

After decalcification, the specimen is bisected by a horizontal section through the external and internal acoustic meatuses in a plane parallel to the plane of the superior surface of the petrous bone (Fig. 31.65). An alternative is a vertical section perpendicular to the superior surface of the petrous bone, parallel to the petrous ridge. Additional cuts parallel to either choice can be made, depending on the size of the specimen.

The instruments used in removal and sectioning of the specimens are important. Unossified or minimally ossified specimens should be removed with a scalpel blade. Because of unossified sutures and minor fontanelles, specimens may crumble even with the use of scalpels unless special care is taken in their removal and sectioning. Partially or extensively ossified specimens require a saw for removal. Adult Stryker saws are usually too large for use in fetuses and newborns. Pediatric Stryker saws are more appropriate and are easily available. Small, sharp bone scissors can be used, but they may cause crushing and fragmentation of the specimen. The use of chisels should be avoided. Sectioning of the appropriately decalcified specimen can be accomplished with a scalpel blade or one of the several available longer, razor-like blades.

More extensive and detailed examinations enter the realm of research and are beyond the scope of this chapter. For instance, if the entire length of the Eustachian tube is desired, a more invasive excision will be required. If the best preservation for histology and immunohistochemistry is desired, the unfixed specimen can be cut into thin serial slices by precision saws. These slices require minimal fixation; various fixatives can be used, and minimal decalcification is required. These slices can be serially microscopically sectioned and stained with a variety of stains and immunohistochemical techniques. The microscopic sections can be utilized for three-dimensional reconstruction to document the details of congenital malformations.

All these histologic procedures are complicated by multiple artifacts. The fixed whole specimen can be studied by CT microscopy [20] or MR microscopy [21]. These techniques avoid the artifacts of histologic procedures and provide excellent anatomic and pathologic detail of the middle and inner ears.

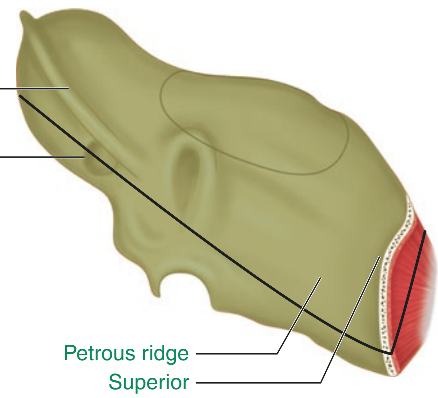

Fig. 31.65 Removed petrous bone showing the preferred plane of section. Often the removed petrous bone includes excess lateral wall of the cranium composed of the squamous part of the temporal bone and possibly the inferior parietal bone. Trim off this excess bone through the squamous part of the temporal bone, flush with the superior horizontal wall of the petrous bone. Locate the internal auditory meatus on the posterior vertical wall of the petrous bone and the cut end of the external auditory canal located on the underside of the anterior surface of the specimen (not shown in this figure). The cut passes through the internal auditory meatus and the external auditory canal. Start the cut on the posterior surface parallel to the petrous ridge and through the internal auditory meatus. Continue the cut forward in the horizontal plane parallel to the superior surface of the petrous bone and through the external auditory canal. The cut bisects the petrous bone in the horizontal plane. Embed the two halves with the cut surfaces down. The histologic sections will include the internal auditory canal cut longitudinally, a longitudinal cut of the cochlea, the vestibule, the middle ear, the tympanic membrane, the external auditory canal (cut longitudinally), and various cuts of the semicircular canals. Multiple microscopic sections of both halves will include all of the structures depicted in the previous photomicrographs. The *black line* is the horizontal plane of section. The *red* is the remnants of the temporalis muscle fibers attached to the cranium. Note the trimmed edge of the squamous part of the temporal bone

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