Paparella: Volume II: Otology and Neuro-Otology

Section 3: Diseases of the Ear

Part 4: Inner Ear

Chapter 40: Sensorineural Hearing Loss in Children - Nongenetic

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This chapter and Chapter 41 are concerned with hearing disorders of childhood. Because children suffer hearing losses owing to all the same causes as for adults (except for presbycusis and otosclerosis), we believe that a proper introduction to this topic will include a classification of the forms of hearing loss, according to the most clinically useful scheme. The otolaryngologist should attempt to apply such a system of classification (differential diagnosis) whenever he or she is faced with the problem of diagnosing a cause of hearing loss. This classification, which has been adopted for this chapter and Chapter 41, is shown in Table 1. The table also provides a reference, whenever the topic is covered in another chapter of this volume.

Detection and Management of Hearing Loss in Children

One of every 750 infants will have a potentially disabling sensorineural hearing loss (Feinmesser and Tell, 1976). The early diagnosis of hearing impairment in children is of utmost importance because of the necessity for proper training in speech and language. A Crib-O-Gram can be used to screen those infants at high risk for additional diagnostic testing to identify newborns who are likely to be hearing-impaired. The following factors identify infants at high risk for hearing impairment, according to the 1982 Joint Committee on Infant Hearing regarding recommendations for screening of hearing of newborn infants:

1. A family history of impaired hearing in childhood.

2. Congenital/prenatal infection (eg, rubella, herpes, cytomegalovirus, syphilis.

3. Anatomic malformations of the head or neck (eg, abnormalities associated with a craniofacial syndrome, cleft palate, abnormalities of the pinna).

4. Birth weight less than 1500 gm.

5. Hyperbilirubinemia at levels exceeding indications for exchange transfusion.

6. Bacterial meningitis, especially from *Haemophilus influenzae.*

7. Severe asphyxia, which may include infants with an Apgar score of 0-3 or those who fail to institute spontaneous respiration within 10 minutes, with hypotonia persisting to 2 hours of age.

Table 1. Classification of Hearing Loss

I. Congenital Sensorineural Hearing Loss

- A. Genetic etiologies
  - 1. Hearing loss occurring alone
    - a. Michel's aplasia
    - b. Mondini's aplasia
    - c. Scheibe's aplasia
    - d. Alexander's aplasia
  - 2. Hearing loss occurring with other abnormalities (syndromes)
    - a. Waardenburg's syndrome (deafness may be delayed)
    - b. Albinism
    - c. Hyperpigmentation
    - d. Onychodystrophy
    - e. Pendred's syndrome
    - f. Jervell's syndrome
    - g. Usher's syndrome
    - h. Trisomies (trisomy 13-15, 18, 21)
- B. Nongenetic etiologies
  - 1. Hearing loss occurring alone
    - a. Ototoxic poisoning (streptomycin, quinine, etc) (see Chap 46, this vol)
  - 2. Hearing loss occurring with other abnormalities
    - a. Ototoxic poisoning (thalidomide) (see Chap 46, this vol)
    - b. Viral infection (maternal rubella, cytomegalovirus)
    - c. Metabolic disorders (cretinism)
    - d. Erythroblastosis fetalis
    - e. Radiatin (first trimester)
    - f. Prematurity
    - g. Birth trauma, anoxia

II. Delayed Sensorineural Hearing Loss

- A. Genetic etiologies
  - 1. Hearing loss occurring alone
    - a. Familial progressive sensorineural deafness
  - 2. Hearing loss occurring with other abnormalities (syndromes)
    - a. Alport's syndrome
    - b. Lysosomal storage disease (Hurler's syndrome, Hunter's syndrome, Fabry's disease)
    - c. Klippel-Feil syndrome
    - d. Refsum's disease
    - e. Alström's disease
    - f. Cockayne's syndrome
    - g. Richards-Rundle syndrome
    - h. Neurofibromatosis
    - i. Crouzon's disease

B. Nongenetic etiologies

1. Bacterial (labyrinthitis, otitis media) (see Chaps 27 and 42, this vol)
2. Spirochetal
3. Viral (meningitis, labyrinthitis, mumps, measles, influenza, etc)
4. Ototoxic poisoning (see Chap 46, this vol)
5. Neoplastic disorders (leukemia, peripheral and central ear tumors, etc) (see Chap 23, this vol)
6. Traumatic injury (acoustic trauma, temporal bone fractures)
7. Metabolic disorders (hypothyroidism, allergies, renal disorders, Ménière's disease, etc)
8. Autoimmune disease
9. Sudden deafness (viral, vascular, perilymphatic fistula).

Although many hospitals screen neonates at high risk for factors indicating auditory problems, 46 per cent of all infants with impaired sensorineural hearing have none of these factors (Menser and Forrest, 1974). Early detection of these infants depends on an adequate understanding by the medical profession and the general public. Alert parents or pediatricians usually will notice that a child does not respond normally to sounds, and they will seek additional consultation.

When a child suspected of being hearing-impaired is brought to the attention of an otolaryngologist, there are several tasks to perform. First, a complete and detailed history must be obtained, covering family background, prenatal and birth history, any etiologic factors that might predispose to loss of hearing, and the developmental history of the child. The history often proves to be the most revealing part of the entire diagnostic workup. Congenital anomalies elsewhere in the body should be looked for. A careful otologic examination should be performed and every means employed to obtain accurate determinations of the extent and type of hearing loss. If hearing loss is discovered, immediate medical or surgical attention or a prescription for a hearing aid, or both, should be given if indicated. Conference with the parents must be held to inform them of their responsibilities with regard to the education and training of their hearing-impaired child.

Audiology can provide a reliable assessment of hearing in children by means of special tests and techniques designed for this purpose (see Chap 5, this vol). Assessment of hearing should begin at the earliest age at which a child is suspected of having impaired hearing. Because of advances in special behavioral testing techniques such as the Crib-O-Gram, as well as advances in evoked-response audiometry, it is now possible to obtain good estimates of hearing status in babies as young as a few weeks of age. This evaluation requires the services of an audiologist with expertise in testing very young children. Not all audiologists have this special training and experience, but they can be located in most larger metropolitan communities. It is important to identify a hearing-impaired child as early as possible in order to initiate plans for special management to prevent serious delay in development of language skills.

The physician can perform simple tests in the office that can provide preliminary information regarding the child's ability to hear. The parents can also furnish information about the child's behavior, which can be of importance in determining the degree of hearing loss. The parents should be questioned about the child's reaction to speech and to sounds such

as the telephone, radio, doorbell, hand-clapping, and so forth. The normal child, after the age of 6 months, will react reliably to sounds such as a bell or a rattle, by attempting to look in the direction of the sound. The physician can, therefore, observe the reaction of the child to such sounds.

The parents should also be questioned about the child's babbling behavior. Around the age of 6 to 9 months, all children, whether or not hearing-impaired, produce babbling sounds. In the normal child, this babbling stage begins to cease around 1 year as she or he starts to develop simple words. While in the babbling stage, the child does two important things: he or she (1) experiments with the mechanisms needed for speech (combining articulation with phonation, gaining control over the respiratory system, and so forth) and (2) establishes the links between motor activity and auditory impressions. Toward the end of the babbling stage, the normal child begins to imitate specific sounds made by adults.

During the babbling stage, the normal child has two routes of reinforcement available to him or her for utterances of sound. One of these is simple acoustic feedback and the other is the reaction of adults to the child's babbling. The hearing-impaired child has only the latter source of reinforcement, and for this reason it becomes vitally important that the parents understand the necessity and means of responding to and encouraging the production of sounds. The parents of a hearing-impaired child must constantly reinforce all sounds produced by the child; otherwise, the babbling may cease much earlier than normal. Visual and tactile information provide the primary means of feedback in this case. It is determined that the child can use a hearing aid, the parents must see that the child hears as much speech as possible and as continuously as possible. They must talk to such a child more than they would to a normal child, and they must be sure that speech is audible to the child. Consultation and instruction may be available to the parents through an audiologic center.

From the age of 12 to 18 months, up to 2 years, the speech of the normal child will develop from simple words such as "mama" and "dada" to a vocabulary containing as many as 200 words. The hearing-impaired child, of course, will have very limited speech or may not produce any sounds at all. In the office, the phyisician can assess the hearing of a child of this age by simple "naming games", or by giving simple commands. The normal child should be able to name a number of common objects or toys, using all the speech sounds, and to perform simple tasks on command. If a hearing loss is suspected, it is necessary to obtain a complete audiologic assessment (see Chap 5, this vol). Failure to obtain a competent audiologic-otologic evaluation and appropriate medial/surgical intervention and/or early educational management at this stage can result in marked retardation in development of language, speech, and learning.

Differential Diagnosis

For each child with sensorineural hearing loss, it is the otolaryngologist's responsibility to make every effort to search for an etiologic diagnosis. This has obvious importance for proper management. The first question asked should be "Is this child's hearing loss congenital, or was it delayed in onset?" The congenitally deaf child should be evaluated with antibody studies to determine the possibility of intrauterine infection. Specific IgM antibody assays for toxoplasmosis, rubella, cytomegalovirus, and herpes will aid in the determination of hearing loss induced by intrauterine infection. Congenital hearing loss may imply aplasia or

dysgenesis of the organ of Corti and related structures and should not be progressive. Delayed hearing loss relates to degenerative changes of the sensory organ and may be progressive.

The second question is "Is the hearing loss genetic (hereditary) or is it nongenetic?" This is important, since approximately half of all disorders involving profound hearing loss in children are genetic in origin. The possibility also exists for a nongenetic type of hearing loss to occur due to a genetic predisposition. For example, microbiologic infections might be considered to be controlled by nongenetic environmental causes; however, with knowledge of the role of the immune response in genes in control of immunocompetence, it is evident that microbiologic infections are conditioned, as are all disorders, to a greater or lesser degree by the genotype (Childs, 1977). Genetic injury may also be induced by environmental mutagens such as ionizing radiation, drugs, and viruses. The third question relates to other anomalies occurring with the hearing loss (syndromes), which can be seen in congenital hearing lorr or in genetic hearing loss that may be either congenital or delayed. The preceding considerations stress the importance of the history in the workup.

Embryologic Considerations

For a complete description of the embryology of the inner ear, the reader is advised to refer to Chapter 1 of Volume I. Here we shall briefly discuss certain aspects of embryology as they help to describe profound hearing loss in children, and the aplasias in particular. The embryo is extremely susceptible to teratogenesis between the 3rd and 9th weeks of gestation, because it is during this period that the organs are being created out of the germ-cell layers. The process of organogenesis is susceptible to injury, regardless of its nature, particularly during the 4th and 5th weeks. The fetal period following organogenesis is mostly concerned with growth, and during this time the fetus is more susceptible to retardation in growth or to injury to already formed organs (Robbins et al, 1984).

The entire membranous inner ear develops from ectoderm. An *otic* (auditory) *placode* first appears in the 3-week-old embryo as a thickening of the ectoderm on the lateral surface of the head, dorsal to the first branchial groove. It then navigates to form an *otic pit*, which continues to deepen until the surface ectoderm closes off, trapping an *otic cyst* (otocyst or otic vesicle) below, surrounded by mesoderm (4 fetal weeks).

After 8 weeks, the mesoderm surrounding the differentiating otic cyst becomes converted into a cartilaginous capsule. Ossification of the cartilage commences at about 16 weeks and is completed by the third trimester of pregnancy. At birth, the osseous labyrinth consists of endosteum (inner periosteum), endochondral (intrachondral) portion, and outer periosteal bone, from within to outward; further growth of the bony labyrinth occurs in the outer periosteal table.

The otic cyst, serving as the primordium for the entire membranous labyrinth, changes its shape at 5 weeks to form a wide dorsal (vestibular) part and a more slender ventral (cochlear) part. During this time a cord of cells grows from the medial side of the otic cyst and soon becomes the endolymphatic duct and sac, serving as a marker to divide the vestibular from the auditory labyrinth. At 6 weeks, the dorsal part forms two pouches, a dorsal pouch (to become the two vertical semicircular canals) and a lateral pouch (to become the lateral semicircular canal). At 7 weeks, the vestibule has begun to divide into a dorsal

utricle and then a ventral saccule. The semicircular canals and utricle are very well established in the 8- to 9-week embryo; the cochlear turns are not yet fully developed. At 12 weeks, the cochlear duct has developed its two-and-a-half turns, while elements of the cochlear duct achieve finer differentiation, continuing into the second trimester.

From this we see the vestibular labyrinth and the three semicircular canals and utricle, or *pars superior,* developing before the auditory labyrinth, saccule, and cochlea, or *pars inferior.* It has been stated that embryology is a reflection of phylogeny. The oder a structure is phylogenetically, the more resistant it is to disease, whether developmental or acquired. As described in this and the following chapter, the two classic examples of developmental changes confined to the parts inferior are those seen in Scheibe's aplasia (genetic), and those resulting from maternal rubella. Similarly, the saccule and cochlea are the structures mainly involved in cases of delayed viral hearing loss, such as from measles and mumps.

The remainder of this chapter is devoted to description and discussion of the most common *nongenetic* causes of sensorineural hearing loss in children. The many *genetic* etiologies of deafness are discussed in the following chapter on genetic hearing loss.

Congenital Hearing Loss Occurring Alone

Ototoxicity

Certain drugs have been shown to cross the placenta and damage the fetal ear (see Chap 46, this vol). Congenital hearing loss and hypoplasia of the cochlea have been described in infants whose mothers received chloroquine or quinine during pregnancy (Hart and Naunton, 1964). Some members of the aminoglycoside antibiotic chemical group, such as streptomycin (Robinson and Cambon, 1964), gentamicin (Kauffman et al, 1975), and tobramycin and amikacin (Israel et al, 1976), have been demonstrated to cross the placenta, and clinical reports have described hearing loss in newborns of some mothers given this group of antibiotics (Rasmussen, 1969; Robinson and Cambon, 1964; Scheinhorn and Angelillo, 1977). The ototoxicity in these children did not depent on the mother's experiencing ototoxicity.

Congenital Hearing Loss Occurring With Other Abnormalities

Ototoxicity

Although ototoxic agents can result in deafness in the absence of other malformations, some drugs, such as thalidomide, produce deafness and a multitude of other malformations as well. Thalidomide-produced embryopathies occurred in England and West Germany in the early 1960s. This tranquilizer produced a variety of malformations, including deformities of the limbs; malformations of the heart, face, lip, and palate; anomalies of the respiratory, digestive, and urogenital systems; and aural atresia with microtia or anotia and palsy of cranial nerves VI and VII and malformation and even agenesis of the inner ear. The hearing loss may be moderate to profound. There also may be an absence of vestibular function. Until the factors that may influence transplacental passage of drugs have been defined, it is important to restrict those drugs known to be ototoxic during pregnancy.

Viral Infection

Maternal Rubella

Maternal rubella (German measles) is a virally induced cause of congenital sensorineural hearing loss. If the mother acquires German measles within the first 3 months of pregnancy, the probability is high that the first 3 months of pregnancy, the probability is high that the child will suffer some degree of hearing loss. In addition to the hearing loss, cardiac malformations, losses in vision, and mental retardation may be present. Following the last epidemic of rubella in the USA ni the 1960s, more than 12.000 infants were born with congenital rubella and hearing loss (Trybus et al, 1980). Although the incidence of rubella has decreased since the introduction of rubella vaccine, there are still approximately 50 infants per year born with hearing loss and congenital rubella (Orenstein and Granes, 1982). Rubella vaccine administered to nonimmune pregnant women can result in the virus's corssing the placenta and infecting the fetus; the risk of hearing loss in these cases, however, is minimal (Preblud et al, 1981). A specific diagnosis of congenital rubella may be made by (1) isolation of rubella virus from urine or throat cultures during the first week of life; (2) identification of IgM antibodies against rubella in serum from the neonate; or (3) an increasing antibody titer to rubella virus in an infant during the first few months of life (Davis and Johnson, 1983).

Most cases of fetal infections with rubella in the first trimester are symptomatic, with the major triad of cataracts, heart disease, and deafness. The incidence of hearing loss among those infants with symptomatic congenital rubella is about 50 per cent. Infants infected with rubella during the second or third trimester are usually asymptomatic. About 10 to 20 per cent of these asymptomatic children are later found to develop a hearing loss (Menser and Forrest, 1974). Most of these children have a bilateral hearing loss that may be asymmetric, with an audiometric configuration that tends to be flat or gradually sloping downward from low to high, though exceptions may occur (Fraser, 1976). In addition to damage to the inner ear, central auditory imperception with delay in development of speech is common in rubella embryopathology and may be associated with cerebral involvement (Ames et al, 1971).

Pathologic findings in temporal bones from these patients have revealed a consistent pattern of cochleosaccular degeneration. There is usually a partial collapse of Reissner's membrane and the saccular wall, as well as strial degeneration. The utricle, semicircular canals, vestibular neuroepithelia, and nerves are usually unaffected. Although the available evidence strongly suggests that rubella virus can cause congenital deafness, the virus has not yet been isolated from the inner ear.

Cytomegalovirus

Cytomegalovirus is the leading cause of fetal viral infection in the USA and accounts for about 4000 cases of sensorineural hearing loss annually in this country alone (Reynolds et al, 1974). The most prominent clinical changes are mental retardation, microcephaly, hepatosplenomegaly, and deafness; however, over 97 per cent of congenitally infected infants show no sign of the disease in the neonatal period. The incidence of sensorineural hearing loss in those infants who are symptomatic at birth is about 30 per cent (Pass et al, 1980). Normal-appearing infants who shed cytomegalovirus in their urine are also at risk to develop

hearing loss. Cytomegalovirus infection can be diagnosed in both symptomatic and asymptomatic infants by isolation of the virus from fresh urine during the first week of life.

The pattern of hearing loss in infants with cytomegalovirus infection is rather inconsistent. Hearing loss can be symmetric, with impairment greater in the high frequencies than the low (Pappas, 1985). An asymmetric or unilateral hearing loss has also been reported (Stagno et al, 1977). Infants and children with asymmetric hearing should be testyed every six months, because progressive hearing loss is prevalent in this group (Pappas et al, 1983). A factor contributing to this degenerative process may be that the virus may remain active for several years following birth and may be reactivated following periods of latent infection (Dahle et al, 1974).

Pathologic evaluation of temporal bones in infants with cytomegalovirus has detected the presence of infected cells in the cochlea, saccule, utricle, and semicircular canals. The cells attacked by this virus are invariably epithelial in origin, and the changes are consistent with those in other organs in the generalized neonatal form of the disease (Meyers and Stool, 1968). Because of autolysis, it has been difficult to judge the condition of the organ of Corti, but it is felt that major degeneration of the hair cells does not occur and that cranial nerve VIII is apparently also spared of pathologic changes. Hydrops of the cochlea and the saccule and collapse of Reissner's membrane have been observed (Davis and Johnson, 1983). The virus can also invade the vestibular mechanism and lead to vestibular symptomatology (Davis et al, 1977). Cytomegalovirus has been cultured at autopsy from the perilymph of a congenitally infected infant, and cytomegalovirus antigen has been identified in the cells lining the membranous labyrinth (Davis et al, 1981).

Metabolic Disorders: Cretinism

Thyroid disease may be associated with hearing loss, as in the syndrome usually referred to as endemic cretinism. It is generally accepted that iodine deficiency is responsible for the cretinism, although genetic factors have been proposed to account for the condition. It is usually found only in certain geographic locations. The hearing loss is of the myxed type, being both sensorineural and conductive.

Erythroblastosis Fetalis

Erythroblastosis fetalis is a hemolytic disease caused by blood group incompatibility between the mother and child. The disease is characterized by excessive destruction of red blood cells, leading to reduction in the oxygen-carrying capacity of the blood and to accumulation and deposition of bilirubin. The disease may vary in severity from congenital anemia to intense jaundice with signs of neurological involvement. The most serious threat in erythroblastosis is damage to the central nervous system, known as kernicterus. In jaundiced cases, the unconjugated bilirubin appears to be particularly toxic to the brain (Robbins et al, 1984).

Zonderman (1959) found that as many as 7 per cent of a sample of 328 hearing-impaired children had hearing loss attributable to Rh incompatibility. This percentage is probably smaller today, because of the improvement in techniques for dealing with the problem. Jaundice, mental retardation, cerebral palsy, and hearing loss may be present shortly

after birth in infants with kernicterus. Postpartum exchange transfusion is the treatment for this problem. However, the child may still have some loss of hearing for high tones; the physician should be alert to this possibility, because acquisition of language may be retarded unless preventive measures are taken. Cochlear pathology, in cases of hearing loss associated with kernicterus, is minimal or absent (Goodhill, 1967), with the auditory lesion occurring at the level of the cochlear nuclei (Gerrard, 1952).

Radiation

Irradiation, in addition to being mutagenic and carcinogenic, is also teratogenic. Malformations such as defects of the skull, spina bifida, microcephaly, blindness, and deafness can occur due to exposure to heavy doses of irradiation during the period of organogenesis.

Prematurity

Sensorineural hearing loss occurs in approximately 9 per cent of infants with low birth weight (Dimitrius et al, 1982). Various causes for this have been suggested, including anoxia, hyperbilirubinemia, hypothermia, ototoxic drugs, and ambient noise. Recent evidence has ruled out otoxotic drugs or ambient noise and suggests that apneic attacks in the neonatal period are the most significant predictors of hearing loss, and that an increased serum bilirubin level in the neonatal period has an additive effect (Abramovich et al, 1979).

Birth Trauma; Anoxia

Injuries at birth may affect any part of the body, but the head, skeletal system, liver, adrenals, and peripheral nerves are most commonly involved. The most common important birth injury is intracranial hemorrhage. There is a tendency to hemorrhage into the inner ear following injury or stress during birth, and it is possible that the damage that occurs to the organ of Corti is due to a toxic effect of the extravasated blood. It has also been suggested that intrapartum asphyxia may lead to hearing loss through toxic damage to the cochlear nuclei (Hall, 1964). The incidence of sensorineural deafness in survivors after severe perinatal asphyxia has been reported as 4 per cent (D'Sauza et al, 1981). The hearing loss is usually bilateral, symmetric, and more severe in the high frequencies.

Delayed (Acquired) Hearing Loss

This section is devoted to those defects in hearing that may manifest subsequent to birth, regardless of whether or not the causal factors are present at or before birth. Nongenetic delayed hearing loss in children may be caused by a number of factors, including viral and bacterial infections, trauma, ototoxic poisoning, and essentially all the other causes of hearing loss, except presbycusis. Even otosclerosis is seen occasionally in teenagers.

Bacterial Causes

Labyrinthitis

The most serious type of labyrinthitis is suppurative or purulent labyrinthitis (see Chap 42, this vol). Suppurative labyrinthitis is characterized by complete deafness due to permanent loss or destruction of the sensory elements of the labyrinth. The labyrinth is vulnerable to bacterial infections through the middle ear, the meninges, and the blood. Bacterial labyrinthitis principally involves the perilymphatic spaces, although there is eventual involvement of the endolymphatic spaces as well. Changes in the inner ear are established successively as formation of serofibrinous exudate, infiltration of inflammatory cells, formation of granulation tissue and, if the infection is unresolved, fibrosis and ossification (Paparella and Sugiura, 1967).

Meningogenic labyrinthitis is a prevalent cause of childhood hearing loss. In a survey of 904 hearing-impaired children, 10 per cent of the questionnaires indicated that meningitis was the factor responsible for the hearing loss (Goodhill, 1950). Hearing loss may be unilateral or bilateral and may vary in degree from mild to profound with no consistent audiometric pattern (Berlow et al, 1980). Although the use of antibiotics has decreased the occurrence of this disease significantly, it remains a source of danger in children as a complication of bacterial infection.

Otitis Media

Sensorineural hearing loss has been demonstrated in patients with chronic otitis media. Paparella and associates (1970) found an increased incidence of a sensorineural hearing loss in patients with chronic otitis media, in all decades of life. Arnold and colleagues (1985) studied 77 children who had otitis media with chronic mucoid effusion and found that 20 per cent had a significant hearing loss that started at 500 Hz. Sensorineural hearing loss also has been reported in cases having chronic otitis media with an effusion of the serous type (Avil and Ostfeld, 1982). Draf and Schultz (1980) described the incidence of sensorineural hearing loss to be as high as 35.8 per cent in children and 87.9 per cent in adults diagnosed as having otitis media with effusion.

In a recent study of data from six centers in five countries, approximately 42 per cent of the ears with chronic otitis media had a loss of 15 dB or greater, and in 16 per cent the loss was 30 dB or greater (Paparella, 1984). These figures were between seven and ten times higher than those in controls. Paparella and coworkers (1970) suggested that the mechanism for sensorineural hearing loss in these patients with chronic otitis media is the passage of inflammatory agents or toxins from the middle ear to the inner ear and that the round window membrane is the most likely portal. The round window membrane has subsequently been shown to be permeable to a variety of substances, including proteins (Goycoolea et al, 1980a; 1980b), toxins (Goycoolea et al, 1980; Schachern et al, 1981), tracers (Tanaka and Motomura, 1981), and antibiotics (Okuno and Nomura, 1984; Harada et al, 1986).

Histologic evidence of hair cell loss or damage to the sensorineural structures has not been demonstrated. Paparella and colleagues (1972) reported findings of inflammatory cells and serofibrinous precipitate localized to the basal turn. Walby and coworkers (1983)

suggested that hair cells may be functionally damaged or suffer injury to their stereocilia, which cannot be observed at the light microscopic level. They also speculated that a local toxic effect may alter the mass, stiffness, or function of the spiral ligament or basilar membrane and result in altered displacement of the cochlear partition in response to sound.

Evidence exists for the presence of clinically undetected otitis media, including chronic otitis media, behind an intact tympanic membrane. Paparella and associates (1980) studied 111 temporal bones of infants and children and found that 54 patients showed histologic evidence of otitis media; of these, only 20 presented with clinical manifestations. He suggested that the remaining cases of continuing but clinically nondetected (silent) otitis media, in these neonates and infants, may explain why certain children are prone to episodes of otitis media, and that this silent condition could play a role in the future pathogenesis and sequelae of the disease.

Spirochetal Causes

Congenital syphilis may manifest in two ways: as secondary syphilis in the first 2 years of life or as tertiary syphilis between the ages of 8 and 20 years, the latter span being more common. In addition to loss of hearing, interstitial keratitis is a common result of congenital syphilis. There may be a long period between involvement of the eyes and the onset of hearing loss. Whenever sudden sensorineural hearing loss occurs in young adults, congenital syphilis should be considered as the possible cause. The hearing loss may occur abruptly and progress rapidly; it is always severe in degree. With congenital syphilis, one ear is usually affected first, then the other ear in turn. Vestibular symptoms may be present, but these gradually disappear as hearing loss increases.

The cochlear pathology associated with congenital syphilis includes marked atrophy of the organ of Corti and severe degeneration of the fibers of the cochlear nerve. Reissner's membrane may be distended, owing to endolymphatic hydrops. The saccule, utricle, and canals may be distorted, with degeneration of the sensory elements (Karmody and Schuknecht, 1966). Diagnosis of the late form may be difficult in that the Wasserman reaction is not reliable after the first few years of age. Associated defects, such as interstitial keratitis and Hutchinson's teeth, may be the most important indications of this etiologic agent.

Hearing loss associated with *acquired syphilis* is also a problem that the otolaryngologist may encounter. Although therapy with penicillin has reduced the number of cases of secondary and tertiary syphilis, more than 27.000 new cases were reported in the USA in 1980 (Morbidity and Mortality Weekly Report, 1981). It is particularly important for the otolaryngologist to be aware of the possibility of syphilis-induced hearing loss, because the hearing loss may be one of the first outward manifestations of the disease beyond the primary stage. The hearing loss usually appears rather suddently and progresses rapidly over weeks or months (although progression over years is also possible). It usually begins near the end of the secondary stage or the beginning of the tertiary stage. Vestibular symptoms and tinnitus may accompany the hearing loss, becoming diminished as labyrinthine destruction increases. There is, however, no consistent audiologic pattern in either congenital or acquired syphilis (Becker, 1979). In a recent study of 38 patients with syphilitic cochleovestibular dysfunction, sensorineural hearing loss was present in 100 per cent of the patients (82 per cent

bilateral, 18 per cent unilateral), 42 per cent had episodic vertigo and 24 per cent had the classic triad of symptoms of endolymphatic hydrops (Steckelberg and McDonald, 1984).

In acquired syphilis, the Wasserman reaction is fairly reliable, both in blood and in cerebrospinal fluid. The test becomes less reliable, however, as the time increases following the initial infection. Tests that are highly specific are the treponemal antibody tests and the FTA-AB test, which uses fluorescent microscopy and is the most sensitive and specific test available. Therapy using penicillin is still the recommended form of treatment. Hearing, in some instances, can be recovered by the systemic administration of steroids.

Viral Causes

Meningitis

Although not clearly established, viral meningitis may cause viral labyrinthitis, resulting in hearing loss. Unlike bacterial labyrinthitis, which principally involves the perilymphatic spaces, viral labyrinthitis primarily affects the spaces of the endolymph.

Mumps

Virally induced hearing loss from infections such as mumps, measles, influenza, and chickenpox is not uncommon in children. Hearing loss associated with mumps (parotitis) occurs in about 5 of every 10.000 cases (Everberg, 1957). Deafness from mumps is usually sudden in onset and profound and may be associated with nausea, vomiting, and vertigo. Tinnitus and fullness in the ear also may be present. The hearing loss is usually unilateral and for this reason may be undiagnosed for some time in young patients. Mumps is probably the most common cause of unilateral acquired sensorineural hearing loss in children.

The first symptoms of mumps are stiffness of the neck and pain in the area of the parotid glands. Tenderness and swelling of one or both parotid glands are the primary signs of mumps. Diagnosis can be confirmed by isolation of the virus from cerebrospinal fluid or the throat, or by a fourfold or greater serologic increase in mumps antibodies in samples of serum from acute and convalescent stages. Pathologic examination of temporal bones from two patients revealed damage mainly in the basal turn, consisting of atrophy of the stria vascularis and organ of Corti, with partial collapse of Reissner's membrane and decreased cochlear ganglia (Smith and Gussen, 1976; Lindsay et al, 1960).

Measles

Measles (rubeola) acquired during childhood may be responsible for hearing loss. The loss is usually symmetric, bilateral, and moderately severe, with the high tones more affected than the low. Tinnitus and vertigo may accompany the hearing loss. During the initial stage of measles, diagnosis may be made by inspection of the buccal mucosa. Small white spots about the size of a pinhead are scattered over the surface of the mucosa, especially in the area around the molars. The typical rash appears four to five days later and the white spots disappear. Symptoms that usually accompany measles include conjunctivitis, diarrhea, vomiting, and laryngitis.

The diagnosis can be confirmed by isolation of the virus from throat culture, by identification of the viral antigen using immunofluorescent staining of exfoliated epithelial cells from the buccal mucosa or pharynx, or by a fourfold or greater serologic increase in measles-antibody titer between samples from the acute and the convalescent stage. Pathologic findings in temporal bones include atrophy of the organ of Corti and vestibular organs, distortion of the tectorial membrane, strial atrophy, and saccular collapse. Degenerative changes seen in temporal bones from patients with deafness from measles were most severe in the basal turn (Lindsay and Hemenway, 1954; Schuknecht, 1974; Suboti, 1976).

Ototoxicity

Although the list of substances known to be ototoxic is vast (see Chap 46, this vol), aminoglycoside antibiotics and diuretics are the two categories that have been studied most extensively. The audiometric pattern of ototoxic damage differs in these two categories. Diuretic ototoxicity usually produces a flat sensorineural hearing loss or a slightly sloping curve across all frequencies. The audiometric pattern of antibiotic ototoxicity is steeply sloping, with the loss mainly in the high frequencies. If damage continues, the curve slopes to include the low frequencies as well. The loss is usually bilateral and symmetric. The site of the ototoxic damage varies among aminoglycoside antibiotics: kanamycin and neomycin result in cochlear toxicity, streptomycin and tobramycin in vestibulotoxicity, and gentamicin may result in damage to both the cochlea and vestibule (Ballantyne, 1983).

The ototoxicity from aminoglycoside antibiotics may not be detected during the period in which the drug is administered but may occur days or even weeks after termination of the therapy (Shambaugh et al, 1959; Theopold, 1977). Interaction of aminoglycoside antibiotics and loop-inhibiting diuretics has been reported in both experimental animals and humans. The interaction appears to be specific for loop diuretics (Brummett et al, 1974) but can occur with divergent antibiotics (Davis and Brummett, 1979).

Some chemotherapeutic agents also have been reported to result in hearing loss. Numerous studies have described the ototoxic effects of cis-platinum. The ototoxicity causes cochlear damage and appears to be dose-related. The hearing loss in humans has been limited to the high frequencies and is usually permanent. Histologic damage in guinea pigs has been described as outer hair cell loss in the basal turn, slight atrophy of the stria vascularis, and severe collapse of Reissner's membrane limited to the basal turn. The inner hair cells are almost completely preserved in all turns (Komune et al, 1981).

Neoplastic Disorders

Leukemia

Patients with leukemia experience a significant incidence of otologic complications secondary to their disease. In a study of 25 patients, 48 per cent were found to have otologic signs or symptoms (Paparella et al, 1973). The major triad of histopathologic findings in the temporal bone of leukemic patients comprises leukemic infiltrate, hemorrhage, and infection. Although these findings are most prevalent in the middle ear, leukemic infiltrate was observed in the scala tympani, saccule, and posterior canal of one patient, and in another patient,

hemorrhage in the inner ear into the scala vestibuli, scala tympani, and lateral semicircular canal was observed.

Peripheral and Central Tumors

Cranial nerve VIII is the most common cranial nerve for origin of tumors. The tumor frequently arises within the internal auditory meatus. Tinnitus, unilateral sensorineural hearing loss, and unsteadiness are early symptoms. Although hearing loss is more common with peripheral tumors, it may also occur with central tumors.

In children, deafness from central tumors can occur in lesions of the brain stem. The most common tumor of the brain stem in children is the pontine glioma. Symptoms include nystagmus, vertigo, tinnitus, and deafness. Symptoms that are gradual in onset are also associated with involvement of the cranial nerves; these have a progressive course. Magnetic resonance imaging is effective in diagnosis of lesions of the brain and cranial nerves.

Traumatic Injury

Fractures of the Temporal Bone

Fractures of the temporal bone can result from a blunt injury to the head. Approximately 70 to 90 per cent of fractures of the temporal bone are longitudinal; 20 to 30 per cent are transverse (Cannon and Jahrsdoerfer, 1983). Although sensorineural hearing loss is relatively uncommon with longitudinal fractures, transverse fractures usually are accompanied by severe sensorineural hearing loss, and loss of vestibular function may occur as well. A study of 199 children with blunt head injuries reported a persistent sensorineural hearing loss of ≥ 30 dB in the high frequencies in 7 per cent of these patients (Vartianen et al, 1985).

Acoustic Trauma

An explosive blast of noise can result in sensorineural hearing loss. The mechanism of cochlear injury in acoustic trauma, as with a blow to the head, is excessive vibratory energy conveyed to the labyrinth; both types of trauma may produce perilymphatic fistula as well as sensorineural loss in the high frequencies.

Metabolic Disorders

Hypothyroidism

As many as 25 per cent of patients with acquired hypothyroidism suffer a moderate to severe hearing loss. Two categories of acquired hypothyroidism affect children: sporadic athyreotic cretinism and juvenile hypothyroidism. Sporadic athyreotic hypothyroidism results from an embryonic defect in the development of the thyroid gland. The athyreotic cretin undergoes normal intrauterine development that, due to the lack of thyroid gland, results in a decrease in circulating thyroid hormone and in subsequent hypothyroidism. Although juvenile hypothyroidism may result from various etiologies, it frequently occurs secondary to

viral infections. The hearing loss in acquired hypothyroidism is usually sensorineural or mixed and responds to thyroid therapy.

Allergy

Allergies have been implicated in sudden and fluctuating hearing loss. Allergic inflammatory disorders may result in a decreased supply of oxygen to the inner ear as a result of endothelial damage and edema, or disruption of red blood cells with subsequent vasoconstriction, platelet agglutination, and hypercoagulation (Jaffe, 1975).

Renal Disorder

Hearing loss in patients undergoing transplant or dialysis occurs frequently, and in spite of the many extrinsic and possibly precipitating factors involved, the hearing loss appears to have a definite association with the renal disease itself. An audiologic study of 290 patients undergoing hemodialysis and renal transplant revealed that in 43 of these patients a significant hearing loss developed that could be directly attributed to the therapy for the kidney problem (Oda et al, 1974). The severity of the clinical and histopathologic findings in temporal bones was directly proportional to the number of hemodialyses and transplants. Histopathologic findings in the cochlea consisted of blue concretions in the stria vascularis and/or vestibular receptors and mild to severe loss of outer hair cells and spiral ganglion cells. In those patients receiving more than 264 hemodialyses and multiple transplants, there was complete absence of the organ of Corti.

Ménière's Disease

Ménière's disease may be due to multiple etiologic factors including metabolic disorder (see Chap 49, this vol). Although Ménière's disease has historically been thought of as an adult condition, approximately 3 per cent of all patients with the disease are in the pediatric age group. Clinical symptoms include vertigo, hearing loss, aural pressure, tinnitus, loudness intolerance, and diplacusis. A peak audiogram occurs in about one-half of the cases. A high-frequency peak at 2000 Hz associated with a moderate hearing loss is the most common type (Paparella et al, 1982). Prevalence of the peak audiogram is affected by the duration and bilaterality of the disease, but not by the degree of hearing loss.

Hydrops of the cochlear duct and saccule is the most important finding, and in advanced cases the endolymphatic hydrops can obliterate and displace the perilymphatic spaces in the scala vestibuli and cisternae vestibuli (Paparella, 1984). The hydrops is presumed to result from dysfunctional absorption of endolymph. Surgery is reserved only for intractable cases of Ménière's disease after prolonged conservative management.

Autoimmune Disease

Autoimmunity is an immune reaction against "self antigens". Ideally, at least three requirements should be met before a disorder can be categorized as truly due to an autoimmunity: (1) the presence of autoimmune reaction, (2) clinical or experimental evidence that such a reaction is not secondary to tissue damage but is of primary pathogenetic significance, and (3) the absence of another well-defined cause of the disease (Robbins et al,

1984). Clinical observations have indicated that there is a sensorineural hearing loss of immunopathologic origin. The clinical symptoms are a bilateral symmetric sensorineural hearing loss, reduced vestibular function, unsteadiness and ataxia in darkness, and temporary facial palsy (McCabe, 1979).

Clinical diagnosis of autoimmune disease is supported by cell-mediated immune responses to stimulation of the membrane of the inner ear. In a recent study of 21 patients with double-sided progressive or fluctuating sensorineural hearing loss of undefined etiology, antibodies against healthy tissues of the inner ear were found in the serum of 15 patients (Arnold et al, 1985). Autoimmune reactivity has also been demonstrated in Ménière's disease (Hughes, 1983). Sensorineural deafness due to autoimmune disease has been treated successfully by steroid therapy.

Sudden Deafness

Sudden deafness is a partial or complete sensorineural hearing loss that develops rather abruptly. The hearing loss is usually unilateral and may be accompanied by tinnitus and mild or transient vertigo. The flat type of audiometric pattern is the most common; however, low-tone, high-tone, or total hearing loss may also occur. Treatment has included various therapies such as perfusion of vasodilators and steroids, isovolemic hemodilution, and hyperbaric oxygen therapy; however, regardless of the type of treatment, approximately one-half of patients with sudden deafness recover some hearing, and about one-third regain normal hearing.

Vascular obstruction, breaks in the cochlear membrane, and viral infections have all been described as possible etiologic factors for idiopathic sudden deafness. Current evidence favors a viral etiology because (1) the pathologic findings in idiopathic sudden sensorineural hearing loss are similar to those occurring with known viral disorders; (2) there is no histologic evidence for breaks in the membrane or healed breaks; (3) fibrous and osseous proliferation such as occurs with vascular causes is absent or insignificant; (4) there is isolated cochlear neuronal atrophy (indicative of viral neuropathy); (5) serologic studies of affected patients are often positive for a viral infection; and (6) the onset of the sudden deafness sometimes occurs in association with an upper respiratory tract infection (Schuknecht and Donovan, 1986).

Although there are no histopathologic findings to support the concept of breaks in the cochlear membrane as a cause for sudden deafness, clinical evidence supports the role of perilymphatic fistula in some of these cases. Perilymphatic fistula of the oval and round window membranes has been reported to occur as the result of exertion (Gray and Barton, 1981; Nedzelski and Barber, 1976), physical trauma such as a blow to the head or ear (Fee, 1968; Althaus, 1977; Emmett and Shea, 1980), barotrauma (Tonkin and Fagan, 1975; Taylor and Bicknell, 1976), acoustic trauma (Grewal et al, 1983; Narula and Marks, 1985), surgical trauma (House, 1967; Harrison et al, 1970; Pulec, 1969), chronic ear disease (McCabe, 1978), and congenital anomalies (Rice and Waggoner, 1970; Supance and Bluestone, 1983) or spontaneously (Goodhill et al, 1973; Arndt, 1984). Goodhill and colleagues (1973) described both implosive and explosive pathways of fistulization. Symptoms of sudden hearing loss, tinnitus, and vertigo may occur alone or in combination.

Spontaneous healing of fistulas can occur; however, if symptoms persist after 5 to 7 days of bed rest with antibiotic therapy and sedation, exploratory tympanotomy is indicated. Tympanotomy should be undertaken in these cases to locate and graft the fistula because of the possibility of meningitis, permanent loss of hearing, or symptoms similar to those found in Ménière's disease. Although surgery is usually effective in relieving vertigo, only a limited improvement in hearing may occur. Supance and Bluestone (1983) reported the presence of fistulas in 66 per cent of 44 years of 33 infants and children who underwent exploratory tympanotomy to verify presumptive diagnosis of perilymphatic fistula. Following surgery, hearing was unchanged in 86 per cent, improved in 5 per cent, and worse in 9 per cent of the ears with fistulas; however, complaints of vertigo subsided in all children in whom a fistula was repaired.