Chapter 4: Pathology of the cochlea

I. Friedmann

The delicate structures of the ear are housed in a comparatively inaccessible part of the skull as Du Verney, a French pioneer in this field, has so aptly described in a postscript to his great thesis *Traité De L'Organe De L'Ouie* (1683): 'Of all the Organs assign'd to the Use of Animals, we have the least knowledge of those of the Senses: but there is none more obscure than that of Hearing; the Minuteness and Delicacy of the Parts which compose it, being inclos'd by other Parts render Enquiries into them more difficult, and their Structure so intricate, that there is much trouble in explaining as there was in discovering them' (Asherson, 1979).

The sensory organ of hearing was first described by Alfonso Corti who was born at Gambarana, near Pavia in Lombardy, Italy, on 15 June, 1822 and died in 1876 at his villa in Mazzolino. He was 19 when he entered medical school at the University of Pavia, but did not complete his course because, at the age of 23, he was attracted by the growing fame of Vienna University where he later received his medical degree. There he attended the Institute of Anatomy and, guided by the great anatomist Joseph Hyrtl, Corti concentrated on the research of the anatomy of the inner ear. Subsequently working with Albert von Kölliker at the University of Würzburg, he was the first to describe the sensory epithelium of the inner ear.

In his experiments, Corti used material as fresh as possible and placed tissue specimens with a diameter of a few millimetres between two slides bonding them with a mastic material. He then allowed a fixative to run between the slides and after fixation, he stained his preparations with a carmine solution. Thus, he was the first to use carmine in histology. In his studies, Corti used a light microscope allowing magnifications of 20-500 times.

Applying this procedure, Corti was not only the first to recognize the bipolar cells of the spiral ganglion, but was able to describe in some detail the basilar membrane, the inner spiral sulcus cells, the pillar cells, as well as the foramina nervosa. Furthermore, he detected the three rows of the outer hair cells and he was the first to describe the tectorial membrane and the stria vascularis in his paper *Recherches sur l'organe des mammifères* in 1851. In spite of the great advances in our knowledge of the organ of Corti, much of the outline given by Corti has remained valid and the organ justly bears his name (Kley, 1986).

Remarkably little has been written about Ernst Reissner (1824-1878) who discovered the vestibular membrane in the cochlear duct. His thesis published in 1851 under the title: *De Auris Internae Formatione* was based on a meticulous study of the fowl embryo ear at different stages of development (Nsamba, 1979).

It is interesting to note that recent intensive research on the fowl and mammalian embryo otocyst mainly in tissue culture, essentially reflects Reissner's method (Fell, 1929; Friedmann, 1959; Orr, 1965; van de Water and Ruben, 1971; Sobkowicz, Bereman and Rose, 1975).
Development of the labyrinth

From the medial aspect of the otocyst, there appears a hollow diverticulum which becomes elongated to form the endolymphatic canal. The otocyst itself divides into the pars superior or vestibular (utricular) pouch and the pars inferior or cochleosaccular pouch. From the vestibular pouch develop three semicircular canals: first, the superior, followed by the posterior and lateral or horizontal canals. The cochlear duct appears around the fifth week as a diverticulum of the cochlear pouch and the saccule develops from its upper portion. This rapid development of the inner ear takes place between the twenty-sixth and the forty-second days: a comparatively short period of time which seems to suffice to transform the simple otocyst into the complicated structures of the membranous labyrinth. After this period, the speed of growth slows down considerably. At this vital period the embryo is most susceptible to teratogenic damage.

The structural differentiation of the cochlea is completed by the third month (length of embryo 25-70 mm). The cochlear nerve fibres induce the sensory epithelium on the inner wall to proliferate, whereas the outer wall continues its longitudinal growth; as a result of this uneven growth the cochlea develops into a spiral organ of two and half coils.

The complete cytological differentiation of the cochlea and the ossification of the otic capsule may be completed between the fourth to the sixth month (embryo length approximately 70-200 mm). It reaches completion with the formation of the three rows of outer hair cells and the single row of inner hair cells with their supporting cells. An area of resorption between the internal and external hair cells leads to the formation of the tunnel of Corti.

Gross anatomy

The inner ear is located in the petrous portion of the temporal bone and is protected by the toughest part of the skull, the otic capsule. The labyrinth, an essential part of the auditory organ, is a complex structure. It consists of a membranous tube lined by epithelium (membranous labyrinth) filled with endolymph and is contained within a bony tube, the osseous labyrinth which is of corresponding complexity of shape and contains the perilymph. The membranous labyrinth is supplied by branches of the auditory nerve and its cochlear branch passes to the organ of Corti.

Classification of hearing loss

The classification of hearing loss has remained complicated and the simple division into conductive, sensorineural and mixed types contrasts sharply with the elaborate schemes developed by various authors.

In trying to distinguish between congenital and acquired deafness, the progress made in recent years has to be considered. The isolation of the rubella virus by Weller and Neva (1962) marked a turning point in the laboratory diagnosis of this condition. This and other advances in virology have thrown some light on the causes of deafness. Furthermore, the rapid progress of genetic and chromosome studies has been contributing to a better
understanding of the genetic influences playing such an important role in the causation of hearing loss.

**Pathogenesis**

Hearing loss in the newborn may be caused by failure to develop one or more parts of the auditory system or to an interruption at any stage in the process of development. It may also be the result of some factor which disturbs or causes the degeneration of the already wholly or partly developed hearing mechanism. Ormerod (1960) tabulated the pathology of congenital deafness as follows:

(1) failure to develop or interruption of development as the result of genetic factors, or toxic influence caused by certain forms of maternal illness during the first 3 months of pregnancy (aplasia)

(2) interruption of development

(3) degeneration of parts of the auditory apparatus which have already developed in some degree or have reached maturity (abiotrophy):

(a) of the cochlear duct or scala media

(b) of the sensory end organs

(c) of the nerve elements.

The pathology of deafness may be conveniently classified according to the following scheme. No new categories are proposed, all have been selected from previous writings on the subject (Friedmann, 1974), although there may be differences of opinion about the interpretation of some of the syndromes.

(1) Pathology of deafness of genetic origin
lesions of the conductive apparatus
lesions of the sensorineural apparatus
aplasia
abiotrophy (heredodegenerative lesions)
chromosome aberrations

(2) Embryopathies
antenatal: rubella, syphilis, toxoplasmosis; other infections - viral and bacterial; hormonal;
perinatal: infections; asphyxia; kernicterus; toxic; hormonal; metabolic
postnatal: infection - viral and bacterial; neoplasms; hormonal; environmental - exposure to noise; ageing; toxic.
**Aplasia**

These are hereditary lesions of a degenerative nature, not apparent at birth but revealed at a later period of life, of a progressive nature and associated with deafness. Several classical types are recognized (Schuknecht, 1967):

1. Michel type (complete failure of development of the inner ear)
2. Mondini type (incomplete development of the bony and membranous labyrinth)
3. Scheibe type (cochleosaccular aplasia)
4. Alexander type (membranous cochlear aplasia).

Membranous cochleosaccular aplasia as described by Scheibe (1892) is the most common pathological lesion in congenital sensorineural deafness of any cause.

Suehiro and Sando (1979) developed a new elaborate classification of labyrinthine anomalies which, however, has not been widely applied and may prove complicated to otologists.

**Heredodegeneration (abiotrophy)**

These conditions are of considerable general interest. Heredodegenerative deafness occurs alone or in combination with other abnormalities in which case they are known as 'syndromes'. There are about 70 phenotypically-distinct types of syndrome which may be classified as mesodermal, ectodermal and neuroectodermal, according to the combination of anomalies which are present:

1. occurring alone: in infants or in adults
2. associated with other abnormalities
   
   a. essentially mesodermal, for example Alport's syndrome; Jervell-Lange-Nielsen (cardioauditory) syndrome; Pendred's syndrome; Hurler's syndrome (gargoylism); Marfan's syndrome
   
   c. essentially neuroectodermal, for example von Recklinghausen's disease; Refsum's syndrome; Jamaica neuropathy.

Chromosomal aberrations are responsible for a number of severe anomalies. The presence of an extra chromosome (trisomy) may lead to anomalies associated with deafness.

**Pathology**

The investigation of the pathology of the cochlea requires the application of a wide range of scientific methods. Histochemical and immunological studies as well as both transmission and scanning electron microscopy have provided an increasing amount of
information on the morphology of the inner ear in health and diseases (Lim and Lane, 1969; Engstrom and Ades, 1973; Hunter-Duvar, 1978). The pathological changes of the different constituents of the inner ear can be assessed in familiar general pathological terms (*Table 4.1*).
### Table 4.1. Histopathology of the cochlea and of the organ of Corti

<table>
<thead>
<tr>
<th>Site</th>
<th>Lesion</th>
<th>Aetiology of deafness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensory epithelium</strong></td>
<td>Total absence or loss (abiotrophy)</td>
<td>Congenital: ageing</td>
</tr>
<tr>
<td></td>
<td>Partial absence or degeneration of the sensory and supporting cells</td>
<td>Noise</td>
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<tr>
<td></td>
<td>Shrinkage: retraction: adhesions</td>
<td>Drugs</td>
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<tr>
<td><strong>Tectorial membrane</strong></td>
<td></td>
<td>Congenital</td>
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<td></td>
<td></td>
<td>Viral (rubella, measles and mumps)</td>
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<tr>
<td><strong>Reissner's membrane</strong></td>
<td>Distension</td>
<td>Anencephaly</td>
</tr>
<tr>
<td></td>
<td>Collapse</td>
<td>Ménière's disease</td>
</tr>
<tr>
<td></td>
<td>Rupture</td>
<td>Anencephaly</td>
</tr>
<tr>
<td><strong>Stria vascularis</strong></td>
<td>Atrophy</td>
<td>Meningitis</td>
</tr>
<tr>
<td></td>
<td>Congestion and hyalinization</td>
<td>Trisomy 22</td>
</tr>
<tr>
<td></td>
<td>PAS-positive deposits</td>
<td>Otosclerosis</td>
</tr>
<tr>
<td></td>
<td>Concrements</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cystic degeneration</td>
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<tr>
<td></td>
<td>Vacuolation</td>
<td></td>
</tr>
<tr>
<td><strong>Spiral limbus</strong></td>
<td>Vacuolation</td>
<td>Ageing, presbyacusis</td>
</tr>
<tr>
<td><strong>Otic capsule</strong></td>
<td>Granulations</td>
<td>Diabetes mellitus</td>
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<tr>
<td></td>
<td></td>
<td>Jervell-Lange-Nielsen syndrome</td>
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<tr>
<td></td>
<td></td>
<td>Toxoplasmosis</td>
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<tr>
<td></td>
<td></td>
<td>Budd-Chiari syndrome</td>
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<tr>
<td></td>
<td></td>
<td>Alport's syndrome</td>
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<tr>
<td></td>
<td></td>
<td>Ototoxic agents</td>
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<tr>
<td></td>
<td></td>
<td>Noise</td>
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Changes of the sensory epithelium may be complex (Friedmann, 1974). The neuroepithelium of the organ of Corti may be totally absent, as in various congenital syndromes, or there may be partial degeneration or absence of the hair cells and supporting cells. Basophilic deposits form in the stria vascularis, the nature of which has remained obscure. The tectorial membrane may be deformed and the ultrastructural changes of the sensory epithelium of the inner ear can be extensive. The cytoplasm of hair cells may show protrusions or ballooning followed by rupture of the outer cell membrane, distension of the rough endoplasmic reticulum with multiple Hensen bodies and marked reduction in the number of the ribosomes. Dense bodies and phagosomes may be present (Table 4.2).
### Table 4.2. Ultrastructural changes

<table>
<thead>
<tr>
<th>Component</th>
<th>Changes</th>
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<tbody>
<tr>
<td>Cytoplasm of hair cells</td>
<td>Protrusion-rupture of outer cell membrane</td>
</tr>
<tr>
<td></td>
<td>Distension of rough endoplasmic reticulum</td>
</tr>
<tr>
<td></td>
<td>Hyperplasia of smooth endoplasmic reticulum</td>
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<tr>
<td></td>
<td>Multiple Hensen bodies</td>
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<tr>
<td></td>
<td>Dense bodies +++</td>
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<tr>
<td></td>
<td>Phagosomes +++</td>
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<tr>
<td></td>
<td>Golgi apparatus - concentration of ototoxic secretory and toxic substances</td>
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<tr>
<td>Ototoxic antibiotics</td>
<td></td>
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<tr>
<td>Mitochondria</td>
<td>Damage and rupture of cristae</td>
</tr>
<tr>
<td></td>
<td>Vacuolation and vesculation</td>
</tr>
<tr>
<td>Nucleus</td>
<td>Aggregation of chromatin</td>
</tr>
<tr>
<td>Ribosomes</td>
<td>Reduction</td>
</tr>
<tr>
<td>Nerves</td>
<td>Bulging and rupture - myelin inclusions, atrophy</td>
</tr>
<tr>
<td>Neurons</td>
<td>Lipofuchsin</td>
</tr>
<tr>
<td></td>
<td>Lysosomes</td>
</tr>
<tr>
<td></td>
<td>Vacuolation</td>
</tr>
<tr>
<td></td>
<td>Nissl substance - reduced</td>
</tr>
<tr>
<td>Basal lamina</td>
<td>Protein crystalline inclusions</td>
</tr>
<tr>
<td></td>
<td>Multiplication and production of long-spaced collagen</td>
</tr>
</tbody>
</table>

The mitochondria are damaged and contain ruptured cristae. Peripheral aggregations of chromatin and intranuclear viral inclusions may be present. Crystalline laminated or striated inclusions may be seen in the hair cells (Friedmann, Cawthorne and Bird, 1965a; Slepecky, Hamernik and Henderson, 1980, 1981).

The stria vascularis forming the lateral wall of the cochlear duct is the site of various well-defined pathological lesions associated with several syndromes and diseases: atrophy in ageing and presbyacusis (Schuknecht, 1974); congestion and hyalinization in diabetes; periodic acid-Schiff (PAS) positive deposits in the Jervell-Lange-Nielsen syndrome; calcification and adhesions in the Budd-Chiari syndrome, toxoplasmosis and Alport's syndrome; vacuolation caused by ototoxic substances and by noise and inflammatory granulations in viral diseases (rubella, measles).

Basophilic deposits in the stria vascularis were studied by Zaytoun (1983). In 42 temporal bones from 22 patients with hearing loss, atrophy of the stria was seen in 12 cases and substrial fibrosis in three; cystic structures were noted in four and the stria appeared to be normal in seven cases.

In 18 cases, bilateral deposits were noted and there were deposits in two or all three coils of the cochlea; the middle coil was the most common site. The deposits presented in the marginal zone of the stria vascularis and protruded into the endolymphatic space. The organ of Corti often showed mild to severe loss of the hair cells and/or total degeneration.
Microscopically, the deposits showed a striking variation of size and shape. Some were elongated or crescent-shaped, others were rounded or polygonal with a concentric lamellar pattern. Still others exhibited a fibrillar pattern. Occasionally, the deposits caused the stria vascularis to be detached from the spiral ligament. In some, the deposits showed a crystalline pattern with sharp edges and fine spicules as described in a case of long-standing profound sensorineural deafness (Nadol and Burgess, 1982) and in Jervell-Lange-Nielsen syndrome (Friedmann, Fraser and Froggatt, 1966; Friedmann, Foggatt and Fraser, 1968).

Ectodermal syndromes

Waardenburg's syndrome

In 1951, P. J. Waardenburg, a Dutch ophthalmologist, described a genetically determined (autosomal dominant) syndrome of which unilateral deafness is a feature. The partial albinism of the hair of the scalp has given the condition one of its names - white forelock syndrome. The commonest and most important feature is sensorineural deafness with eyelid deformity and heterochromia or deep blue eyes.

The histopathology of the temporal bones of a child with Waardenburg's syndrome studied by the author showed total absence of the organ of Corti, atrophy of the stria vascularis and absence of the neurons of the spiral ganglion (Friedmann, 1974).

Since the original description over 1200 cases of the syndrome have been reported, not only in patients of Dutch extraction but also in English, American, African, Indian, Oriental and Black persons (Hageman, 1977; Wang, Karmody and Pashayan, 1981; Galich, 1985). Waardenburg's syndrome seems to consist of two genetically distinct entities, which can be differentiated clinically into Waardenburg's syndrome with or without dystopia canthorum (type 1 and type 2 respectively). Congenital deafness in both ears may occur in about 25% of the patients with Waardenburg's syndrome type 1 and in about 50% of those with type 2.

Usher's syndrome

This consists of retinitis pigmentosa and sensorineural deafness. The histopathological findings include malformation of the cochlea, cochleosaccular dysplasia and degeneration of the spiral ganglion (Usher, 1914).

Cogan's syndrome

Non-syphilitic interstitial keratitis associated with vestibuloauditory dysfunction was first described by Cogan in 1945. Twenty-seven cases were reviewed by Cody and Williams (1960) and two cases were added by Bellucci, Grobeisen and Sah (1974). Fifty-three cases have been reviewed by Cheson, Bluming and Alroy (1976) (including one of their own). In 72% of the affected patients there was an underlying systemic, often vascular, process. Ten per cent had fatal or near fatal aortic valvular disease, which proved to be amenable to surgical intervention. Other systemic manifestations have included congestive heart failure, gastrointestinal haemorrhage, adenopathy, splenomegaly, hypertension, musculoskeletal involvement and eosinophilia.
The aetiology and pathology of the syndrome remain obscure. It has been suggested that the syndrome is a manifestation of polyarteritis nodosa (Cheson, Bluming and Alroy, 1976). The pattern of multisystem involvement can be almost identical in these entities and, in fact, sudden nerve deafness may occur in polyarteritis nodosa.

The clinical course of Cogan's syndrome is as variable as its modes of presentation. Some patients have died within months of onset; others have lived up to 15 years after diagnosis. Most patients regain and retain good vision, but permanent hearing loss is the rule (Wolff et al, 1965) (see Chapter 15).

**Histopathology**

Necrotizing vasculitis, affecting many organs may be present, affecting the heart, aorta, kidneys and gastrointestinal system. The inner ear shows degeneration of the organ of Corti and of the spiral ganglion. Endolymphatic hydrops and ossification of the labyrinth may occur.

**Mesodermal syndromes**

**Alport's syndrome**

This can be defined as familial nephropathy, usually accompanied by sensorineural deafness (Alport, 1927; McDonald, Anderson and Ott, 1978). It is inherited as an autosomal dominant trait and is more severe in males. The disease begins in childhood, usually with haematuria following an acute upper respiratory infection. Hearing loss is slowly progressive and asymmetrical. The discrimination score remains normal until severe hearing loss ensues.

**Histopathology**

The changes in the stria vascularis range from mild perivascular oedema with thickening of the capillary walls and fragmentation or splitting of the basement membrane, to complete degeneration and atrophy. The spiral prominence is less affected, although severe perivascular oedema may be present. In cases of severe deafness there is a loss of inner and outer hair cells and of ganglion cells, particularly in the basal turn. Non-specific basophilic deposits may occur (Gregg and Becker, 1963; Crawford and Toghill, 1968; Nadol and Arnold, 1987).

However, according to Fujita and Hayden (1969), consistent inner ear pathology is conspicuous by the absence of any characteristic histological findings. A normal organ of Corti with a normal spiral ganglion and acoustic nerve was found in some cases (Wood and Knight, 1966; Arnold, personal communication). It has been suggested that many of the degenerative changes noted in the hair cells of the organ of Corti could be attributed to autolysis (Miller et al, 1970).

The pathogenesis of the inner ear hearing loss is not completely understood. It is not clear whether this undoubted congenital disorder is based on the primary degeneration of the inner ear or whether the sensorineural hearing loss resulted from a special type of glomerulonephritis (Arnold, 1984). Since deafness has been reversed after renal transplantation
The mechanism causing hearing loss may be considered to be secondary to renal disease.

The renal changes combine various features of chronic glomerulonephritis, pyelonephritis and interstitial nephritis. Lipid-laden foam cells are present in the tissues, often forming long rows and clusters in the renal cortex, a characteristic feature of hereditary nephritis (Krickstein, Gloor and Balough, 1966).

The association of certain clinical problems existing simultaneously in the kidney and the ear has been recognized (Bergstrom et al., 1973). The ultrastructural organization of both these organs displays certain similarities of functional importance. Evidence of a shared antigenicity between the two organs has been noted, suggesting an immunological basis for Alport's syndrome (Quick, Fish and Brown, 1973).

**Jervell-Lange-Nielsen syndrome**

The Jervell-Lange-Nielsen, or cardioauditory, syndrome consists of congenital deafness with an abnormal electrocardiogram and fainting attacks, frequently causing the sudden death of a child so affected. This rare syndrome was first described, in 1957, by Jervell and Lange-Nielsen in four of six siblings of a Norwegian family (Jervell, Thingstad and Thor-Østen, 1966). The fainting attacks had originated in childhood and three of the children had died at the ages of 4, 5 and 9 years respectively. The deaf children showed striking abnormalities of the electrocardiogram, previously undescribed, and characterized mainly by a gross prolongation of the Q-T interval. Levine and Woodworth (1958), during the screening of several thousand deaf persons, described the syndrome in a boy of Finnish ancestry who died suddenly at the age of 13. Nine further cases in Britain and Ireland were ascertained (Friedmann, Fraser and Froggatt, 1966; Friedmann, Froggatt and Fraser, 1968). The attacks are considered to be syncopal as a result of cardiac insufficiency secondary to cardiac arrest or some transient arrhythmia, and the syndrome is inherited in an autosomal recessive manner.

**Histopathology**

The most common finding is a widespread degeneration of the sensory end organs of the cochlea and of the vestibular apparatus; Reissner's membrane is collapsed and adheres to the stria vascularis, to the tectorial membrane and/or the remnants of the organ of Corti. The stria vascularis in every coil contains unusual spherical inclusions of some eosinophilic hyaline matter which seem to be most abundant in the apical coils. The deposits filling distended vessels protrude into the cochlear duct. The ragged surface of the stria vascularis appears to have been ruptured by the underlying fibrillar or crystalline material forming the deposit or inclusion. The deposited material is PAS-positive. This suggests that it contains mucopolysaccharides or allied substances.

Special investigation of the conducting system of the heart revealed considerable narrowing of the sinusatrial artery with intimal hyperplasia. The gradual narrowing of this artery and its intraneural branches may result in arrhythmia; should this become uncontrollable, death may ensue during a fainting attack.
Pendred's syndrome

Pendred's syndrome consists usually of bilateral profound childhood deafness and the development in childhood of diffuse or nodular colloid goitre. The mental and physical development of the child is otherwise normal. Histopathology of the ear shows malformed cochlear structures and degenerative changes in the inner ear.

Hvidberg-Hansen and Jorgensen (1968) described the temporal bone findings from a 60-year-old man who had been born deaf and from about the age of 25 had developed a goitre which was first removed at the age of 49. The histological diagnosis was of a colloid nodular goitre. At the age of 60, the recurrent goitre had to be removed after unsuccessful replacement therapy.

Histopathology

The bilateral developmental arrest of the labyrinth was of the Mondini type. Apart from this malformation, however, there were also signs of atrophy of the organ of Corti and of the tectorial membrane, endolymphatic hydrops, connective tissue formation in the saccule and utricle, and an increased amount of periotic connective tissue with endosteal ossification of the cochlea.

A recent study by Johnsen, Jorgensen and Johnsen (1986) of five temporal bones from four patients with Pendred's syndrome has confirmed an earlier finding that the malformed cochlea resembled a Mondini-type cochlea.

Mucopolysaccharidoses

These form a group of lysosomal storage diseases caused by inherited deficiency of an enzyme capable of degrading glycosaminoglycans. Hurler's disease (mucopolysaccharidosis (MPS I)) is an autosomal recessively inherited lysosomal storage disease caused by alpha-L-iduronidase deficiency. Therefore, in Hurler's disease, glycosaminoglycans (mucopolysaccharides) accumulate in the tissues and are excreted in the urine. Hurler's disease is distinct from the X-linked recessively inherited Hunter's disease (MPS II), the severe variants of which superficially resemble the former clinically.

Deafness is a well-recognized component of the clinical phenotype in both Hurler's and Hunter's diseases (Hurler, 1919; Kittel, 1963). Although both of these diseases are invariably fatal, deafness often makes an appreciable contribution to the overall morbidity in the earlier stages of their clinical evolution. Hearing loss is also an important practical problem in the clinically milder syndromes associated with alpha-L-iduronidase deficiency (Scheie disease MPS IS) and Hurler Scheie disease (MPS IH/S) and in the mild variants of Hunter's disease. The intellect is well preserved relative to the non-neurological manifestations in both these groups, so that handicaps such as deafness are particularly important in relation to the individual patient's quality of life.
**Histopathology**

Characteristic vacuolated Hurler or gargoyles cells were noted disrupting the fascicles of the vestibulocochlear nerve within the temporal bone in two cases of Hurler's disease (Schachern, Shea and Paparella, 1984; Friedmann et al, 1985). The perivascular spaces of the mastoid process contained many vacuolated cells, and large areas of the mastoid process were replaced by accumulated Hurler cells. The neuroradiological features in these cases were described by Watts et al (1981) and post-mortem biochemical and general pathological studies were reported by Crow et al (1983).

**Idiopathic sudden sensorineural hearing loss**

The challenging diagnostic and therapeutic problems of idiopathic sudden sensorineural hearing loss have attracted a great deal of attention. The condition can be defined as spontaneous sudden hearing loss in patients with apparently no previous otological problems. Its pathogenesis has remained speculative despite some, mainly empirical, improvement in its clinical management.

The pathology has been extensively studied by Schuknecht and Donovan (1986).

**Histopathology**

The pathological changes resemble those occurring in labyrinthitis of known viral aetiology.

The principal histopathological changes involve the organ of Corti and the tectorial membrane with less frequent and less severe lesions of the stria vascularis and of vestibular labyrinth.

In two of the 12 cases studied, the severe hearing loss was attributed to the atrophy of the tectorial membrane and one of the cases showed atrophy of the cochlear neurons as the probable cause.

A histological study of sudden deafness resulting from rupture of cochlear membranes first in the left ear, and then 3 years later in the right ear, in a patient with vertebrobasilar arteriosclerosis was reported by Gussen (1983). Two healed ruptures were shown on the right side, one in the hook portion of the cochlea, and one in the area of the promontory; the latter was adherent to the saccule, distorting it inferiorly. In the left temporal bone, a healed rupture was shown. Although the patient's vertebrobasilar artery disease and her sudden deafness are considered separate entities, one must at least consider whether such long-standing vascular insufficiency might predispose to more readily ruptured membranes with sudden pressure changes in the inner ear.

**Viral diseases**

The ear is potentially open to infection by any of the respiratory viruses and it is a widely accepted assumption that bacterial otitis is often preceded by viral otitis. Although
some respiratory viruses have been isolated from the middle ear, on occasions, there is no
evidence that any of them could invade the middle ear and cause a pure viral otitis media.

Various viruses can cause fetal damage and congenital malformations affecting the ear,
and the role of certain specific viruses is well established; for example rubella,
cytomegalovirus, herpes simplex, varicella-zoster, influenza, mumps and measles.

The ear in maternal rubella

The special vulnerability of the eye, ear and heart of the developing fetus in maternal
rubella during the first trimester of pregnancy is well recognized and, although the period of
greatest danger to the fetus from rubella is in the first trimester, infection in the second and
third trimester can cause deafness.

Histopathology

By contrast with the rapid progress of the epidemiology and virology, new knowledge
of the histopathology of rubella deafness has remained fragmentary, because of the relatively
small number of temporal bone specimens available (Friedmann and Wright, 1966; Lindsay,
1973).

Microscopy of the cochlea showed partial collapse of Reissner's membrane with
adherence of the membrane to the stria vascularis and organ of Corti. Small granulomata may
be present between the stria vascularis and Reissner's membrane. The tectorial membrane was
found to be rolled up lying in the internal sulcus. Collapse of the saccule was observed, and
the membrane was found to be collapsed and adherent to the macula sacculi suggestive of a
recent acute inflammatory process. Few changes were present in the organ of Corti, in the
examined cases. The hair cells were plentiful, as were the pillar cells, and appeared to be
normal. There were some areas of cystic dilatation at the junction of Reissner's membrane and
the spiral ligament.

The granulomatous lesions described by several authors appear to have occurred when
the organ of Corti had reached morphological maturation (Friedmann and Wright, 1966;
Bordley and Hardy, 1969; Brookhauser and Bordley, 1973; Lindsay, 1973). This could be
interpreted as consistent with the degeneration of the preformed neuroepithelial structures,
reflecting continued virus cell interaction, as suggested by other stigmata of the rubella
syndrome.

Prenatal rubella is recognized as a cause of congenital deafness but its importance may
not be fully appreciated (Brookhauser and Bordley, 1973). One reason is that a woman may
have a silent rubella infection during pregnancy and pass the virus to the fetus without any
clinical evidence of her own infection (Menser, Dods and Harley, 1967). Out of 84 pregnant
women infected with the rubella virus, but without clinical disease, 10 gave birth to children
from whom the virus was isolated (Bordley et al, 1968).

A study of the effect of rubella on the frequency of congenital deafness for 5 years
after an epidemic in 1960, in an island population, revealed that of 87 congenitally deaf
children born the year after the epidemic, 86 had suffered deafness as the only demonstrable
congenital abnormality. Only 20 gave a history of first trimester rubella, so by the usual classification, the remaining 67 cases would be labelled as idiopathic, all known causes having been ruled out. However, serological tests for rubella antibodies on 30 of the 'idiopathic' deaf children were positive in 74% compared with 30% in a control group born within the same year (Karmody, 1968).

In the investigation of congenital deafness in a child, a test for rubella antibodies should be performed. With increasing age a positive result becomes less significant, but the absence of rubella antibodies would exclude the virus as a cause and focus attention on other factors.

**Herpes zoster oticus**

The classical syndrome, described by Ramsay Hunt in 1907, is not common, and it is a more complicated disease than the original conception of 'geniculate ganglionitis' would indicate. Multiple cranial nerves may be affected, but the facial nerve and its ganglion is perhaps the most commonly involved.

The case described by Blackley, Friedmann and Wright (1967) involved the seventh and eighth cranial nerves. The patient, a 69-year-old woman who complained of sudden deafness and right facial palsy, died of carbon-monoxide poisoning some 214 days from the onset of herpes zoster of the ear.

**Histopathology**

The most striking feature of the histopathology was the presence, 7 months after the herpetic eruption, of intense perivascular, perineural and intraneural round cell aggregations in the facial nerve, the auditory nerve, the cochlea and in the mastoid process. The organ of Corti was damaged and, with the atrophic stria vascularis, covered by the collapsed Reissner's membrane.

Sections of the temporal bone of the clinically affected side contained extensive lymphocytic or round cell infiltration of the facial nerve throughout its length and also of the auditory nerve. There was considerable perivascular 'cuffing' by lymphocytes in the modiolus, in the perineural tissue of the facial nerve, the chorda tympani and the skin of the external auditory meatus. The vestibular, spiral and geniculate ganglia contained numerous apparently normal neurons, although there was scattered lymphocytic infiltration of the surrounding nerve tissue. These findings were in complete accordance with the main histopathological findings of the four cases previously described: that is profuse and widespread lymphocytic infiltration in the facial nerve which is in striking contrast to the microscopical findings in Bell's palsy (Friedmann, 1974).

**Mumps**

Mumps appears to be the virus infection most commonly associated with sudden deafness. It may be a more frequent cause of deafness since mumps infection without parotitis is not uncommon and can remain undiagnosed.
**Measles**

Endolymphatic labyrinthitis caused by infection with measles virus is well recognized. The virus may reach the endolymphatic system from the blood stream and cause destruction of the neuroepithelium.

Lindsay and Hemenway (1954) described the histopathological findings in the temporal bones of a 7-month-old deaf child following measles infection.

**Viral encephalopathy**

Viral labyrinthitis may be associated with viral encephalitis. The temporal bones of three children between the ages of 12 months and 13 years have been studied and the microscopical changes included various degrees of degeneration of the organ of Corti and of the stria vascularis. There was marked round cell infiltration of the modiolus (Karmody, 1983).

**Syphilis**

Invasion of the central nervous system by *Treponema pallidum* occurs during the early stages of infection. Deafness may occur in both acquired and congenital syphilis.

**Congenital syphilis**

The stillborn or young infant may exhibit syphilitic changes in the middle ear and cochlea which may become ossified. Severe endolymphatic hydrops and degeneration of the organ of Corti and spiral ganglion have also been described (Karmody and Schuknecht, 1966).

**Acquired syphilis**

The pathology of the deafness is obscure. The principal lesions are those of the tertiary stage of the disease, which may become manifest within a few or many years after infection. The skin and cartilage of the external ear may be affected. The middle ear and temporal bone may be the sites of destructive gummatous processes of tertiary syphilis.

**Deafness associated with chromosomal aberrations**

Chromosomal aberrations are responsible for many severe anomalies (Friedmann, 1974). The presence of an extra chromosome (trisomy) may lead to anomalies associated with deafness (Suehiro and Sando, 1979). Cochlear anomalies associated with the presence of the additional chromosome in trisomy 13-15 include Patau syndrome, characterized by deafness, ocular defects and absence of the olfactory bulbs and tracts. Deafness is common in Down's syndrome (trisomy 21). Multiple malformations of the ear were described in trisomy 18 (Edward's syndrome) (Suehiro and Sando, 1979) and trisomy 22 (Nadol and Arnold, 1986). Anatomical details of the affected inner ear have been summarized by Suehiro and Sando (1979). Here, only the description of the cochlear changes will be mentioned.
Trisomy 13-15 syndrome

The changes in the cochlea include: absence of hook portion, absence of apical and middle turns, rudimentary and deformed cochlea, shortened cochlea, anteriorly situated cochlea, malformed scala vestibuli, underdeveloped modiolus, absence of Rosenthal canal in lower basal turn, absence of lumen of osseous spiral lamina in lower basal turn, scala communis between apical and middle turns, scala communis between middle and basal turns, wide cochlear aqueduct, tectorial membrane rolled up and covered by single epithelial layer.

Trisomy 18 syndrome

Alterations found in the cochlea include: absence of apical turn; deformity of cochlea; scala communis between apical and middle turns; wide cochlear aqueduct; absence of cochlear duct; underdeveloped stria vascularis.

Trisomy 21 syndrome

A shortened cochlea may be found.

Hearing loss due to noise

The effect of noise or any acoustic trauma is of immense industrial and public health importance. Repeated exposure to high levels of noise is a potent cause of deafness, particularly in certain industrial occupations and in places of public or private entertainment where there is overamplification of sound. Proximity to explosions or to gunfire is also liable to result in deafness. Noise induced degenerative patterns in the human ear exhibit a characteristic 'knife-sharp' demarcation line between the damaged and undamaged areas.

Acoustic trauma may cause sensory cell damage by direct mechanical action, by metabolic disturbances resulting from impaired blood circulation, or as a result of the altered permeability of the cell membrane. The inner hair cells are more resistant to acoustic trauma regardless of their site (Bohne, 1976), but greater hearing loss is caused by the loss of the inner than the outer hair cells. By contrast, the outer hair cells display a varied susceptibility in different coils of the cochlea. The morphological changes include proliferation and vacuolation of the endoplasmic reticulum, swelling of the mitochondria, degeneration of the cuticular plate. The swollen sensory cell may rupture and perish.

The sensory cells are joined by attachment zones and gap junctions as first described in tissue cultures of the otocyst (Friedmann and Bird, 1961a). Subsequently it has been shown that the cell junctions of the organ of Corti are disrupted by noise (Beagley, 1965).

The hair cells and the cochlear nerve endings can degenerate within days following excessive exposure to sound. In the cochlear nucleus, the small cochlear nerve endings are especially susceptible to acoustic trauma. It is noteworthy that there is evidence for both a differential sensitivity of inner and outer hair cells and for a selective susceptibility of different auditory pathways in the central nervous system to acoustic overstimulation (Kent and Bohne, 1983).
Even lower levels (below 100 dB) of noise may damage the outer hair cells. High intensity sound (noise) produces considerable changes in the cilia, which may be converted into large complex 'giant' structures affecting the function of the sensory cells. Lim (1986), in a recent comprehensive review, has drawn renewed attention to the important role of the ciliary apparatus in the normal transduction of sound and any damage may considerably impair its function. Various stereociliary changes may be caused by acoustic trauma (also by ototoxic agents). These have been described as floppy, fanned-out, fractured, fused, giant and dissolved cilia. Following mechanical overstimulation or acoustic trauma, the stereocilia show a reduction in stiffness, as measured directly in isolated organs of Corti. They may return to their pre-exposure stiffness in about 15 minutes, following mechanical stimulation (Miller, Canlon and Flock, 1985; Saunders and Flock, 1985).

Splayed (fanned-out) stereocilia may be caused by the tightening of the contractile proteins that are attached to the rootlets in the cuticular plate (Friedmann, Cawthorne and Bird, 1965b; Slepecky, Hamernik and Henderson, 1980, 1981). Another mechanism could be the result of the altered consistency of the cuticular plate because of depolymerization, leading to an exaggerated pivoting of the rootlets. Such macromolecular changes may represent the underlying mechanism of the reduction of stereociliary stiffness by mechanical overstimulation or acoustic trauma. Seemingly minor changes of the stereociliar-cuticular plate complex have a profound effect on the auditory and/or vestibular function (Friedmann, Cawthorne and Bird, 1965b; Lim, 1986).

**Ototoxic drugs**

There is a wide range of drugs which are capable of causing deafness and/or dizziness, either by causing toxic degeneration of the inner ear, or of the higher centres of hearing and equilibrium. The peculiar sensitivity of the eighth nerve has not yet been satisfactorily explained. Many ototoxic drugs have no apparent chemical similarity (for instance thalidomide, ethacrynic acid and atoxyl), but most ototoxic antibiotics belong to the 'useful but unruly' family of basic streptomyces antibiotics (Hawkins, 1959), or aminoglycoside antibiotics and to the so-called 'loop diuretics'.

**Histopathology**

It has been shown that the effect of some ototoxic antibiotics differed from that of acoustic trauma which usually started at the base of the cochlea extending to its apex. This applies equally to neomycin, gentamicin and kanamycin. Neomycin seemed to act initially upon the hook area and apical coil, whereas gentamicin and kanamycin would initially cause simultaneous destruction of the outer hair cells in the upper basal coil and in the hook area. Neomycin may also act on the apical inner hair cells which are only seldom damaged by gentamicin or kanamycin (Hawkins, 1959; Friedmann and Bird, 1961b; Friedmann, Dadsell and Bird, 1966). The lesions caused by atoxyl usually start at the apex (Anniko, 1976; Anniko and Wersall, 1976).

There exist great variations among individual animals (and humans) in their reaction to the ototoxic antibiotics necessitating the evaluation of the hair cell population of each animal (human) individually.
Transmission electron microscopy

As has been shown in animals and in tissue culture ototoxic antibiotics are ribosomal and mitochondrial poisons (Friedmann and Bird, 1961b).

The earliest ultrastructural signs of degeneration of the organ of Corti, regardless of the antibiotic administered, occur in the outer hair cells. The cisternae along the outer cell membrane become distended and dense bodies accumulate in the subcuticular cytoplasm of the hair cells. Subsequently the distended cisternae become vacuolated and eventually the outer cytoplasmic membrane will rupture. The intracellular organelles are expelled into Nuel's space leading to their complete disintegration.

Sensorineural deafness may be caused by the 'loop diuretics', frusemide and ethacrynic acid, which inhibit cellular metabolism and the enzymes participating in electrolyte transport. Ethacrynic acid causes oedema and cystic degeneration of the stria vascularis. Studies of the combined effect of kanamycin and ethacrynic acid show that the concurrent administration of two or more ototoxic drugs has an enhanced toxic effect on the inner ear. On the other hand, the selective ototoxicity of atoxyl can be employed as a model system for comparative studies of various ototoxic agents (Anniko, 1976; Anniko and Wersall, 1976).

The effect of prussic acid on neurons has been demonstrated on tissue cultures of the isolated fowl embryo otocyst exposed to sodium cyanide (Friedmann and Bird, 1972). The degenerative changes observed were comparable to those observed in patients with the cassava syndrome. Cassava root is a widely consumed food in Africa, which contains a cyanogenic compound, linamarin; and it has been recognized that multiple neuropathy associated with deafness might ensue in persons consuming this otherwise simple food.

Scanning electron microscopy

The effect of gentamicin has been studied by scanning electron microscopy on guinea-pigs (Forge, 1985; Lim, 1986). A variety of lesions have been noted at the hair cell apex. The stereocilia were fused or foreshortened, apparently disintegrating. The surfaces of the outer hair cells where stereocilia were almost completely destroyed appeared to be roughened. The cuticular surfaces were bulging and became detached from the reticular lamina.

'Crooked' rootlets with bent stereocilia, floppy cilia, fusion of stereocilia and giant cilia have been observed on cochlear hair cells exposed to ototoxic agents.

The detached hair cell remnant could be seen beneath the surfaces of the expanded or swollen supporting cell, possessing microvilli, and occluding the space beneath the vanishing hair cell debris (Forge, 1985; Lim, 1986). This process is probably electrochemical in nature and acts through the gap junctions linking the two cell groups. This type of necrosis of the cell has been linked by Forge (1985) to the 'apoptosis' occurring in developing organs which require a programmed regularly timed cell death (Wyllie, 1981).

A partial or total loss of outer hair cells alone, in a given segment of the cochlea, was not associated with any corresponding rarefaction or loss of neurons. When the inner hair cells had also degenerated, the number of neurons in the spiral ganglion and spiral osseous
lamina was markedly reduced, provided the survival time was long enough for degeneration to have run its course. The secondary degeneration of first order neurons following any damage to the organ of Corti, appeared to be a delayed phenomenon; its full development was not apparent until at least 4 weeks after the cessation of treatment with gentamicin.

**Ageing and hearing loss**

Hearing loss and degeneration of balance control in the aged is of gradual onset and forms part of the progressive deterioration of the physiological functions associated with the ageing process. These are of a general nature, affecting any cell of any tissue or organ, although different cell systems may become vulnerable in particular ways.

The true nature of the pathogenesis of hearing loss of the aged (presbyacusis) has remained obscure. Two principal lesions may be recognized: a loss of neurons and nerve fibres of the spiral ganglion and spiral nerve; and vascular changes and atrophy affecting the stria vascularis (Schuknecht, 1974; Suga and Lindsay, 1976; Nadol and Arnold, 1987).

Four distinct clinical patterns have been recognized in the ageing population with typical histopathological correlates:

1. degeneration and loss of neural elements or 'neural presbyacusis'
2. degeneration and loss of hair cells or 'sensory presbyacusis'
3. inner ear biochemical defect or 'metabolic presbyacusis'
4. degeneration or inefficiency of inner ear supportive elements or 'mechanical presbyacusis'.

**Neural presbyacusis**

Early degeneration affects the dendritic processes of the osseous spiral lamina. In areas of severe degeneration there may be marked loss of spiral ganglion cells and afferent axons.

**Sensory presbyacusis**

There is a loss of inner and outer hair cells in the basal turn. Secondary cochlear neuronal degeneration is common. In cases of severe degeneration, the supporting elements may be missing and the organ of Corti may be replaced by a single layer of flat 1/1 epithelial cells.

**Metabolic presbyacusis**

Schuknecht (1964) described a common type of sensorineural hearing loss which has its onset in middle age, is slowly progressive, and is characterized by a flat audiometric pattern. It is associated with degenerative changes of the stria vascularis of the middle and apical turns of the cochlea. Atrophy of the stria vascularis is an important cause of sensorineural hearing loss of ageing. The pathological changes consist of degeneration of all
three layers of the stria vascularis, most prominently in the apical region of the cochlea, affecting most severely the marginal cells, then the intermediate and least severely, the basal cells.

There are other cellular and subcellular processes participating in various degenerative syndromes which find expression in extreme old age. The hair cell population decreases with age in parallel with atrophy of the spiral nerves. The vestibular end organs may also be affected and there is an age-related progressive reduction of the number of vestibular sensory cells and nerve fibres over the age of 40 years. The cells contain a great deal of lipofuchsin yet the physiological ability of such persons may not be substantially impaired, probably as a result of compensation by the surviving cells.

**Mechanical presbyacusis**

**Microscopy**

The observed loss of hair cells, neuronal elements and stria vascularis is insufficient to explain the degree of hearing loss. In such cases a variety of abnormalities of supporting elements of the inner ear has been found. These include degeneration of the spiral ligament and rupture or thickening of the basilar membrane (Nadol and Arnold, 1986).

**Vascular diseases causing hearing loss**

Progressive or sudden hearing loss can be caused by localized or systemic vascular disease. In the first category, the vessels of the stria vascularis and the internal auditory artery and its branches which are terminal arteries, play a significant role for example in diabetes mellitus and in various congenital syndromes associated with deafness. The vestibular end organs appear to be more resistant than the organ of Corti to the effects of surgical severance of the labyrinthine artery.

The cause of so-called idiopathic sudden deafness varies. A vascular disorder such as spasm, oedema or arteritis, or a combination of several vascular factors, have been incriminated. Polyarteritis nodosa and Wegener's granulomatosis involving the ear may cause deafness (Friedmann and Bauer, 1973).

**Delayed effects of ionizing radiation on the ear**

Patients with cancer of the brain, nasopharynx, tonsil, and parotid are often treated with doses of radiation which range from 5000-7000 cGy over a period of 5-7 weeks. Depending on the size and site of the tumour, one or both temporal bones may receive a nearly equivalent dose of radiation. Several studies have shown that some patients so treated developed hearing difficulties during therapy (Bohne, Marks and Glasgow, 1985).

The question of damage to the ear from exposure to ionizing radiation was studied by exposing groups of chinchillas to fractional doses of radiation (200 cGy per day) for total doses ranging from 4000-9000 cGy. In order to allow any delayed effects of radiation to become manifest, the animals were sacrificed 2 years after completion of treatment and their temporal bones examined. The most pronounced effect of treatment was degeneration of
sensory and supporting cells and the loss of eighth nerve fibres in the organ of Corti. The
degree of damage found in many of these ears was of sufficient magnitude to produce a
permanent sensorineural hearing loss.

**Anencephaly**

Anencephaly is probably the result of failure of the closure of the neural groove and
consequent failure of development of the forebrain. Histopathological studies of the temporal
bones of six anencephalics have yielded some interesting findings (Wright, Phelps and
Friedmann, 1976; Friedmann, Wright and Phelps, 1980).

The cochlea was malformed and showed Mondini-type malformation as described by
Gussen (1968). A short, poorly developed modiolus reached the malformed basal coil opening
into a wide-open bulbous or pear-shaped space replacing the upper coils and forming a scala
communis. The overall size of the cochlea appeared to be considerably reduced and the otic
capsule showed enhanced ossification.

The neuroepithelial elements of the organ of Corti appeared to be well differentiated
where preserved, but the cochlear duct was distended as in Ménière's disease. Reissner's
membrane was bulging or collapsed onto the tectorial membrane and onto the epithelium of
the organ of Corti. There was some evidence of rupture and repair.

**Systemic bone diseases affecting the ear**

The temporal bone is affected by systemic or local diseases of the bone. These include
developmental abnormalities, inflammatory conditions, otosclerosis, metabolic and endocrine
conditions, achondroplasia, osteogenesis imperfecta, Paget's disease, osteopetrosis,
histiocytosis X, fibrous dysplasia, lipidoses involving bone, tumours of bone (see Table 15.2).

**Osteogenesis imperfecta**

Osteogenesis imperfecta is a rare condition characterized by fragility of the bones,
leading to multiple fractures associated with blue sclerae and deafness. The temporal bone
may be affected by this generalized skeletal abnormality, which may result from a specific
dominant gene abnormality.

The lesions may present in two forms: as osteogenesis imperfecta congenita at birth,
and as osteogenesis imperfecta tarda, when the changes become evident during childhood or
adolescence (Seedorff, 1949).

**Histopathology**

In the congenital form the lamellar bone is replaced by a spongy network of non-
lamellar bone, which permeates the entire temporal bone or the otic capsule, and may involve
the oval window region and stapes, when it can be difficult to distinguish from otosclerosis.
In older individuals, the bones are brittle ("fragilitas ossium"). The histological features display
no characteristic pattern that might be of differential diagnostic significance. The changes may
be regarded as the result of a functional abnormality of osteoblasts.
Paget's disease of the temporal bone

The aetiology of Paget's disease has remained obscure. Cytoplasmic inclusions morphologically similar to the nucleocapsids of the paramyxoviridae family have been identified under the electron microscope. Evidence has been presented by Mills et al (1984) in support of the hypothesis that Paget's disease of bone is a slow viral infection of the paramyxoviridae family.

Paget's disease affecting the skull may cause obstruction of the external auditory meatus, inducing conductive deafness. Obliteration of the labyrinth and sensorineural deafness are less common symptoms. Some of the features which distinguish it from otosclerosis include the later age of onset, lack of family history, sensorineural deafness showing rapid deterioration, tinnitus, radiological evidence of Paget's disease of the skull.

Histopathology

Histologically there is evidence of disordered and very active reconstruction of the bone (Friedmann, 1974). There are, in the active phase, numerous multinucleate osteoclasts, lying in the perivascular fibrous tissue or in the deep lacunae they have produced. Elsewhere, chains of osteoblasts are prominent, lining newly formed bony trabeculae. Alternating resorption and apposition of bone culminates in the classical mosaic of irregular cements lines. In the inactive lesion, remodelled bone, displaying the characteristic mosaic pattern of cement lines, has been formed. This must not be confused with the similar pattern observed in the sclerotic mastoid bone following chronic infective diseases. The author has studied the temporal bones of a woman who died at the age of 81. The petrous temporal bones were almost totally affected by the process. Her deafness was, in fact, only moderate and it had been easy to communicate with her. The process obstructed the external auditory meatus and obliterated the tympanic cavity but not the cochlea; the organ of Corti was present. There is a similarity with otosclerosis, in that there is a sharp zone of demarcation between the disease and the normal bone.

Fibrous dysplasia of bone

No less than 33 different names had been used by various authors to describe this disease before the term fibrous dysplasia was introduced by Lichtenstein (1938). The disease is characterized by the development in one or more bones of circumscribed lesions consisting of bone-forming tissue: monostotic or polyostotic fibrous dysplasia. The aetiology is obscure.

Fibrous dysplasia usually occurs as lesions of long bones, but it is not uncommon in the skull, and particularly in the maxilla. It may affect the temporal bone alone.

The primary histological component consists of connective tissue with metaplastic new bone formation; the bone is of woven pattern and a lamellar organization is usually lacking. There are relatively slender trabeculae of immature bone containing many immature osteoblasts staining unevenly and surrounded by fibrous connective tissue. Osteoclasts can be seen tunnelling into the mineralized interior of trabeculae scalloping and fragmenting them. The resorbed areas become filled with a cellular fibrous tissue.
Osteopetrosis (marble bone disease or Albers-Schönberg disease)

This is a rare disease, only about 300 cases have been reported (Hamersma, 1970). Recurrent progressive facial palsy and deafness are frequently encountered. Acute recurrent attacks of facial palsy identical with Bell's palsy usually start in childhood. The disease is probably the result of a congenital metabolic disorder of bone resulting in a failure of resorption of cartilage and mature bone.

Histopathology

The abnormality is caused by a failure of adult bone formation and the failure of resorption or replacement of primitive bone. Myers and Stool (1969) examined the temporal bones of a 2.5-year-old Negro girl who died of the sequelae of osteopetrosis (anaemia and pulmonary haemorrhage). Sections of the temporal bones showed that the enchondral layer was most severely affected and there was bony obliteration of the mastoid air cell system. There were no inner ear changes attributable directly to the abnormal bone.

Xanthoma of the ear

Xanthomatous deposits in the temporal bone (or mastoid process) are rare (Friedmann, 1974) but may imitate chronic mastoiditis. Their aetiology is unknown. Clinically or pathologically recognizable deposits of cholesterol and other fats in the skin, tendons and bone occur in many diseases, such as diabetes. Groups of foam cells may be seen in inflammatory granulation tissue or in the exudate of otitis media.

The xanthomatoses may be the result of metabolic disturbances of steroid metabolism, lipid metabolism or both, and are associated respectively with high levels of cholesterol and high levels of neutral fats in the blood; they may, however, be found in the absence of any detectable alteration in blood chemistry.

The pathological lesions are formed by the accumulation of lipid-laden macrophages in the affected tissues. The cytoplasm of these macrophages has a foamy appearance, caused by the presence of finely dispersed droplets. At operation, much creamy fluid may be noted in the temporal bone.

Idiopathic histiocytosis (non-lipid histiocytosis, histiocytosis X or Langerhans cell histiocytosis)

This non-committal title describes a triad of diseases: Letterer-Siwe disease, Schuller-Christian disease and eosinophilic granuloma of bone. All these conditions have in common focal accumulations or large macrophages in various organs. These cells often contain cholesterol, especially in the more chronic forms of the condition, but this is apparently secondary (Ornvold, Nielsen and Clausen, 1985).

Eosinophilic granuloma of bone

Solitary eosinophilic granuloma is frequently localized in the temporal bone of children and the presenting symptoms and signs may be interpreted as chronic otitis media.
(Friedmann, 1974). There is discharge from the ear, and polypoid granulations may be found in the external auditory meatus. In other cases, the granuloma presents as a painful, bony swelling infiltrating the postauricular area and it has to be distinguished from a malignant neoplasm. Radiologically, an area of destruction may be noted.

**Histopathology**

A network of proliferating histiocytes encloses large numbers of eosinophils containing Charcot-Leyden crystals. There are occasional foam cells or xanthomatous cells, accompanied by multinucleated giant cells. Recently S-100 protein has been recognized in the cytoplasm and in the nuclei of the proliferating histiocytosis X cells of eosinophilic granulomata. Although the demonstration of Birbeck granules by electron microscopy is considered to be diagnostic for histiocytosis X, the immunohistochemical detection of S-100 protein can serve as a helpful marker.

**Sensorineural deafness and otosclerosis**

Large otosclerotic foci may reach the cochlea and damage the spiral ligament; Kelemen and Linthicum (1969) suggested a correlation between the atrophy of the spiral ligament and the extent of the sensorineural hearing loss, subsequently confirmed by others. Schuknecht and Barber (1985) have cast doubt on the significance of the involvement of the cochlear endosteum on inner ear function. However, they reported one case where they accept that otosclerosis has resulted in sensorineural deafness without stapes fixation.

**Immunology**

Immunological mechanisms may play an aetiological role in ear diseases, many of which have been considered to be of idiopathic nature (Arnold, Altermatt and Gebbers, 1984). Various cellular constituents of the immune system, as well as immunoglobulins, have been identified within the inner ear, suggesting that it may possess an active immune system. While it is possible that many of the idiopathic diseases will eventually prove not to be immunologically mediated, the result of the intensive investigations carried out will assist in a better understanding of some of the basic mechanisms of host immunity involved in ear disease.

**Miscellaneous infective and neoplastic causes of deafness**

Purulent labyrinthitis complicating acute or chronic otitis media and purulent meningitis may lead to partial or complete ossification of the cochlea.

Schwannomata may form satellite tumours in the cochlea and various malignant neoplasms can spread to the cochlea for example rhabdomyosarcoma, malignant paraganglioma, malignant melanoma, malignant lymphoma. Leukaemic deposits may occur.

(The so-called acoustic neuroma is a misnomer but, because of custom and surgical practice, is being used throughout this work. The most precise histopathological term is vestibular schwannoma as it most commonly arises from the Schwann cells of the vestibular
division of the eighth cranial nerve. Strictly speaking a neuroma is a non-neoplastic overgrowth of nerve fibres, Schwann cells and other components of scar tissue.)