

Paparella: Volume II: Otology and Neuro-Otology

Section 3: Diseases of the Ear

Part 4: Inner Ear

Chapter 41: Sensorineural Hearing Loss in Children - Genetic

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Although virtually all diseases can be said to arise out of or be affected by the genotype, this chapter is restricted to those types of hearing loss in which the genetic component plays a major role. Approximately 50 per cent of all hearing loss can be ascribed to genetic factors. This is a particularly disturbing statistic in view of the fact that in the majority of these cases treatment is of no avail. Prevention remains the primary means of reducing the high incidence of genetic hearing loss. Prevention can, of course, be accomplished only through genetic counseling of high-risk individuals - that is, persons who possess a gene that includes hearing loss in its manifestation.

There are three clear forms of inheritance: autosomal dominant, autosomal recessive, and X-linked. Autosomal dominant inheritance occurs when one of the parents, who is usually heterozygous for the trait, passes the condition on to approximately half of the offspring. The normal children will not be carriers. In autosomal recessive inheritance, both parents (heterozygotes) carry the same recessive gene but are not affected by the disease. Theoretically, one-fourth of their children will be affected, having a double dose of the gene (being homozygous), and one-half of their offspring will be carriers of the gene (heterozygous). If both parents are affected and homozygous for the same recessive gene, all offspring will be affected.

X-linked inheritance may occur through either dominant or recessive transmission; however, almost all conditions that include deafness so transmitted are X-linked recessive. Almost all patients with X-linked disorders are males (hemizygotes), and all of the daughters of an affected male are carriers (heterozygotes). The probability is that one-half of the male children of female carriers will be affected. An homozygous female (father is affected; mother is carrier) is fully affected; an heterozygous or carrier female is normal or may partially express the condition (lyonization). There is no male-to-male transmission, but all the daughters of an affected male are carriers. If the X-linked hearing loss is a dominant trait, all daughters of an affected male will be affected, but none of his sons, whereas half of the daughters and half of the sons of an affected female will express the condition.

The majority of genetic hearing loss is transmitted through recessive genes. Approximately half of all types of recessive hearing loss have no accompanying abnormalities. Thus, thorough family histories must be obtained to ascertain whether the defect may be genetic.

Whenever a person is affected with, or is suspected of being a carrier for, hereditary hearing loss, genetic counseling should be given to inform the patient of the probabilities of there being affected offspring. There are many types of hereditary hearing loss, so that the

likelihood of two persons possessing the same genetic defect is small. In some communities, however, where consanguineous marriage (ie, marriage between persons with recent common ancestors) is frequent, the incidence of genetic hearing loss (and other hereditary diseases) is greatly increased. Even though hearing-impaired people tend to marry other hearing-impaired people, this does not necessarily account for an increase in inherited hearing loss, because of the small probability that the parents possess the identical genetic defect.

Differential diagnosis of genetic hearing loss is the responsibility of the otolaryngologist. Accurate assessment of the etiology provides the foundation for adequate management of the problem, whether medical, educational, or consultative. Cytogenetic analysis (ie, examination of a patient's karyotype) can be used to identify disorders arising out of chromosomal abnormalities with a high degree of certainty and may, in appropriate cases, even be established antenatally. In mendelian disorders without alteration of the karyotype, diagnosis can often be established by the combined use of biochemistry and genetics. Because heredity plays such a large in hearing loss, it is important that the otologist be aware of the various forms in which genetic impairment of hearing can occur. Since one-third of hereditary hearing losses are associated with a known syndrome, familiarity with the features of some of the more common syndromes is necessary.

The organization of this chapter is based on the distinction between congenital (aplastic) and delayed (heredodegenerative) hearing loss of genetic origin. A further differentiation between hearing loss occurring alone and hearing loss occurring in association with other abnormalities (syndromes) will be used to facilitate clinical categorization of the problem. In each of these categories we shall consider only genetic *sensorineural* hearing losses. The reader may wish to refer to Bergstrom and Stewart (1971), Bergstrom and colleagues (1971), Black and coworkers (1971), and Konigsmark and Gorlin (1978) for classifications that include hereditary conductive hearing loss.

Other distinctions in classification have been suggested for genetic hearing loss. For example, Konigsmark (1969) and Konigsmark and Gorlin (1978) categorized hereditary hearing loss according to other systems involved in the syndromes (eg, integumentary, visual, skeletal, etc). Proctor and Proctor (1967) classified genetic hearing loss according to dominant and recessive modes of transmission. In this chapter we differentiate between congenital and delayed manifestations of hereditary hearing loss, although this distinction is not always used, since all genetic hearing loss may be considered to be congenital in origin. However, the time of appearance of a hearing loss is important for early clinical diagnosis and management; therefore, the otolaryngologist should be familiar with disorders in which genetic hearing loss is manifested at the time of birth (congenital or aplastic) and those that develop subsequent to birth (delayed or heredodegenerative).

Congenital Genetic Hearing Loss Occurring Alone

Those types of hearing losses characterized by agenesis or dysgenesis of the components of the inner ear are common congenital hereditary problems with hearing. The following classic types of aplasia are differentiated on the basis of anatomic severity and the site of the developmental failure.

Michel's Aplasia

Michel's aplasia (Michel, 1863) is characterized by total lack of development of the inner ear. In some cases even the petrous portion of the temporal bone is not developed, whereas in others it is present but is underdeveloped at the usual site of the labyrinth. Spaces may be found in the petrous bone, but these do not resemble components of the inner ear. The external and middle ears may be normally formed and apparently capable of functioning. In the case originally reported by Michel, the malleus, incus, and tensor tympani muscle were fully developed but the stapes was missing. There is an unfortunate dearth of well-documented reports of Michel's aplasia in the recent literature. Absolute diagnosis must rely on postmortem histopathologic findings, since x-ray studies do not demonstrate a differentiation between Michel's aplasia and labyrinthitis ossificans.

Mondini's Aplasia

This type of malformation (Mondini, 1791) has been described as a flattened cochlea with development only of the basal coil. Instead of two and one-half turns in the bony cochlea, there may be only one and one-half turns, with the middle and apical turns occupying a common space or cloaca. The agenesis is rarely symmetrically bilateral, but the other ear always shows some degree of malformation. Similar bony malformation may be found in normal subjects (Polvogt and Crowe, 1937).

The vestibular structures and their associated neural elements may be similarly underdeveloped. There appears to have been an interruption in the development of the cochlea at the stage in which it is represented by a short, curved tube (about the 6th week of gestation). Vestibular structures may be recognizable in some cases; in others there is no membranous labyrinth. Occasionally some sensory epithelium may be present; this implies some possibility of function. An enlarged endolymphatic duct and sac and a deficient utriculoendolymphatic valve are commonly found associated with collapse of Reissner's membrane or an absence of endolymphatic hydrops (Gussen, 1968; Paparella, 1980). Lesions of the end-organ of Corti may be present or absent. The stria vascularis and spiral ligament are often normal. Mondini's deformity may be associated with an absence of the oval and round windows along with other aplastic lesions of the middle ear.

The Mondini type of deafness may first become manifest in childhood or early adult life. Auditory function ranges from marked deafness to normal hearing. Mechanisms of hearing loss in Mondini's aplasia may be explained on the basis of pathologic findings in the inner ear or middle ear, including dysgenesis of the end-organs and associated neural elements sufficient to cause a sensorineural hearing loss; aplasia of the oval or round windows, which might explain manifest "sensorineural hearing loss" in the presence of normal-appearing organs of Corti; and aplasia or infection of the middle ear causing a conductive loss. Because of the probability that some residual hearing may be present, amplification should be attempted.

Scheibe's Aplasia

In this type of aplasia (Scheibe, 1892), the bony labyrinth is fully formed, as are the membranous utricle and semicircular canals. The parts inferior (sacculle and cochlear duct) is

represented by mounds of undifferentiated cells. The tectorial membrane is reduced in size. The scala media is collapsed and Reissner's membrane may lie directly on the mound of undifferentiated cells and the stria. The stria vascularis and organ of Corti show abortive strands of connective tissue. The wall of the saccule is flattened and lies on the aplastic sensory epithelium and otolithic membrane.

Scheibe's aplasia is the most common form seen in inherited congenital hearing losses, especially those having autosomal recessive inheritance. The pathologic condition is similar to that seen in animals with genetic congenital hearing loss. An audiogram may show some residual hearing in the low frequencies. Since a few hair cells can usually be seen histologically, there may be some hearing remaining, and amplification may be of some use.

Alexander's Aplasia

This type of inherited hearing impairment is characterized by aplasia of the cochlear duct (Alexander, 1904). The organ of Corti and adjacent ganglion cells of the basal coil of the cochlea are most affected, resulting in a high frequency hearing loss. The patient with Alexander's aplasia should be able to use amplification to an advantage since hearing remains in the low frequencies.

Congenital Hearing Loss Associated With Other Abnormalities

Congenital hearing loss may accompany disorders of other systems. In some cases the hearing loss may be the first symptom of a previously unsuspected disease. Therefore, it is important that the otologist be alert to the possibility of other defects associated with the hearing loss. The number of described genetic syndromes involving hearing loss is so large as to make detailed discussion of each impossible. Therefore, we will discuss only a few of the more common syndromes and describe briefly the remaining ones that the otolaryngologists may expect to encounter. For more information on rarer, more unusual syndromes, the reader is referred to the literature (Konigsmark, 1969; Konigsmark and Gorlin, 1978; Proctor and Proctor, 1967).

Waardenburg's Syndrome

Waardenburg's syndrome (Waardenburg, 1951) occurs in about 2 of 100,000 births and is estimated to account for 2 to 3 per cent of all congenital hearing loss in the USA. It is heterogeneous, and there are two distinct forms. Both have autosomal dominant inheritance, with individual characteristics having variable expression. In type I, the primary features of the syndrome include lateral displacement of the medial canthi and lacrimal points (in 100 per cent of cases), a flat nasal root (75 per cent), hyperplasia of the eyebrows (50 per cent), partial or total heterochromia of the irises (25 per cent), partial albinism in the form of a white forelock (20 per cent), and congenital hearing loss (25 per cent). In type II, there is no dystopia canthorum. The degree of hearing impairment varies from an almost total loss of hearing to a moderate loss with preservation of the high frequencies (Fisch, 1959). The pathologic condition of the temporal bone associated with Waardenburg's syndrome includes atrophy of the organ of Corti and the stria vascularis, with reduction of the number of nerve cells in the spiral ganglion.

Albinism

Albinism is the hereditary inability to synthesize melanin. There are two chief clinical variants: ocular albinism, which has X-linked recessive inheritance, with the lack of pigmentation being restricted to the eye; and oculocutaneous albinism, inherited as an autosomal recessive trait, with the lack of pigmentation in the hair, skin, and eyes. Sensorineural hearing loss of varying severity is usually associated with the oculocutaneous type but also has been reported in the ocular form (Reed, 1967).

Hyperpigmentation

Severe sensorineural hearing loss has been found in persons affected by hyperpigmented areas of skin (the leopard syndrome). The pigmentary defects progress from small spots in localized areas in childhood to larger lesions over the whole body in adults. Transmission of this syndrome is autosomal dominant. Vestibular functioning may be depressed.

Onychodystrophy

The association of congenital dystrophy of the fingernails and toenails with congenital sensorineural hearing loss was first described by Feinmesser and Zelig (1961) in two offspring of a consanguineous marriage, suggesting autosomal recessive inheritance. The affected siblings had short, small fingernails and toenails, and severe high-frequency hearing loss. The syndrome may also include defects of the teeth, hair, and sebaceous glands.

Pendred's Syndrome

The triad constituting Pendred's syndrome (Pendred, 1896) has been defined as congenital perceptive hearing loss, goiter, and a pathologic perchlorate test. It is characterized by abnormal metabolism of iodine, resulting in enlargement of the thyroid. Increase in size usually appears in adolescence, and nodules develop in adulthood. Affected persons are usually born with hearing impairment. It has been estimated that this syndrome may account for as many as 10 per cent of the cases of recessive hereditary hearing loss. Hearing loss is usually bilateral and more severe in the high frequencies. Positive recruitment is frequently found (Nilsson et al, 1964), suggesting that the auditory defect is in the organ of Corti. Tomographic (Illum et al, 1972) and histologic (Hvidberg-Hansen and Jorgensen, 1968) findings reveal cochlear malformation of the Mondini type. Vestibular and semicircular canals have been found to be normal.

Jervell's Syndrome

The main characteristics of Jervell's syndrome (Jervell and Lange-Nielsen, 1957) include a prolongation of the Q-T interval, Stokes-Adams attacks, and congenital, bilateral severe hearing loss. It has been estimated that this disease comprises 1 per cent of all recessive hearing loss.

Syncopal attacks begin to occur in childhood, and affected persons usually suffer sudden death in childhood. Postmortem examinations have not revealed any gross cardiac

defects. The pathologic condition of the temporal bone includes severe atrophy of the organ of Corti, loss of spiral ganglion, accumulation of PAS-positive aggregates of hyalin in an atrophic stria vascularis, and atrophy of the sensory epithelial cells of the utricle and saccule (Friedmann et al, 1966).

Usher's Syndrome

Usher's syndrome (Usher, 1914) affects 3 in every 100,000 individuals. Inheritance is autosomal recessive. It is the major cause of combined deafness and blindness after childhood and accounts for 6 to 10 per cent of the congenitally deaf population (Forsius et al, 1971). Features of the syndrome are progressive retinitis pigmentosa and congenital severe to moderate sensorineural hearing loss.

Those children affected with the syndrome are born either deaf or with severe bilateral hearing loss. Loss of visual acuity occurs gradually during childhood as deposits of pigment occur in the periphery of the retina. Cataracts may occur also. The absence of cochlear microphonic potential points to a malfunction of the hair cells as the cause of the hearing impairment (Abraham et al, 1977). This is supported by histopathologic findings of sensory degeneration of the cochlea (Belal, 1975). An end-organ lesion in the basal turn of an otherwise normal membranous labyrinth can be found.

Trisomies

Chromosomal anomalies, which account for some cases of congenital hearing loss, are not truly hereditary but represent cases in which there is added or missing chromosome material (partial or whole chromosomes). Normally, humans have 46 chromosomes: 22 pairs of autosomal chromosomes and 1 pair of sex chromosomes. The chromosomes are numbered by pairs (1 through 22) and these pairs are grouped according to similar morphologies. Thus, the term trisomy 13 indicates that there is an extra chromosome 13. Likewise, trisomy 18 and trisomy 21 indicate that there is an extra chromosome 18 and 21, respectively. Usually, parents have a normal karyotype and are normal in other respects, but the mother may be older.

Trisomy 13

Trisomy 13 occurs in 1 of every 6000 births. Infants with this syndrome have the most severe malformation of all those born alive with chromosomal abnormalities. Clinical features include microcephaly and mental retardation; scalp defects; microphthalmia; cleft lip and/or cleft palate; postaxial polydactyly; rocker-bottom feet; small, low-set, malformed pinnae; absence of the external ear canal or the middle ear; apneic spells and myoclonic seizures; cardiac dextroposition and interventricular septal defects; and other visceral defects. The congenital malformations are so extreme that only a few infants survive longer than 1 year, and most die within the first few months after birth. Histopathologic changes in the ear include a shortening of the length of the cochlea, cystic lesions in the stria vascularis, a patent cochlear aqueduct, anomalies of the semicircular canal, abnormalities of the angulation of the facial nerve, and saccular dysplasia or degeneration (Miller et al, 1971; Sando et al, 1975; Tomoda et al, 1983).

Trisomy 18

Trisomy 18 occurs in about 1 in 5000 to 10.000 live births. The average life span of these infants is about 10 weeks, with 13 per cent surviving beyond the age of 1 year. The malformations are severe and wide-ranging. Clinical features include mental retardation; prominent occiput; micrognathia; low-set and malformed pinnae; hypertonicity; flexed and overlapping fingers; cardiac, renal, and intestinal defects; and deformities of the sternum, pelvis, and hip. Histopathologic findings include ossicular malformations, decreased spiral ganglion, incomplete development of the stria vascularis, enlarged endolymphatic duct, malformation or absence of the horizontal semicircular canal, and absence of the utriculoendolymphatic valve (Sando et al, 1970; Kos et al, 1966; Miglets et al, 1975).

Trisomy 21 (Down's Syndrome)

Down's syndrome is the most common of the chromosomal disorders. The incidence in newborns is about 1 of 1000 births in the USA. Maternal age has a strong influence on the incidence of Down's syndrome. It occurs in 1 of 1550 live births in women under the age of 20 and in 1 of 25 live births in women over 45 years of age (Thompson and Thompson, 1986). The clinical features include mental retardation; flat facial profile; oblique palpebral fissures; muscular hypotonia; hyperflexibility; broad, short trunk; dysplastic pinnae, pelvis, and middle phalanx; epicanthic folds; and congenital heart disease. Down's syndrome is one of the leading causes of mental retardation, which is often severe. Although 40 per cent of these children die by age 10, patients frequently survive into adult life.

Estimates of hearing loss in patients with Down's syndrome range from about 40 to 77 per cent. The hearing loss can be conductive, sensorineural, or mixed. Histopathologic findings in temporal bone include residual mesenchyme in the middle ear, a wide angle of the facial genu, vestibular changes ranging from mild to severe, endolymphatic hydrops, shortened cochlear spirals, and in some cases smaller vestibular measurements (Igarashi et al, 1977; Harada and Sando, 1981).

Delayed Genetic Hearing Loss Occurring Alone

All hereditary disorders involving hearing loss, whether they occur at the time of birth or develop subsequent to birth, have a genetic basis that is present at the time of conception. It is important for the clinician, however, to recognize a hearing loss as early as possible and to advise the patient accordingly. Thus the aplasias (genetic hearing loss at birth) are generally to be considered stable and nonprogressive, whereas those disorders that develop after birth (delayed) represent a hereditary degeneration of a fully formed organ of Corti and are usually progressive.

Familial Progressive Sensorineural Hearing Loss

Familial progressive sensorineural hearing loss (Cawthorne and Hinchcliffe, 1957) has a clinical similarity to other types of sensorineural hearing loss. Correct diagnosis, therefore, depends primarily on a careful history of the problem in relation to its occurrence in other members of the family. The audiometric patterns of familiar sensorineural hearing loss typically show either a loss in the high tones, or a flat or basin-shaped loss. The hearing loss

is usually bilateral and transmission is considered to be autosomal dominant. It manifests during childhood (8 to 12 years of age) or in early adult life (late teens and thereafter) and progresses in severity during adulthood. Genetic progressive hearing loss, characterized by a bilateral sensorineural loss with good discrimination, is commonly seen in young adults and may be confused with the somewhat uncertain clinical entity called cochlear otosclerosis, causing sensorineural hearing loss without a conductive component. Indeed, these may represent variants of the same problem. Temporal bone studies of familial hearing loss have shown absence of the organ of Corti in the basal turn, degeneration of the spiral ganglion in the basal turn, and irregular degeneration of the stria vascularis (Paparella et al, 1969).

Hearing Loss Occurring With Other Abnormalities

Other genetic syndromes that include delayed sensorineural hearing defects exist, but for the most part they differ from those described below only by the addition or involvement of another symptom. Konigsmark (1969), Konigsmark and Gorlin (1978), and Proctor and Proctor (1967) have compiled extensive lists of such syndromes.

Alport's Syndrome

Alport's syndrome is characterized by nephritis accompanied by sensorineural hearing loss and various disorders of the eye, including posterior cataracts, corneal dystrophy, and dislocation of the lens. Males are affected more frequently and more severely than females and in males the disease is more likely to progress to renal failure and deafness. The symptoms appear at ages 5 to 20, with the onset of renal failure at 20 to 50 years. The mode of inheritance of this syndrome is usually autosomal dominant, but in some families an X-linked dominant mode of genetic transmission is seen.

Hearing loss is usually bilateral, symmetric, and slowly progressive, affecting the high frequencies most severely. Histologic reports of pathologic findings in temporal bones vary from a normal-appearing organ of Corti to severe degeneration. Loss of cells in the spiral ganglion and destruction of the neuroepithelium of the cristae and semicircular canals have also been reported (Winter et al, 1968; Fujita and Hayden, 1969; Myers and Tyler, 1972; Celis-Blaubach et al, 1974). Audiologic findings of bilateral, symmetric sensorineural hearing loss, high scores on the short increment sensitivity index, type II Békésy tracings, and tone decay within normal limits point to the cochlea as the site of the lesions (Miller et al, 1970).

Lysosomal Storage Diseases

There is a group of metabolic diseases characterized by an enzymatic deficiency that results in lysosomal accumulation of material that would otherwise be metabolized. These storage diseases have been divided into subgroups based on their accumulated metabolites as glycogenoses, sphingolipidoses, mucopolysaccharidoses, and mucolipidoses. Hearing loss has been reported only in some entities from these various subgroups; however, because entities within a category resemble one another clinically as well as biochemically, the otolaryngologist should be aware of the possibility of hearing loss in patients with any of these disorders. Following are examples of some of these disorders.

Fabry's Disease

Fabry's disease (angiokeratoma corporis diffusum universale) is part of the subgroup of sphingolipidoses and has X-linked recessive inheritance. Hemizygous males are affected more severely than heterozygous females. This progressive disorder results from the systemic accumulation of the glycosphingolipid trihexosyl ceramide in the endothelial, perithelial, and smooth-muscle cells of blood vessels and in the ganglion cells, the autonomic nervous system, reticuloendothelial cells, connective tissue, myocardial cells, epithelial cells of the cornea, and the glomeruli and tubules of the kidney. Skin lesions, corneal opacities, and peripheral edema occur in childhood or adolescence, with death in adulthood resulting from cardiovascular, central nervous system, and renal involvement. The hearing loss is usually bilateral and sensorineural, occurring mainly in the high frequencies. Tinnitus and vertigo are common. Histopathologic findings in temporal bones include atrophy of the stria vascularis and spiral ligament, reduced numbers of cells in the spiral ganglion, and evidence of accumulation of glycosphingolipids in the vascular endothelial cells and various ganglion cells. Findings in the middle ear include otitis media (Schachern et al, 1989).

Hurler's Syndrome

Hurler's syndrome (MPS-IH) is one of several variants of mucopolysaccharidoses that have been classified MPS-I through VII. The mucopolysaccharidoses are forms of lysosomal storage diseases that involve the accumulation of various mucopolysaccharides. In Hurler's syndrome, the mucopolysaccharides that are accumulated are dermatan sulfate and heparan sulfate. The disease is a relatively rare autosomal recessive disorder, which occurs as seldom as 1 in 100,000 persons. The clinical manifestations of this syndrome include dysostosis multiplex, dwarfing, cloudy corneas, mental retardation, and hearing loss. The characteristic phenotype is usually not recognized until after the 1st year of life and survival is rare, after the 14th year. The hearing loss is usually mixed, with the sensorineural component usually greater in the high frequencies. Histopathologic findings in six temporal bones included otitis media, incomplete pneumatization due to residual mesenchyme, cells containing PAS-positive material within the mesenchyme, atrophy of the spiral ligament, basophilic concretions in the stria vascularis, and, in some cases, degeneration of the organ of Corti (Schachern et al, 1984).

Hunter's Syndrome

Hunter's syndrome (MPS-II) is the only mucopolysaccharide disorder with X-linked recessive transmission, the others having autosomal recessive inheritance. Hunter's syndrome, like Hurler's syndrome, involves the accumulation of heparan and dermatan sulfates. The clinical features of the disorder resemble Hurler's syndrome, with the following exceptions: (1) patients generally have a longer life span and usually are not as severely retarded; (2) clouding of the corneas does not occur, but retinal degeneration and nodular infiltrates of the skin do occur. The hearing loss may be conductive, sensorineural, or mixed. Examination of the temporal bones revealed otitis media, persistent mesenchyme, ossicular malformation, and PAS-positive histiocytes (Zeckner and Altmann, 1968; Hayes et al, 1980).

Klippel-Feil Syndrome

Klippel-Feil syndrome is characterized by a congenital defect of the spine resulting from a reduction or fusion of cervical vertebrae (McLay and Maran, 1969). Other defects may include spina bifida, scoliosis, and torticollis. The hearing loss is usually of the profound sensorineural type but conductive and mixed losses also occur. A high incidence of hypoplasia of the inner ear and of anomalies of the middle and external ear has been demonstrated by tomography (Windle-Taylor, 1981). A pathologic report of findings in temporal bones demonstrated underdevelopment of the bony and membranous labyrinth, cochlea, auditory nerve, and ossicular deformation (McLay and Maran, 1969).

Refsum's Disease

Refsum's disease (heredopathia atactica polyneuritiformis) is characterized by retinitis pigmentosa, ichthyosis, polyneuropathy, ataxia, and hearing loss (Refsum, 1946). Visual symptoms usually begin after age 20. Cerebellar ataxia and peripheral neuropathy may appear in childhood or in early adulthood. Approximately 50 per cent of patients with Refsum's disease have progressive sensorineural hearing loss. The pathologic condition of the temporal bone includes degeneration of the stria vascularis and atrophy of the organ of Corti. The vestibular system (pars superior) is normal. The syndrome has autosomal recessive transmission.

Alström's Syndrome

The primary features of Alström's syndrome are retinitis pigmentosa, diabetes mellitus, obesity, and progressive hearing loss (Alström et al, 1959). The retinal degeneration may begin as early as the first year of life, with nearly total visual loss by 20 years of age. The hearing loss appears around the age of 10 and is slowly progressive. The syndrome has autosomal recessive transmission.

Cockayne's Syndrome

In 1938, Cockayne reported a syndrome of dwarfism, retinal atrophy, and deafness. Variable manifestations include microcephaly, mental retardation, pigmentary retinal degeneration, photosensitive dermatitis, disturbance in gait, and peculiar facies including large ears. The onset of the disease is in late infancy, in infants of normal birth weight with normal development during the first months of life. Hearing loss is progressive and varies in degree from mild to severe. It is largely sensorineural, with degeneration of the spiral ganglion and transsynaptic degeneration in the ventral cochlear nucleus, medial dorsal olivary nucleus, and inferior colliculus (Gandolfi et al, 1984). This syndrome exhibits autosomal recessive inheritance.

Richards-Rundle Syndrome

The main features of Richards-Rundle syndrome include mental deficiency, ataxia, hypogonadism, and severe hearing loss (Richards and Rundle, 1959). All the symptoms appear in childhood, and the hearing loss is severe by 5 to 6 years of age. Transmission of the syndrome is autosomal recessive.

Neurofibromatosis

Neurofibromatosis is a relatively common autosomal dominant disorder, occurring in 1 in 3000. There are several forms of neurofibromatosis, the most common being the classic form characterized by multiple neural tumors, numerous pigmented lesions on the skin, and hamartomas of the pigmented iris. When acoustic neuromas occur in classic neurofibromatosis, they are unilateral; in the central or acoustic form of neurofibromatosis, bilateral acoustic tumors are invariably present. The central form of the disease is characterized by pigmented lesions of the skin and by an absence of hamartomas of the pigmented iris. Skin tumors may or may not be present.

Crouzon's Disease

Craniofacial dysostosis, or Crouzon's disease (Crouzon, 1912), is characterized by premature synostosis of the cranial sutures, exophthalmos, "parrot-nose" (hook-nose), short upper lip and protruding lower lip, atresia of the auditory meatus, and mixed hearing loss. The syndrome has autosomal dominant inheritance.