Chapter 15: Diseases of the temporal bone

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Many different systemic diseases may involve the temporal bone and they invariably result in a sensory hearing loss; occasionally there are associated vestibular symptoms and, in some instances, middle ear function is also compromised.

Several diseases have been excluded from this chapter, or considered only briefly, as they are covered more appropriately in other sections. Thus, the many causes of severe childhood deafness, in particular teratogenic, hereditary and metabolic, are largely excluded. Secondary involvement of the temporal bone by neoplasms, reticuloses, or by the leukaemias are also described elsewhere, together with the diseases of the cardiovascular, haemopoietic, respiratory and renal systems (Chapter 17). This chapter concentrates upon disorders of bone which may involve the petrous temporal structures and those caused by infective, granulomatous, metabolic and dietary-induced diseases. The developing contemporary field of autoimmune inner ear disease is also considered.

Systemic bone diseases

The bony labyrinth differs histologically and biologically from all other skeletal tissues. Maurer (1967) studied the mineral content of the bone of the otic capsule and ossicles, and compared it to the composition of bone from the mastoid cortex and general skeleton. He found that the calcium and phosphorus content of the woven bone of the otic capsule and ossicles was significantly greater than that of the ordinary haversian bone of the mastoid cortex and other regions. In addition, alkaline phosphatase activity was one-third to one-sixth lower in this woven bone, indicating that there are fundamental metabolic differences compared to general skeletal bone. Recent animal studies have shown that otic bone takes up radioactively labelled calcium significantly slower than does femoral bone, a reflection of its reduced metabolic rate (Ross, 1979). It is also relevant that the metabolic regulation of the entry of calcium into bone varies with both sex and age (Bronner, 1973; Preston et al, 1975). There is a reduced entry of calcium in women, compared with men and with increasing age. These basic physiological differences between otic capsule and other bone will clearly affect the likelihood of preferential involvement of the petrous temporal bone as a localized manifestation of a more generalized bone disorder.

The temporal bone may be affected by many specific conditions (Table 15.1). Table 15.2 summarizes the biochemical, radiological and other characteristics encountered in the most important of these conditions. Somewhat paradoxically, however, the temporal bone is relatively infrequently involved in many of the generalized systemic bone diseases. Perhaps the lower metabolic rate of the bony labyrinth confers some degree of protection, although it must be appreciated that any cochleovestibular symptoms are probably often overshadowed by other more generalized features.

Direct involvement of the otic bone which supports and protects the delicate cochlear and vestibular neuroepithelial structures, by other rarefactive or sclerotic processes, can lead to secondary degenerative changes in the spiral ligament, stria vascularis and cochlear hair cells, either by local ischaemia or by the toxic effect caused by the release of enzymes, as has
been postulated and generally accepted in cochlear otosclerosis. This is the likely pathogenesis in most conditions, although, in addition, sustained biochemical aberrations may cause adverse effects in other ways. Calcium is involved with many cellular functions, including the regulation of membrane permeability and the control of neuromuscular excitability. Active transport mechanisms, which maintain the differential biochemical integrity of the inner ear fluids which is vital for normal cochlear function, are probably calcium dependent. Deficiency of ionized calcium may also adversely affect transmission of the nerve action potentials generated by the cochlea by inhibiting the release of transmitter substances at the neural synapses.

Table 15.1. Systemic bone diseases

(1) Osteogenesis imperfecta (Van der Hoeve syndrome)
(2) Osteitis deformans (Paget's disease)
(3) Fibrous dysplasia
(4) Osteopetrosis
(5) Neurofibromatosis
(6) Genetic craniotabular hyperostoses
   (a) hyperostosis corticalis generalisata
   (b) sclerosteosis
   (c) congenital hyperphosphatasia
   (d) progressive diaphyseal dysplasia
(7) Genetic craniotabular dysplasias
   (a) craniometaphyseal dysplasia
   (b) frontometaphyseal dysplasia
(8) Craniofacial dysostosis
(9) Osteopathia striata

Osteogenesis imperfecta

Osteogenesis imperfecta or fragilitas ossium is a relatively rare disease. Its incidence varies between 2 and 15 per 100,000 births (Smärs, 1961; Morrison, 1967; Pedersen, 1985). It is an hereditary disorder of collagen synthesis (Smith, Francis and Haughton, 1983) and occurs in two main forms. In the congenita form, multiple fractures occur in utero and early death is commonplace. In the tarda form, multiple fractures occur with relatively minor trauma in childhood but tend to become less frequent after puberty. Abnormal fracture alignment frequently results in excess callus formation and skeletal deformity of the limbs. It is generally accepted that the tarda form has a dominant mode of inheritance with variable penetrance. Thus asymptomatic 'carriers' exist in some families. Sporadic cases have also been encountered. The congenita form has a recessive mode of inheritance.

The chief manifestation is spontaneous fractures which occur in more than 95% of cases (Smärs, 1961). These usually follow relatively minor trauma and may exceed 60 in number in any one individual. Eighty-five per cent of cases have blue sclerae, which may also be seen in other conditions where a collagen differentiation defect is present, for example Ehlers-Danlos syndrome and Marfan's syndrome. Many healthy children under 3 years of age also have blue sclerae, so that scleral colour is an unreliable diagnostic feature. Approximately 50-605 of affected individuals eventually develop a hearing loss (Smärs, 1961;
Table 15.2. Summary of features of specific conditions affecting the temporal bone

<table>
<thead>
<tr>
<th>Condition</th>
<th>Type of hearing loss</th>
<th>Biochemistry</th>
<th>Radiology</th>
<th>General features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteogenesis imperfecta</td>
<td>Conductive and/or sensorineural</td>
<td>Ca and PO$_4$ normal</td>
<td>Alkaline phosphatase occasionally raised</td>
<td>Acid phosphatase normal</td>
</tr>
<tr>
<td>Paget's disease (osteitis deformans)</td>
<td>Conductive and/or sensorineural</td>
<td>Ca usually normal</td>
<td>PO$_4$ hypercalcaemia - immobilization</td>
<td>Alkaline phosphatase elevated in active disease</td>
</tr>
<tr>
<td>Fibrous dysplasia</td>
<td>Conductive</td>
<td>Ca usually normal</td>
<td>PO$_4$ always normal</td>
<td>Alkaline phosphatase may be raised in active disease, especially polyostotic form</td>
</tr>
</tbody>
</table>
Skeletal survey to exclude polyostotic
Pathological fracture
Café-au-lait pigmentation may be present (either type)

Osteopetrosis
(a) Albers-Schönberg
  Conductive
  Occ. mixed
  Ca normal
  PO₄ normal
  Alkaline phosphatase may be markedly elevated
  Acid phosphatase may be markedly elevated
  Urinary HDP usually normal
  Symmetrical increase in bone density; bones appear structureless
  Sclerotic foci - 'bones within bone'
  Thickening of vertebral end-plates ('rugger jersey')
    Thick dense brittle bones
    Pathological fracture
    Facial palsy
  Occ. osteomyelitis of mandible after dental extraction
  Mild anaemia

(b) Malignant recessive
  Sensorineural
  As above
  Transverse bands in metaphyseal regions of long bones and longitudinal striations
  Proximal humerus and distal femur - flask-shaped
  Vertebrae - rugger jersey
    Facial palsy
    Blindness
    Pathological fracture
    Mental retardation
    Liver and spleen enlargement
    Haemolytic anaemia and thrombocytopenia

Genetic craniotabular hyperostoses
(a) van Buchem's (autosomal recessive)
  Conductive and/or sensorineural
  Ca normal
  PO₄ normal
  Alkaline phosphatase frequently raised (50-250%)
  Diffuse, symmetrical increase in bone density
  Cortical bone - abnormally thick but bones not increased in size
  Hyperplasia diaphysis long and short bones
  Endosteal thickening diaphysis - tubular bones
    Normal stature
    Facial palsy
    Clavicles - thickened and palpable
Overgrowth of brow and mandible

(b) Sclerosteosis (autosomal recessive)

Conductive and/or sensorineural

Ca normal
PO₄ normal
Alkaline phosphatase markedly elevated in nearly all patients
Acid phosphatase normal
Bones show increased density but only minor degree of bony modelling, if present
Progressive bony thickening
Tubular bones markedly undermodelled with lack of usual diaphyseal constriction
Syndactyly and digital malformation
Facial paralysis
Tall stature
Distortion of face and jaw
Chronic headache
Raised ICP
Anosmia
Majority Afrikaners

(c) Congenital hyperphosphatasia (autosomal recessive)

Conductive with decreased bone conduction
Ca normal
PO₄ normal
Alkaline phosphatase consistently elevated
Acid phosphatase consistently elevated
Similar to Paget's
Marked irregular thickening of skull
? Narrowing of EAM
Tubular bones - width greatly increased, bowing and lacking of modelling
Multiple fractures
Dwarfing
Blue sclerae
(?
increased serum uric acid and leucine aminopeptidase)

(d) Progressive diaphyseal dysplasia (autosomal dominant)

Combined with big air-bone gap
Ca normal
PO₄ normal
Alkaline phosphatase normal
Acid phosphatase normal
Generalized sclerosis of skull base; vault less commonly severely affected
Marked thickening of cortices of leg bones and medullary canals narrowed; external bony contours irregular

Morrison, 1975; Quisling et al, 1979; Pedersen, 1985). When multiple fractures, blue sclerae and deafness occur together they constitute the syndrome ascribed to van der Hoeve and de Kleyn (1918). It is now known that this eponymous association is rather unsatisfactory because the syndrome was in fact described 6 years earlier by Adair-Dighton (19120, while Bronson (197) independently published 19 cases of the same triad at an earlier date. In some family members, hearing impairment and blue sclerae are present without the tendency to fractures (Morrison, 1979; Stoller, 1982).

Altered collagen synthesis results in defective connective tissue with a tendency to hypermobility and laxity of joints, 'thin' skin and subcutaneous bruising. The abnormal formation of dentine and cracking of the overlying enamel results in yellow-stained irregular teeth, the so-called amelogenesis imperfecta. The appearances are reminiscent of tetracycline staining of the permanent teeth. This feature is found in about 155 of patients with osteogenesis imperfect and may be the only manifestation. The diagnosis of this feature is made radiologically by demonstration of obliteration of the root canals.

**Otological features**

Characteristic features of the hearing loss in osteogenesis imperfecta are its age of onset and progression. Although only 10-20% of affected individuals will be deaf in childhood or adolescence, by middle age the figure exceeds 50% (Smärs, 1961; Pedersen, 1985) and usually progresses significantly from the third decade. The hearing loss may increase during pregnancy, while rather surprisingly, there is no correlation between its severity and that of the disease as indicated by the degree of physical handicap.

The hearing loss in osteogenesis imperfecta is clinically indistinguishable from otosclerosis. Characteristically it commences soon after puberty when fractures become less frequent. A conductive component is present in nearly 80% of cases, although more often than not this is part of a mixed loss. The deafness can be entirely sensorineural and total deafness may result in a few instances.

Tympanometry studies using a probe tone of 220 Hz show a tendency to high normal or raised compliance values. Although fixation of the stapes footplate is invariably present in cases with a conductive loss, hypermobility of the tympanic membrane (Carruth, Lutman and Stephens, 1978; Pedersen, 1984, or fracture or aplasia of stapedial crura may coexist (Shea and Postma, 1982; Pedersen, 1985). Carruth, Lutman and Stephens (1978) suggested that the reduced stiffness of the fibrous layer of the tympanic membrane, which has the same embryological origin as the sclera, was the more important factor leading to increased membrane mobility, possibly due to defective cross linkage between the circular and radial fibres. In ears with a fracture of the stapedial arch, very high compliance values are present combined with a stapedius reflex of high amplitude providing there is not too large a contralateral conductive hearing loss. Carhart notches are not seen, and despite the widespread changes in the temporal bone neither is the Schwartze sign.

Vestibular symptoms have been reported as rare (Smärs, 1961; Morrison, 1979; Quisling et al, 1979) or as frequently as 20% of affected cases (Shea and Postma, 1982; Pedersen, 1984). Johnsson et al (1982) described extensive bilateral endolymphatic hydrops in a case where temporal bone microdissection was undertaken. Morrison (1979) described
two patients with amelogenesis imperfecta and Ménière's syndrome, in whom abnormal sclerosis of the otic capsule was demonstrated on polytomography. However, secondary hydrops appears to be an unusual feature of the condition.

Changes in the labyrinthine capsule on petrous temporal bone tomography are virtually indistinguishable from those of labyrinthine otosclerosis. Demineralization, which is perhaps more widespread, and sclerosis produce a mottled appearance which is, however, not so marked as in Paget's disease of bone.

Histologically, there are some similarities to otosclerosis, although the disorders are considered distinct entities (Wullstein, 1960; Bretlau, Jorgensen and Johansen, 1970; Shea and Postma, 1982; Pedersen, 1985). In about two-thirds of cases stapedial fixation is due to a focal lesion in the footplate which, histologically, resembles the early active stages of otosclerosis. However, there is a greater degree of disorganization in the new bone formation in the osteogenesis imperfecta footplate compared with that seen in otosclerosis (Brosnan et al, 1977). In other cases, fixation is the result of a diffuse structural alteration of the entire footplate. Biochemical assays of serum calcium, phosphorus and calciferol are normal, which alkaline phosphatase levels may occasionally be elevated. Photon absorptiometry has demonstrated that patients with osteogenesis imperfecta have a reduced thickness of cortical bone, while other generalized features include reduced dermal and central corneal thickness (Pedersen, 1985). These features are not found in otosclerosis. It is considered very likely, therefore, that the temporal bone features in osteogenesis imperfecta represent a local manifestation of the generalized skeletal and connective tissue disorder.

Treatment

There is no known curative treatment for the condition. In a typical case, new fractures cease to occur in adolescence, but skull involvement continues causing the characteristic 'soldier's helmet' appearance and deafness. Rehabilitation using an appropriate hearing aid is the mainstay of treatment, although stapedectomy may have a place in patients with a large air-bone gap and good cochlear function.

Surgical results are generally satisfactory and can give hearing improvement similar to that obtained in otosclerosis if delayed until several years after the cessation of fractures (Patterson and Stone, 1970; Kosoy and Maddox, 1971; Shea and Postma, 1982; Stoller, 1982; Pedersen, 1985). The fixed footplate is often very thick and soft, while middle ear mucosa around the oval window appears to be more vascular than normal. A high risk of a 'floating' footplate has been reported (Kosoy and Maddox, 1971; Brosnan et al, 1977), although this is not the experience of others (Pedersen, 1985). Extra care is required not to fracture the long process of the incus when crimping a wire prosthesis.

Paget's disease (osteitis deformans)

Sir James Paget described the detailed clinical and pathological features of this bone disease in 1877. The alternative term osteitis deformans introduced by Czerny in 1873 is inappropriate because there is no evidence that the basic pathology is inflammatory, and marked skeletal deformity rarely occurs. The disease is characterized by spreading osteolytic and osteoblastic changes, most frequently affecting the pelvis, lumbar spine, skull, femur and
tibia. However, the archetypal patient displaying the full clinical picture with an enlarged skull, progressive kyphosis, bowed legs and short stature is now rarely seen. It affects males four times more often than females and has a curious racial and geographical distribution, being very common in the UK (Woodhouse, 1973; Detheridge, Guyer and Barker, 1982), where estimates suggest that some three-quarters of a million people have the disease. The incidence is also high in Australia and New Zealand and in other populations of British origin, such as North America and South Africa. Surveys have revealed a marked geographical disease variation, and within the UK the prevalence has been shown to be considerably higher in Lancashire than elsewhere, but decreasing from high to lower levels over short distances (Barker et al, 1980).

As described by Paget himself, the onset of the disease occurs in middle age. It is rarely seen before the age of 40 years and is more commonly encountered after the age of 55 years. Hereditary aspects are not easy to evaluate because of this relatively late age of onset, but it has been thought to be inherited by a simple autosomal Mendelian dominant gene (McKusick, 1972).

Three-quarters of patients with the disease have pelvic involvement, while the skull is affected in some 28%. An increased tortuosity and hypertrophy of the anterior terminal branch of the superficial temporal artery may be seen in many patients with skull involvement in Paget's disease, but it is by no means characteristic of the condition. Of those with widespread active disease, bone pain is a troublesome symptom, and probably occurs in as many as 20% sufficient to warrant treatment. Expansion of bones around foramina at the base of the skull and in the orbit can lead to neurological defects and optic atrophy. Early workers suggested that narrowing of the internal auditory meatus and the nerve channels in the bony modiolus with compression of the nerve fibres might account for the sensorineural loss, but this is not supported by histological studies (Schuknecht, 1974).

While the exact aetiology is unknown, it is now widely accepted that Paget's disease is an example of primary osteoblast dysfunction in which the pathogenesis involves an increase in the number and activity of osteoblasts. The stimulus for this increase is unknown, but as a result of the bone resorption, there is a compensatory increase in bone formation, leading to a greatly enhanced rate of bone turnover. The normal lamellar structure of the collagen of the ground substance becomes grossly distorted and replaced by adjacent areas of osteolytic and sclerotic bone of increased vascularity. This results in bone softening, a tendency to fractures and deformity and typical biochemical changes. The serum calcium is usually normal, even though the rate of turnover of calcium in bone is enormously increased. Immobilization as a result of this disease, however, causes even greater bone resorption and formation so that both hypercalcaemia and hypercalciuria can occur. Serum alkaline phosphatase activity is elevated in active disease, particularly if it is widespread. Activity of this enzyme is related to bone formation by osteoblasts and probably also by osteocytes. Serum acid phosphatase is an index of osteoclastic activity and is often increased in Paget's disease, particularly when the alkaline phosphatase is quite high, but its measurement is of little diagnostic value. Urinary hydroxyproline is an amino acid found exclusively in collagen and levels may be greatly elevated in Paget's disease, when the condition is active, reflecting the breakdown of bone collagen.
The most interesting recent hypothesis is that the disease results from a slow virus infection of the osteoblasts. Rebel et al (1980) demonstrated inclusion bodies only in the osteoblasts, which are morphologically analogous to those seen in proven paramyxovirus (PMV) infections - measles or respiratory syncytial virus. Clinicopathological aspects of Paget's disease have several features in common with other proven slow virus disorders, and Harvey (1984) has recently reviewed the evidence for this proposed association. If a viral aetiology is confirmed, co-factors are almost certainly necessary, perhaps on a genetically susceptible background.

**Otological features**

Despite the frequency of Paget's disease, it is only rarely recognized as a cause of deafness in clinical practice. In many instances the disease may be asymptomatic apart from the otological features and the diagnosis can therefore easily be missed. However, in other cases, although hearing loss is present it may not be directly due to the disease. In patients with deafness due to Paget's disease, one would usually expect to see obvious signs in the plain skull X-rays. Davies (1968) reviewed 236 patients with the disease, finding skull involvement in 70% and deafness in 41%. Of the 97 patients with deafness, there was no radiological skull abnormality in 14. Vertigo and tinnitus, which was characteristically pulsatile, were present in 36% and 32% respectively. Harner, Rose and Facer (1978) studied 1066 patients with objective evidence of Paget's disease over a 5-year period. More than 43% had a hearing loss which was usually sensorineural. However, when the records were carefully reviewed they concluded that the hearing loss was not usually part of the disease process and most patients had no direct evidence of temporal bone involvement. In their series, 17% of patients had tinnitus and 22% dizziness. The most common vestibular symptoms were postural and positional unsteadiness. However, in those with radiological evidence of skull involvement, the incidence of mixed hearing loss was statistically greater than expected and the incidences of tinnitus and dizziness were also higher than in the group as a whole.

The type of hearing loss most commonly encountered is progressive and mixed with both conductive and sensorineural components (Davies, 1968). It is usually fairly symmetrical. In the earlier stages of the disease, conductive deafness is present in more than two-thirds of affected ears. Davies found that the air-bone gap averaged 30 dB for females and 20 dB for males, and was most marked at the 500 Hz frequency. The stapedius reflex is often present and preserved with moderate conductive hearing losses. By contrast, in patients with otosclerosis and in osteogenesis imperfecta, as little as 15 dB of hearing loss due to stapedial fixation abolishes the reflex. The greater age of onset also helps to distinguish Paget's disease from otosclerosis.

There are still relatively few histological studies of the temporal bone in Paget's disease. Changes are rarely present in the stapes footplate, while pagetic changes in the other ossicles and the formation of bony spurs in the epitympanum interfering with incudomalleal mobility are the common findings accounting for a conductive hearing loss (Davies, 1970; Schuknecht, 1974).

A progressive sensorineural hearing loss mainly affecting the higher frequencies is seen in 20% of patients and can also be associated with an additional conductive element (Davies, 1968). Pagetoid osteitis involving the endosteal layer of the otic capsule results in
degenerative changes in the stria vascularis with atrophy of both the cochlear duct and vestibular labyrinth (Kornfield, 1967; Rüedi, 1968; Lindsay and Lehman, 1969; Schuknecht, 1974). The basal turns of the cochlea are most severely affected and Schuknecht suggested a local toxic effect caused by pagetic disease of the bony labyrinth, similar to that observed in cochlear otosclerosis. Secondary endolymphatic hydrops of the cochlear duct and saccule, and atrophy of the membranous semicircular canals have been described. The vascular shunts connecting vessels of diseased pagetic bone with those of the spiral ligament described by Rüedi (1968) have not been confirmed by others. Thus, in the early stages, the inner ear loss is mainly sensory with relatively well preserved speech discrimination, but later, secondary neuronal degeneration occurs. Bony softening and deformity of the skull base can lead to acquired basilar impression and possibly sensorineural hearing loss by torsion of the eighth nerve or its associated vasculature. Vestibular symptoms are usually rather non-specific, taking the form of transient vertigo or imbalance, although exceptionally they assume a Ménière-like character when secondary hydrops has occurred.

In the early stages, small areas of lucency and dense patches which fade into one another are seen on X-ray. There is often a typical mixture of lytic and sclerotic areas and the skull is thick where it is affected, predominantly over the vertex. Some coarse trabeculae are nearly always visible except in the most advanced cases. Osteoporosis circumspecta is a different manifestation of the disease causing a total radiographic disappearance of bone which always stops short of involving the whole structure (Kasabach and Gutman, 1937; du Boulay, 1980). The radiological appearance of the temporal bone in the established disease is pathognomonic and variations from minimal demineralization of the petrous apex to demineralization of the entire petrous pyramid including the otic capsule are encountered.

The temporal bone changes frequently correlate with the degree of skull involvement. In the initial stage when extensive demineralization primarily affects the medial aspect of the petrous pyramid, the labyrinthine capsule stands out more clearly than normal. Involvement of the internal auditory meatus consists of demineralization of the walls without evidence of narrowing and, when surrounded by featureless homogeneous pagetoid bone, it may no longer be identifiable as a distinct structure. The otic capsule is spared until advanced changes are present. Involvement of the labyrinthine capsule begins in the outer periosteal layer; the middle endochondral layer is more resistant and the greatest resistance is present in the endosteal layer, but with extensive involvement these three layers can no longer be distinguished. Eventually the medial ends of the petrous pyramids become tilted upwards due to bone softening causing acquired basilar impression. High resolution computerized tomography may yield additional information about bone architecture (Lloyd, Phelps and du Boulay, 1980; Swartz et al, 1985).

Treatment

It is generally agreed that the results of reconstructive middle ear surgery are unsatisfactory in Paget's disease. There are several reasons for this surgical pessimism. There is no consistent defect responsible for the conductive loss and, indeed, several may coexist in some cases. The frequently associated sensorineural hearing loss is another significant factor mitigating against the prospects of a successful surgical outcome. Perhaps it sensitizes the cochlea to further diminution of function during the footplate manipulations of a
stapedectomy procedure. Finally, and probably most important, the long-term results in most reported cases are poor.

Morrison (1975) performed stapedectomies on two patients with 40-50 dB air-bone gaps. In each case the stapes was found to be normal. Both patients experienced a hearing gain which was unfortunately only temporary and was followed by progressive conductive and sensorineural hearing loss. This experience has been shared by others (Sparrow and Duval, 1967; Davies, 1968). Stapes or ossicular mobilization has also generally produced a less than favourable long-term outcome. Morrison (1975) described two good hearing results after mobilization which reverted to preoperative levels within a few months. A normally mobile stapes with or without a mobile malleus handle may, however, provide scope for other reconstructive techniques which can be worth pursuing, particularly in the younger patient.

The effects of medical treatment with calcitonin on hearing loss have been studied by several groups, although with conflicting results. Calcitonin causes a rapid inhibition of osteoblast activity, while continued therapy leads to a reduction in the rapid turnover of calcium and a gradual remineralization of bone (Woodhouse, 1973). Successful treatment results in a fall in the serum alkaline phosphatase and urinary hydroxyproline excretion. A typical protocol consists of daily subcutaneous injections of 10-50 mg of calcitonin which can be reduced to an alternate day regimen when biochemical parameters become normal, after about 2 weeks. Shai, Baker and Wallach (1971), Morrison (1975 and Moffat, Morrow and Simpson (1977) all reported hearing improvement following calcitonin treatment, while Grimaldi, Mohamedally and Woodhouse (1975) and Walker et al (1979) found no significant differences between treated and untreated groups. The Otologic Medical Group of Los Angeles have very recently reported the results of a comprehensive study of calcitonin therapy in this disorder (El Sammaa et al, 1986). Twenty six patients with hearing loss due to Paget's disease seen by one clinician received calcitonin regularly for periods ranging from 5 to 8 years and were compared to 19 patients, seen concurrently by other colleagues, who received no treatment. They found that, although there was no significant hearing improvement in the treatment group, their hearing thresholds were effectively stabilized, in contrast to the untreated group in whom a mean increase hearing loss of more than 25 dB was observed. Such long-term treatment is certainly expensive and may be affected by antibody formation with calcitonin of porcine or salmon origin.

Disodium etidronate (EHDP) is a diphosphonate which seems to possess all the biological properties of pyrophosphate including the ability to inhibit bone resorption. The drug appears to inactivate osteoclasts and osteoblasts and these effects have led to its clinical usage in Paget's disease (Kanis and Russell, 1981). Although the drug is effective, long-term administration may result in histological osteomalacia. It has the distinct advantage that it may be taken orally, but so far, only one short report of its use in the deafness of Paget's disease has been published (Gennari and Sensini, 1975). Five patients were treated and their pure-tone audiograms showed a significant improvement in the air conduction threshold of greater than 15 dB in three cases. Recently, it has been shown that short-term high dosage treatment with EHDP may well maximize suppression of disease activity but decrease exposure to unwanted secondary effects (Preston et al, 1986).

Severe hearing loss, particularly in younger adults, with evidence of rapidly progressive disease would seem a clear indication for medical treatment, while the enhanced
patient acceptability of EHDP, as a result of oral administration, makes the decision for a therapeutic trial in other cases easier to make. Such treatments are clearly not devoid of risk and must be undertaken in close conjunction with a metabolic physician.

**Fibrous dysplasia**

Fibrous dysplasia is a fairly common benign disorder of fibro-osseous tissue of unknown aetiology which was not recognized as a specific disease entity until the 1940s. It can affect one or several bones and while the dominant features are skeletal, occasionally certain endocrinopathies, abnormal pigmentation of skin and mucous membrane, and other abnormalities may form part of the disease process. The craniofacial skeleton is a predilective site and the temporal bone is affected in more than 15% of cases with skull involvement. For many years, fibrous dysplasia of bone was not distinguished from primary hyperparathyroidism, and both kinds of osseous lesions were described pathologically and radiologically as osteitis fibrosa cystica.

Three separate types of fibrous dysplasia are now described.

**Type I: monostotic**

This type is limited to one bone, usually the femur, tibia, ribs or facial bones. The mandible and maxillae are the most frequent sites of facial bone involvement.

**Type II: polyostotic**

In this type more than one bone is involved, most frequently of the lower limbs. In the skull, the lesser and greater wings of the sphenoids, and the vertical and horizontal processes of the frontal bones are mainly affected. The frontal and sphenoid sinuses are frequently obliterated.

**Type III: disseminated and extraskeletal manifestations**

This is also known as the McCune-Albright syndrome (McCune, 1936; Albright et al, 1937). Bone distribution is similar to the polyostotic form but is commonly unilateral, with areas of skin hyperpigmentation and endocrine disturbances, particularly hyperthyroidism. The disorder primarily affects females who characteristically display precocious puberty.

The monostotic form, which accounts for about 70% of cases (van Tilberg, 1972), generally becomes arrested at puberty. The polyostotic form, on the other hand, may progress beyond the third or fourth decades. Initial clinical symptoms usually appear during childhood or early adolescence - a period of active skeletal growth (Lichtenstein and Jaffe, 1942) - and include pain, deformity and recurrent fractures.

In the disease, normal bone is replaced by fibrous tissue consisting of spindle cells and poorly formed trabeculae of immature woven bone. Increased osteoblastic and osteoclastic activity is usually present and islands of cartilage may be observed. It primarily involves cancellous bone, although tissue expansion may give rise to distortion and structural weakness. As the lesions enlarge, the overlying bony cortex becomes thinner, although its
histological structure usually remains normal. The disease has been considered variously as an arrest of bone maturation (Reed, 1963), as a disturbance of postnatal cancellous bone maintenance (Aegerter and Kirkpatrick, 1968), or as a misdifferentiation of the bone-forming mesenchyme (Lichtenstein and Jaffe, 1942). Carcinomatous degeneration is very rare (Schwartz and Alpert, 1964) and has never been reported in the temporal bone.

Otological features

In 1982, Nager, Kennedy and Kopstein reviewed the literature and summarized the findings in 69 cases of fibrous dysplasia involving the temporal bone. The male to female sex incidence was 2:1 and a majority of the patients had the monostotic form of the disease. The mean age of onset of the clinical symptoms was 15 years, although the range extended to 59 years. The mean age at clinical presentation was 28 years.

The commonest presenting symptoms were progressive hearing impairment (57%), localized swelling of the temporal bone (51%) and progressive bony occlusion of the external auditory meatus (42%). About 15% of the patients with hearing loss had a total or profound sensorineural deafness and the remainder had an early conductive loss. Vestibular symptoms and tinnitus were uncommon. In 11 cases, marked constriction or obliteration of the external auditory meatus was associated with an underlying epidermoid inclusion cyst or cholesteatoma. The pathogenesis is similar to other situations with acquired stenosis of the meatus, when desquamation of normal meatal skin and tympanic membrane continues medial to an obstruction (Brookes and Graham, 1984). Labyrinthine involvement was present in three of the cases; five developed facial nerve paralysis. For this reason an obliterated external auditory meatus should be explored surgically and reconstructed. Three patients presented with massive temporal bone involvement and features of an intracranial space-occupying lesion. The increased size of the temporal bone was usually postauricular often causing an anteroinferior protrusion of the auricle, but occasionally swellings of the preauricular and supra-auricular regions were present. Blockage of the eustachian tube leading to serous otitis media may occur. Rarely bone narrowing of the internal auditory meatus develops with progressive impairment of function of the seventh and eighth cranial nerves.

Typically the serum calcium and phosphorus levels are normal, while the alkaline phosphatase level may be raised in the presence of an active lesion. If several bones are involved hyperparathyroidism must be carefully excluded, although on occasions it appears that the two conditions may occur together. X-ray studies generally reveal an enlarged temporal bone associated with sclerosis, or a uniform 'ground glass' appearance. Areas of radiolucency and cortical thinning may occasionally be seen. The radiological appearance of the disease is a function of its histological structure. A predominance of osseous elements renders the lesion more opaque, while the mixture of fibrous and bony elements produces the 'ground glass' appearance. The predominance of fibrous elements produces a radiolucent cyst-like picture. The high resolution CT features have recently been documented (Swartz et al, 1985).

Treatment

At present there is no known conservative treatment for the control of fibrous dysplasia. Nevertheless, the prognosis is usually good and the decrease in disease activity at
puberty is greater in the monostotic form. The presence of a lesion in the temporal bone does not in itself justify surgical intervention. However, more than one-half of the patients will probably undergo operative treatment. The main indication is external auditory meatus stenosis, while reduction of the unsightly local swelling for cosmetic reasons accounts for most of the other cases. The diseased bone has characteristic macroscopic features. It is vascular, spongy and crumbly with a gritty consistency and can be readily removed by curettage. Half the cases reviewed by Nager, Kennedy and Kopstein (1982) underwent two or more operative procedures, but surgery was rarely curative. Management should therefore be conservative. Spontaneous decrease in disease activity may well help to reduce the recurrence in rate. Radiotherapy appears to have a predisposing propensity to malignant generation of lesions in other sites (Schwartz and Alpert, 1964).

Osteopetrosis (marble bone disease)

Osteopetrosis is a rare inherited bone disorder which occurs as a benign dominant form, otherwise known as Albers-Schönberg disease, and a malignant recessive form. Pathologically there is a failure of resorption of cartilage and excessive formation of immature bone leading to thickening of the cortex and narrowing or obliteration of the medullary cavity. This may cause anaemia and a susceptibility to infection. Failure and impairment of bone maturation result in thick, dense and brittle bones. The skull may become extremely thick and when remodelling involves the cranial foramina, stenosis and compression of emergent nerves and vessels may occur. The optic, trigeminal, facial and auditory nerves are those most frequently affected (Myers and Stool, 1969; Hamersma, 1970).

Otological features

Histological studies of temporal bones show that the labyrinth and ossicles mainly consist of dense calcified cartilage. Typically, pneumatization of the mastoids is absent. The internal auditory meatus may be narrowed, but the otic capsule remains unaffected (Myers and Stool, 1969; Hawke, John and Bailey, 1981). The serum alkaline and acid phosphatase may be markedly elevated, while the urinary hydroxyproline levels are usually normal (Johnston et al, 1968).

Most of the patients with malignant recessive disease die in early childhood and certainly none survive into their twenties. The associated hearing loss in these cases is sensorineural. In contrast, many patients with the benign disease may be asymptomatic, the diagnosis only being made radiologically. Common symptoms are bone pain and fractures. The hearing loss is usually conductive, but occasionally, is mixed and is caused by impaired ossicular mobility by osteopetrotic bone (Jones and Mulcahy, 1968; Hamersma, 1970). Recurrent facial palsy, which behaves like a typical Bell's palsy, is a frequent manifestation. There is a tendency to progressive residual facial weakness with synkinesis and contracture. Clinical experience indicates that surgical intervention to alter the natural history of these recurrent facial palsies should ideally include decompression of the proximal facial nerve in the fallopian canal by a middle fossa approach.
Neurofibromatosis

This is a common disorder of neural tissue which was described by von Recklinghausen in 1882. It is characterized by multiple areas of cutaneous pigmentation (café-au-lait spots), multiple naevi and neurofibromata of peripheral or cranial nerves. Within the cranial cavity, neurofibromata most often occur on the eighth nerve and are frequently bilateral (see Chapter 21). In addition, there is an increased incidence of gliomata and meningiomata, which may be multiple. The disease is familial with an autosomal dominant inheritance, although sporadic cases do occur.

Bone lesions occur in about one-half of the cases (Hunt and Pugh, 1961; Nordin, 1973; Beighton, 1978). Common skeletal abnormalities include severe scoliosis, defects of the walls of the orbits, erosive defects caused by adjacent neurogenic tumours, apart from disorders of bone growth. The facial bones, mandible, occipital and temporal bones may be deformed and hypoplastic. The figure shows the famous patient of Sir Frederick Treves, Joseph Merrick (alias the elephant man), who was treated at the London Hospital. It can be seen that he had marked narrowing of the right external auditory meatus resulting in a conductive hearing loss. There is no evidence, however, that one of his numerous misfortunes included an acoustic neuroma.

Genetic craniotabular hyperostoses

Hyperostosis corticalis generalisata (Van Buchem's disease)

This disease was first described by Van Buchem and his colleagues in 1955, who have since added further reports (Van Buchem et al, 1962; Van Buchem, 1971). It is an autosomal recessive condition, in which normal stature but overgrowth of bone in the skull and skeleton are associated with facial palsy and conductive deafness.

There is osteosclerosis of the skull, mandible, clavicle and ribs and hyperplasia of the diaphyseal cortex of the long and short bones. The skull and mandible may enlarge from the age of 10 years onwards with thickening of the calvaria, skull base and clavicles. The facial paralysis may be unilateral or bilateral, and the gradually symmetrical hearing loss may be noted from the early teenage years. In some a sensorineural hearing loss and in others a mixed loss may occur. Optic nerve involvement is a late complication. The serum calcium and phosphorus remain normal, but the alkaline phosphatase is frequently raised by as much as 50 to 250%.

Sclerosteosis

This is an autosomal recessive condition in which skeletal overgrowth is associated with syndactyly and digital malformation; facial palsy and deafness are common complications and raised intracranial pressure may develop (Truswell, 1958).

The hearing loss may be bilateral, sensorineural, mixed, or conductive. Facial nerve paralysis is often unilateral in childhood, becoming bilateral in late adolescence. There is also decreased sensory function of the ophthalmic and maxillary divisions of the fifth cranial nerve, anosmia and chronic headache.
The alkaline phosphatase is markedly elevated in nearly all patients, although other biochemical skeletal indices are usually normal. Radiologically, the bones show increased density but abnormalities of bone modelling, if present, are of minor degree (Beighton, Crenin and Hamersma, 1976; Beighton, Durr and Hamersma, 1976).

**Congenital hyperphosphatasia (osteoectasia)**

This is a rare autosomal recessive condition with skeletal deformity developing in the second or third year of life. It is associated with dwarfing, fractures and blue sclerae. There is marked irregular thickening of the skull and enlargement of the calvaria. The external auditory meatus may become narrowed and there is a progressive mixed hearing loss, which becomes evident from the fourth to the fourteenth year. Typically the hearing thresholds average about 70 dB. The serum alkaline and acid phosphatase levels are both consistently elevated.

**Progressive diaphyseal dysplasia**

*(Camurati-Engelmann's disease; osteopathia hyperostotica sclerositans multiplex infantilis)*

This is an autosomal dominant condition principally involving the long bones, but the skull may be mildly affected. Generalized sclerosis of the base, similar to osteopetrosis, may be seen but in the vault of the skull fewer bones are involved and are less severely affected.

Sparkes and Graham (1972) have reported the case of a 26-year-old man with progressive hearing difficulty leading to total deafness on the right side associated with a facial paralysis. Bilateral decompression of the slit-like internal auditory meatus was carried out and some initial improvement was noted. More recently, two cases who underwent surgery have been described (Miyamoto, House and Brackmann, 1980). The first was a 26-year-old man who complained of bilateral hearing loss, right-sided facial paralysis and chronic unsteadiness. X-rays showed bilateral massive overgrowth of dense bone involving the petrous apex and mastoid bone. Both internal auditory meatus were partially obliterated by such bone. The second case was that of a 30-year-old woman with bilateral sensorineural hearing loss, occurring suddenly 14 months earlier on the right side and 9 months later on the left. Both cases were explored surgically by a middle cranial fossa approach, the first to improve the facial nerve function and the second to decompress the internal auditory meatus on the right side. Following surgery, the hearing of the second patient has remained stable and further X-rays did not show evidence of recompression.

The genetic craniotabular dysplasias, craniofacial dysostoses and osteopathia striata are extremely rare conditions. They are usually only seen in infancy and are listed in Table 15.1 for completeness.

**Dietary and metabolic diseases**

**Osteomalacia (vitamin D deficiency)**

Vitamin D deficiency has recently been recognized as an uncommon cause of bilateral sensorineural hearing loss (Brookes and Morrison, 1981; Brookes, 1983). It is a condition
which occurs primarily in Asian immigrants and socio-economically deprived populations. Since changing hospital appointments to a predominantly middle class practice in postgraduate hospitals without a metabolic medical unit on site, one of the authors (GBB) has not seen a single new case for well over 2 years.

Vitamin D refers to a group of steroids which play an essential role, with parathyroid hormone, in the regulation of calcium and bone metabolism. The main metabolic pathways is shown in the figure. Most is synthesized in the skin and, under normal circumstances, dietary requirements are minimal.

Rickets and osteomalacia are the juvenile and adult forms respectively of a group of disorders characterized by defective mineralization of bone and usually result from quantitative and qualitative impairment of vitamin D activity. A less common cause is hypophosphataemia and secondary hyperparathyroidism is occasionally associated. A high incidence of osteomalacia has recently been recognized among Asian immigrants living in the UK, due to a combination of dietary and genetic factors (Editorial, 1976). In the classical deficiency state, the serum calcium and phosphate levels may be low, while the alkaline phosphatase is usually elevated. These biochemical parameters are often normal, however, due to compensatory metabolic mechanisms. Reduced mineralization may produce an altered trabecular bone pattern and pathological fractures on X-ray, but radiology in most early cases is normal, when the clinical condition is termed 'biochemical osteomalacia'. Serum assay of metabolic derivatives of vitamin D - 25-hydroxy vitamin D, the storage form, and 1,25-hydroxy vitamin D, the active form - are invariably low in vitamin D deficiency states including biochemical osteomalacia.

Otological features

The otological features and treatment results of 27 patients presenting to the London Hospital with deafness and low vitamin D levels have recently been summarized (Brookes, 1985a). More than half were Asian immigrants and two-thirds reported associated tinnitus. Vestibular symptoms were infrequent. Nearly 50% had a progressive cochlear deafness. A characteristic trough-shaped pure-tone audiogram centred around 1-2 kHz frequencies was seen in two-thirds of these cases. Figure is the audiogram of a 35-year-old Asian man at presentation. Three months later, when the diagnosis was established, his hearing had fallen to a mean level of 85 dB. Electrocochleography showed features of endolymphatic hydrops. Cochlear tomography demonstrated bilateral demineralization. However, this has only been present in less than 15% of cases. All except one of the remaining patients in the London Hospital series had otosclerosis.

Covell first reported the histopathological effects of acute vitamin D deficiency in 1941. He studied a group of rats who were maintained on a vitamin D deficient diet for 3 weeks, followed by a vitamin replacement diet for 1 week. Pathological features were thus modified by various degrees of healing. Newly formed osteoid was found in the periosteal and endochondral layers of the otic capsule, together with slight degenerative changes in the cochlear nerve.

The effects of acute vitamin D deficiency alone on both cochlear function and morphology have recently been studied in the albino rats (Brookes, Lilly and Hawkins, 1983).
A significant reduction in the amplitude of the brainstem evoked responses and impaired mean hearing thresholds were seen in the vitamin D deficient animals, following a vitamin depleted diet for 10 weeks, compared with a control group. Preliminary morphological studies showed narrowing and, in some places, obliteration of the capillaries in the stria vascularis, features suggesting early strial atrophy.

Treatment

Patients have been treated with replacement vitamin and mineral supplements, the dosage being dependent upon the degree of deficiency. Those with a 25-hydroxy vitamin D level of 5-10 ng/mL have received combined vitamin D and calcium tablets, two or three per day, to provide a dose of 1000-1500 units of vitamin D. Patients with levels less than 5 ng/mL have received treatment with the parent vitamin D3, calciferol, in doses of 3000-6000 units per day. Calcium and occasionally phosphate supplements have been added to this latter group if the patient’s general diet was considered unsatisfactory. Careful biochemical monitoring is essential during replacement treatment because prolonged increases in plasma calcium and phosphate may lead to extraskeletal calcification. Overall, the results have been generally disappointing, with a significant (greater than 10 dB) hearing improvement occurring in less than 15% of cases.

Vitamin D resistant rickets (hypophosphataemic)

Familial hypophosphataemic vitamin D resistant rickets is the commonest form of the genetically determined osteomalacias. It is due to a reduced renal tubular reabsorption capacity for phosphate and is most frequently transmitted as an X-linked dominant condition. Sporadic cases due to a new mutation are not uncommon. Davies, Kane and Valentine (1984) recently described the results of their survey of 16 families with the condition and found a high incidence of sensorineural hearing loss in 25 patients. General skeletal radiographs show osteosclerosis with an increase in bone density and a coarsened trabecular pattern (Davies and Stanbury, 1981). The petrous temporal bones in many of the 25 cases also showed a generalized increase in bone density, and in some, narrowing of the internal auditory meatus was present. Similar radiological features were reported by Stamp and Baker (1976) who described two children from a first cousin marriage. The audiological features indicated a cochlear dysfunction but did not, however, support the original theoretical pathogenesis for hearing impairment suggested by Stamp and Baker, which was a retrocochlear loss due to pressure on the cochleovestibular nerve bundle in the narrowed internal auditory meatus. Nearly 75% of the cases were subsequently found to have typical features of endolymphatic hydrops on transtympanic electrocochleography (O'Malley et al, 1985), while two displayed classical features of Ménière’s syndrome.

The other main form of hypophosphataemic osteomalacia is recessive in type. Weir (1977) described two pairs of siblings who were known to suffer from this disorder. Three out of four developed some degree of sensorineural deafness, and all demonstrated the radiological finding of marked narrowing of the internal auditory meatus. In the X-linked hypophosphataemic variety, alkaline phosphatase levels return to normal on cessation of growth, but in the recessive form continued biochemical activity persists on attaining adult stature and maintenance therapy with vitamin D is necessary.
Vitamin D intoxication

Cohen et al (1979) reported a patient with pseudohyperparathyroidism, who had continued to take calciferol 2.5 mg daily. Four years later a severe conductive hearing loss was present, and examination showed marked calcification of the tympanic membranes and cornea. Radiological investigation demonstrated extensive calcification of the kidneys and blood vessels, while the mastoids were cellular. Unfortunately the hearing loss was unchanged by treatment. One of the authors (GBB) has encountered a similar case. in 1972, a 4-year-old child, whose father was a serviceman stationed abroad, was eventually found to be suffering from a very rare growth disorder due to a primary growth hormone deficiency. The diagnosis of rickets had been made initially and calciferol treatment taken for more than 2 years. A bilateral hearing loss was present in addition to partial blindness and impaired growth. Calcification of the tympanic membranes and cornea was present, although the nature of the hearing loss could not be fully evaluated.

Osteoporosis

Most cases of osteoporosis are classified as idiopathic and typically affect the spine and long bones in the elderly. Pathologically there is a reduction in total bone mass due to loss of both the trabecular bone matrix with widening of the vascular channels and deficient mineralization. Radiologically there is rarefaction of bone, which is indistinguishable from osteomalacia. However, in this latter condition the histopathology is quite different because the bone matrix framework remains intact. Blood biochemistry is normal, although metabolic studies may show a negative nitrogen balance and evidence of calcium malabsorption.

Otological features

One of the very few accounts of the otological features associated with osteoporosis was reported by Henkin, Lifshitz and Larson (1972). They diagnosed a sensorineural deafness, significantly greater than their age related mean level, in five or seven patients with confirmed osteoporosis who presented with severe bone pain. The hearing loss commenced at the onset of symptoms of bone disease or soon after and was almost invariably bilateral and progressive. Temporal bone radiology showed increased sclerosis of the otic capsule in five cases.

The biochemistry is frequently normal and the diagnosis may not be straightforward. Normal serum calcium, phosphate and alkaline phosphatase indices are also often seen in vitamin D undernutrition when clinical features of osteomalacia are also frequently absent and radiological bone changes are only found in the well established case. The association of osteoporosis and sensorineural loss clearly requires further investigation. The potential benefit of such studies for the hearing impaired population could be enormous. It is common knowledge that the body's positive calcium balance deteriorates with increasing age, particularly in postmenopausal women when plasma oestrogen levels are no longer maintained. It is quite possible therefore that this condition may well be an important contributory factor in the aetiology of presbyacusis, perhaps in association with relative vitamin D undernutrition which is also associated with increasing age. It is of great interest that the current treatment advocated for osteoporosis consists of a vitamin D metabolite, in conjunction with oestrogens in postmenopausal women. Calcium supplements are not
considered necessary providing that the diet is satisfactory (Crilley et al, 1981). The efficacy of such treatment on pre-existing hearing loss requires further study.

Hyperparathyroidism

The disorder may be primary, usually due to a parathyroid adenoma, or secondary, due to chronic renal disease. Occasionally it may be associated with osteomalacia. When the condition causes skeletal changes due to mobilization of phosphorus and calcium from bone, it is termed osteitis fibrosa cystica or von Recklinghausen's disease of bone. Plasma calcium levels are high and invariably diagnostic. Phosphate levels are often low, while elevation of the alkaline phosphatase, an index of osteoblastic activity, reflects bone involvement.

The condition is only rarely encountered in otological practice. Rüedi (1968) described the temporal bone changes in two patients with osteitis fibrosa cystica, and Lindsay and Suga (1976) subsequently reported another. The histopathological features were very similar to those seen in Paget's disease. Morrison (1979) detailed the clinical features of one case; a 64-year-old man presenting with a one-month history of a rapidly progressing hearing loss. Calcium deposits were observed beneath the tympanic membrane and a mixed hearing loss was found on pure-tone audiometry. The patient was lost to follow-up, but terminal hypercalcinosi was subsequently diagnosed a few months later.

Acromegaly

Acromegaly is a chronic disease of middle life resulting from the action of excessive growth hormone usually caused by an eosinophil adenoma of the anterior pituitary gland. It occurs after fusion of the bony epiphyses and is characterized by enlargement of the bones, especially of the hands, feet, skull and mandible. The enlargement of bones is caused by deposition of new bone upon the surface of original cortex causing an increase in thickness but not in length. About 30% of patients develop over diabetes mellitus.

Otological features

Richards (1968) investigated 15 patients. Five ears showed a marked conductive deafness, but otherwise the remainder developed a sensorineural loss which was substantially lower than in the 'normal' population, with the general tendency for the hearing loss to deteriorate with age. There was no relationship with the duration of the disease or the plasma growth hormone levels and hearing loss. Subsequently Doig and Gatehouse (1984) assessed the hearing in 56 patients with acromegaly requiring pituitary surgery and compared them with matched controls. They were unable to find any significant difference in hearing levels between the two groups nor any correlation with diabetes, growth hormone levels, blood pressure or other factors. In addition, no change in the hearing occurred after surgery to remove the tumour. In this series, three ears of the acromegalics showed evidence of otosclerosis compared with one in the control group.

Three cases of acromegaly with temporal bone involvement were reported by Graham and Brackman (1978). Radiology demonstrated massive thickening of the mastoid cortex and posterior bony canal wall with secondary lengthening of the bony external meatus. Some overgrowth diminishing the lumen also occurred. However, the internal auditory meatus,
cochlea and vestibule appeared normal and the structure of the otic capsule including the facial nerve, remained in normal relationship.

**Infective and granulomatous diseases**

**Syphilis**

The effects of syphilis on the temporal bone are often seen in clinical practice. It is a disease which should be suspected in any patient presenting with tinnitus and/or vertigo and/or sensorineural hearing impairment, particularly if fluctuant and of sudden onset. Prompt recognition and treatment may halt or possibly reverse the progressive audiovestibular symptoms, and prevent the development of serious systemic involvement in the tertiary stage, if this is not already present. These serious systemic features include cardiac and aortic involvement and parenchymatous neurosyphilis, manifested by general paralysis of the insane and tabes dorsalis. Both the congenital and acquired forms of syphilis can be complicated by inner ear disease.

The last half century has witnessed a dramatic decline in the number of reported new cases. Thus the incidence of new cases of congenital disease in the UK fell from 2439 in 1931 to 1223 in 1950 and more recently the numbers have stabilized at about 150 per annum (Chief Medical officer, 19740. in 1980, only eight new cases were diagnosed in children under 2 years of age (British Medical Journal, 1982). The universal antenatal serological screening programme in the UK has undoubtedly played an important part in the control of congenital syphilis; an untreated syphilitic mother has about a 50% chance of bearing a syphilitic child. Failure to eliminate this form of the disease altogether is probably due to the difficulty in administering antenatal care to some social groups. During the same period, the overall reported incidence of new cases of both congenital and acquired types fell from the post-war peak of nearly 28,000 cases per year to about 4,500 cases in 1980. The current prevalence in 1984 was 6.4 cases per 100,000 (British Medical Journal, 1986). A transient rise in the incidence was noted during the early 1970s and has been attributed to male homosexual transmission. Currently well over 50% of syphilitic infections in men are reported to have been homosexually acquired. The male:female incidence is now about 4:1 and new cases of acquired syphilis are about 25 times as frequent as congenital ones.

**Diagnosis**

Of the established screening tests for syphilis, the Venereal Disease Research Laboratory slide test (VDRL) is most commonly undertaken in clinical practice. Although the test is frequently negative in previously treated cases, and false positives may occur, it does give an indication of disease activity. It is invariably strongly positive in high dilution in early untreated cases and is usually accompanied by an elevated erythrocyte sedimentation rate.

More specific serological tests are now routinely employed, for example Treponema pallidum haemagglutination test (TPHA); Treponema pallidum immobilization test (TPI) and the fluorescent treponemal antibody absorption test (FTA abs). of these the FTA abs is the most sensitive (Dunlop, King and Wilkinson, 1969; Hughes and Rutherford, 1986). A positive result confirms previous syphilitic infection but does not reflect disease activity and stays positive even following adequate treatment.
Examination of the cerebrospinal fluid in patients with syphilitic ear disease is essential to look for possible evidence of central nervous system involvement which is more likely to be seen in the late acquired form. Typical cerebrospinal fluid abnormalities of neurosyphilis, apart from positive serological tests, include slightly raised globulin and IgG levels and a lymphocytosis. Such investigations and treatment are best coordinated by a venereologist, who will also need to examine possible contacts in cases of acquired syphilis.

**General features**

Congenital syphilis may be associated with other abnormalities outside the cochleovestibular systems. The ocular manifestations of interstitial keratitis and choroidoretinitis result in corneal opacity in about 90% of patients with otological symptoms. Such features may only be apparent on careful slit-lamp examination by an ophthalmologist and may be of diagnostic value. Hutchinsonian thickened wedge-shaped incisors which are occasionally notched are found in 20% of cases. The typical facies of frontal bossing of the skull due to periostitis of the cranial bones and saddle nose due to involvement and collapse of the nasal septal cartilage and bone are only present in about 10% of cases (Morrison, 1975; Belal and Linthicum, 1980). Other features such as 'sabre tibia' are rare.

Tabes dorsalis and general paralysis of the insane are manifestations of neurosyphilis and both are now rare. The neurological features include 'lightning' pains, early optic atrophy, Argyll Robertson pupils, bladder dysfunction and sensory loss from dorsal column involvement resulting in impaired vibration sense and joint disruption - Charcot's joints (Catterall, 1977). However, previous treatment which may have been inadequate often results in atypical features.

A not infrequent clinical dilemma is posed by patients from the West Indies, Central America and Africa, who may display positive serological test results and similar clinical manifestations but who are suffering from yaws. This disorder is caused by a different spirochete, *Treponema pertenue*, and typically is spread by direct contact among children. Old scarring from previously healed cutaneous ulcers is characteristically present on the lower legs. When these scars are absent, the patient from these countries should certainly be considered to be suffering from syphilis and treated accordingly.

**Otological features**

**Histopathology**

Two distinct types of histopathology are recognized. Treponemal labyrinthitis is the typical lesion in early congenital syphilis, and meningolabyrinthitis in the acute meningovascular phase of secondary and tertiary disease. In this latter form, the small blood vessels of the meninges show endarteritis obliterans. There is increased fibrosis of the meninges, with small areas of the necrosis and a diffuse infiltrate by plasma cells and lymphocytes. The eighth nerve may be involved in association with the infective basal meningitis, and the inflammatory process spreads from the spiral ganglion to the cochlear duct and membranous labyrinth (Goodhill, 1939).
In late congenital and acquired disease, the main lesion is a rarefying gummatous osteitis of the temporal bone with secondary involvement of the membranous labyrinth (Mayer and Fraser, 1936; Goodhill, 1939; Schuknecht, 1974). All three layers of the otic capsule are involved in the osteitis, which is associated with underlying endarteritis and infiltration with chronic inflammatory cells and multinucleated giant cells. The inner ear features are dominated by endolymphatic hydrops and progressive degeneration of the neuroepithelial structures, particularly the cochlear neurons and organ of Corti, which may be severe.

It has long been held that the pathogenesis of the hydrops is probably by direct involvement of the endolymphatic duct which becomes obliterated. However, treponemal spirochetes have been found in many different sites in humans with late syphilis following treatment, including the aqueous humour of the eye, cerebrospinal fluid, synovial fluid, temporal artery, lymph nodes and liver (Collart, Borel and Durel, 1964; Smith and Israel, 1967; Goldman and Girard, 1967; Rice, Jones and Wilkinson, 1969; Mack et al, 1969; Dunlop, 1972). This continued presence of spirochetes in spite of apparently adequate previous antibiotic treatment, may well be a significant factor in the pathogenesis of the hearing loss (see below; Immunology and the temporal bone).

Early syphilis

Congenital syphilis is contracted by the developing fetus in utero as a consequence of acquired maternal syphilis. The early infantile form is usually fatal due to multisystem involvement which dominates the features of otolabyrinthitis. As noted above, it is now exceedingly rare in the UK. Probably about 50% of cases develop bilateral hearing loss eventually. Earlier studies, for example Karmody and Schuknecht (1966), tended to underestimate the incidence because of the proportion of younger individuals who could be expected to develop symptoms later on.

Secondary syphilis is typically, although not exclusively, seen in adult homosexual men. The first symptoms last for a few weeks and include malaise, slight pyrexia, non-specific headaches, skin eruptions, pharyngitis and lymphadenopathy. They are relatively trivial and are hence frequently ignored by the patient until sudden hearing loss develops which is often bilateral. There may be some transient vestibular symptoms which are frequently positional in character and tinnitus. Ocular palsies and facial paralysis may occur as well in the acute meningovascular type of secondary disease. The sensorineural hearing loss preferentially affects the high frequencies; elevated stapedius reflex thresholds, possibly with reflex decay, are frequently present. Speech discrimination is often significantly worse than is suggested by pure-tone audiometry and the caloric responses are reduced. Increased latency and/or reduced wave V amplitude on brainstem evoked audiometry has been recently reported (Rosenhall, Löwhagen and Roupe, 1984). These audiovestibular symptoms may be partly reversible. If left untreated, the infection tends to run a benign course but the hearing loss remains.

Late syphilis

Late syphilis affects the temporal bone between 10 and 50 years after the primary infection. Once established, the untreated disease carries a poor prognosis with relentless
progression to profound deafness, although fluctuations are common. There are some grounds, however, for optimism with antitreponemal agents and systemic steroids.

In general, the clinical features are similar in both the congenital and acquired forms of the disease, although the former is more common in females. It is often difficult to assign a patient to one of these groups, particularly since previous antibiotics have invariably been taken. The otological features in congenital cases can occur at any stage, but they are uncommon after middle age. In contrast, patients with late acquired disease are usually over 40 years of age. The hearing loss is typically symmetrical in congenital cases but more frequently unilateral in the acquired group, sometimes for many years. In about 20% the onset of aural symptoms is sudden and fluctuations are seen in 30%, particularly in early stages (Hahn, Rosin and Haskins, 1962; Dawkins, Sharp and Morrison, 1968; Kerr, Smyth and Cinnamond, 1973). Apart from fluctuation, there are other features which closely mirror the symptoms of Ménière's disease and are a reflection of the underlying endolymphatic hydrops (Schuknecht, 1974). The early hearing loss is sensory in character with predominantly low or peaked patterns of pure-tone audiometry. Half the patients exhibit episodic attacks of vertigo which may be indistinguishable from those occurring in classical Ménière's disease.

The results of transtympanic electrocochleography in a series of 18 cases of late syphilitic deafness have been described by Ramsden, Moffat and Gibson (1977). An enhanced negative summating potential (SP) was found in nearly 80% of ears tested in association with a small cochlear microphonic (CM), both features indicating established endolymphatic hydrops. The summating potential characteristically affected the descending limb of the compound action potential (AP). This feature, however, is not pathognomonic and in the authors' experience occurs relatively infrequently. Syphilitic hydrops tends to remain relentlessly active in the majority of cases, in contrast to idiopathic Ménière's disease where only a relatively small proportion of patients have hydropic pathology which is not self-limiting to some degree. Secondary neuronal degeneration associated with more profound degrees of hearing loss is therefore more frequent. The pattern of pure-tone audiometry now becomes flattened or high-tone in character. Alteration of the stapedius reflex to a retrocochlear pattern with elevated thresholds and decay is now evident in association with a relative greater impairment of speech discrimination.

Progressively severe peripheral vestibular damage leading to increasing imbalance and ataxia is also quite common. However, compensation for such a slowly developing deficit can significantly reduce the degree of disability, particularly in the younger patient, and may only come to light on formal vestibular assessment.

Two eponymous otological phenomena which are sometimes present in late congenital syphilis are worthy of mention. Hennebert's (1911) sign consists of a transient positive fistula test without clinical evidence of middle ear disease. Tullio's sign consists of transient vertigo and nystagmus following exposure to sudden high intensity sound. These phenomena are believed to be due to sound energy transmission through the stapes footplate on to the distended saccule, and are occasionally seen in other diseases associated with endolymphatic hydrops.
Treatment

Penicillin is still the most effective antibiotic for the treatment of syphilis. Its main bactericidal effect occurs when the organisms are dividing. This has been shown to take place much less rapidly in the late form of the disease, and hence the duration of treatment is as important as the maintenance of effective serum concentrations. In the presence of confirmed allergy, one of the cephalosporins is probably the second choice of drug to use.

The proven effective therapeutic regimen consists of 600,000 units of procaine penicillin by intramuscular injection daily for 21 days. This aqueous solution only has to be injected once a day and results in an effective serum level for 24 hours (Catterall, 1977). Oral probenecid 500 mg 6-hourly inhibits excretion of the drug and helps to raise tissue levels. This regimen has proved satisfactory for outpatient treatment (Dunlop, A.I.-Egaily and Houang, 1981). An alternative protocol which is probably as effective in patients who show good treatment compliance is high-dose ampicillin. A dosage of 1.5 g is prescribed four times daily for 4 weeks (Adams et al, 1983). Unfortunately, there is no evidence that penicillin treatment alone prevents the progression of cochleovestibular manifestations.

There is now, however, considerable clinical evidence that systemic steroids alone can improve the hearing at least temporarily, in up to 50% of cases with late syphilitic deafness (Hahn, Rodin and Haskins, 1962; Karmody and Schuknecht, 1966; Morrison, 1969; Kerr, Smyth and Cinnamond, 1973) and suggests an immunological basis for at least part of the hearing loss. Steroids are also indicated to prevent the adverse effects of a possible Herxheimer reaction. This is a systemic phenomenon occurring within 2-12 hours of the first antitreponemal injection and is characterized by fever, followed by headache, malaise, flushing and sweating. The reaction lasts a few hours and is often accompanied by worsening local tissue involvement and has been known to cause sudden increased hearing impairment. The reaction has been attributed to complement activation and to complex immunological reactions involving a hypersensitivity response to the disintegration productions resulting from sudden destruction of large numbers of spirochetes (Catterall, 1977).

Prednisolone 30 mg 8-hourly is therefore commenced prior to institution of antitreponemal treatment and continued for 4 weeks. Others have preferred to use ACTH (Kerr, Smyth and Cinnamond, 1973; Adams et al, 1983). If there is no evidence of improvement in the auditory and vestibular symptoms by 6 weeks, it is discontinued. Improved hearing thresholds are more likely in patients with fluctuant symptoms and are an indication for longer term treatment on a maintenance dose of 2.5-5 mg daily. Unfortunately, any hearing gains often relapse on withdrawal of steroids which may well therefore need to be taken on a long-term basis to maintain improvement. Of course, prolonged steroid treatment has well recognized side-effects and the decision to maintain steroids must be weighed carefully in each individual case. Discontinuation of steroids should be followed by a further course of antibiotics. Initial optimism about the successful outcome of treatment of late syphilis with penicillin and steroids has been tempered in recent years, although long-term results show that this regimen frequently prevents further hearing impairment and almost invariably preserves some hearing (Adams et al, 1983).
Tuberculosis

Increasing numbers of patients with tuberculosis are currently presenting to various specialist departments in the UK, most often from among immigrant communities. Unfortunately it can no longer be considered a disease of the past. Although the infection primarily affects the middle ear, it may cause secondary involvement of the bony labyrinth.

Otological features

The possibility of tuberculous involvement is usually entertained by the presence of certain atypical features of chronic suppurative middle ear disease. Windle-Taylor and Bailey (1980) recently comprehensively reviewed a series of 22 patients with tuberculous ear disease who presented to The Royal National Throat, Nose and Ear Hospital, London, over a 30-year-period and found one-half to be under 20 years of age. None had a past history of pulmonary tuberculosis, although 18% had previously diagnosed disease at other sites. The middle ear features are dominated by the presence of florid, pale granulation tissue. Occasionally, as in other granulomatous disorders, the tympanic membrane may be intact, but more often breakdown has occurred, characteristically resulting in multiple perforations. Coexistent secondary infection by other organisms is frequently found.

Concomitant sensorineural hearing loss is encountered much more frequently than in 'conventional' chronic suppurative otitis media, and often results in a disproportionately large hearing loss. Windle-Taylor and Bailey did not detail the precise sensorineural hearing loss, but their data indicated that 60% had inner ear involvement, and in 25% this loss was total.

Treatment

Management obviously involves surgical excision and drainage of middle ear and mastoid disease in conjunction with antituberculous treatment. As in patients with syphilis, referral to a physician for general assessment, coordination of medical treatment and tracing of possible infective contacts is mandatory. Although there have been isolated reports of ototoxicity by rifampicin and ethambutol the risk is very considerably lower than following streptomycin therapy, which has therefore been largely discontinued.

Sarcoidosis

Sarcoidosis is a rare systemic granulomatous disease of unknown aetiology. Head and neck manifestations are uncommon and, when encountered in otolaryngological practice, the disease usually involves the parotid gland, facial nerve, nasal cavity and larynx. The nervous system is affected in only 5% of cases, although this rises to 50% if uveoparotid fever is present. The central nervous system lesion is presumed to be a granulomatous meningitis that directly infiltrates the cranial nerves or causes them to be compressed from involvement of adjacent intracranial structures. Any of the cranial nerves may be affected by the facial nerve is most frequently involved (see Chapter 24) while the eighth cranial nerve is fourth in order (Hybels and Rice, 1976). The disease has a higher incidence rate among negroes and Puerto Ricans in America.
The organs most affected are the lymph nodes, lung, liver, spleen, skin and eyes, but any tissue may be affected and certain manifestations are known to be associated with particular HLA types. The course of the disease is usually chronic with minimal constitutional upset.

Serum angiotensin-converting enzyme levels are raised in nearly two-thirds of cases of active sarcoidosis, but false positive elevation of this enzyme can occur. False positives, however, are extremely rare in the Kveim test. de Remee and Rohrbach (1980) noted that serum angiotensin-converting enzyme levels closely paralleled and occasionally antedated changes in clinical status in patients either undergoing spontaneous remission or being treated with steroids and suggested that enzyme determination should be of value in management. However, it must be appreciated that serum angiotensin-converting enzyme levels may also be raised in other conditions, such as Gaucher's disease and leprosy.

All patients with the disease should have assessment of their liver and renal function. The alkaline phosphatase is frequently raised and may be due to involvement of either liver or bone. Approximately 5-10% of patients with sarcoidosis have elevation of their serum calcium and this is thought to be due to hypersensitivity to vitamin D. There is hypoglobulinaemia in about 25% and this may also reflect disease activity. Electrophoresis of the serum proteins usually shows increased alpha-2 and gamma-globulins. The full blood count is frequently normal but erythrocyte sedimentation rate may be raised in the active stages. It is a characteristic feature of sarcoidosis that infiltration of old scars often occurs and these may provide welcome biopsy material.

**Otological features**

Sarcoidosis involving the ear may be associated with other signs such as uveitis (80%), parotid swelling (20%), facial nerve palsy (43%) and lymphadenopathy (55%). However, 40% of cases have shown no other neurological involvement.

The hearing loss may be sudden, fluctuating or progressive and the degree may vary from slight to severe to even total loss. It is usually bilateral although one side is more affected. Pure-tone audiometry may show either a high or low frequency loss while caloric testing usually shows reduced or absent responses (Gristwood, 1958; Hooper and Holder, 1970; Kane, 1976). The mechanism by which the deafness is caused is undecided. From the 36 recorded cases it would appear that the hearing loss is most probably sensorineural, but electrocochleography in two recent cases suggested the lesion may be retrocochlear with normal hair cell function (Majumdar and Crowther, 1983).

The temporal bones from a 32-year-old man deaf for 5 years from central nervous system sarcoidosis, have been examined histologically (Babin, Liu and Aschenbrener, 1984). It was found that the acoustic, vestibular and facial nerves were involved in a striking perivascular lymphocytic infiltration resulting in myelin and axonal degeneration. The cochlear and labyrinthine neuroepithelium and stria vascularis had degenerated. Babin, Liu and Aschenbrener hypothesized that sensorineural deafness and vestibular dysfunction in sarcoidosis start as a reversible neuropathy; in some patients an ischaemia secondary to the vasculitis results in irreversible damage to the inner ear neuroepithelium.
Steroids remain the only form of treatment but their effectiveness is not assured, especially in those with a profound or total hearing loss.

**Histiocytosis X**

Eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease are considered to be related disorders because of the similarity in the pathological lesions which consist of an inflammatory reticuloendotheliosis (Lichtenstein, 1953). There are, however, major differences in the severity and prognosis of the disorders (see also Chapters 10 and 23).

**Eosinophilic granuloma**

Eosinophilic granuloma is the mildest form of these granulomatous disorders. The features of 19 cases recorded over a period of nearly 40 years at the Armed Forces Institute of Pathology Registry, Washington, DC, have been reviewed by Sweet, Kornblut and Hyams (1979). Eosinophilic granuloma occurs typically in children and young adults, and there is a male predominance. It usually appears as a solitary osteolytic lesion in the long bones, skull including the temporal bone, ribs and vertebrae. It was considered for some time that there are no systemic manifestations, but later findings have suggested that multiple sites can be involved by the disease (Michelson and Bonfiglio, 1977). Although the tumour-like disorder is usually initially asymptomatic, growth progression in the temporal bone eventually may produce erosion of the mastoid cortex, tegmen, tympanic or sigmoid plates, and the bony labyrinth, leading to pain and local tenderness.

Histopathology demonstrates sheets of benign histiocytes and scattered collections of small eosinophils. There may be areas of haemorrhage and necrosis with giant cells (Schuknecht, 1974). Treatment is by local curettage with low dosage irradiation, and is invariably curative.

**Hand-Schüller-Christian disease**

Hand-Schüller-Christian disease usually appears in childhood before 5 years of age, but has been reported in young adults. Multiple lesions similar to eosinophilic granuloma are present at diagnosis or develop within a few months. Skull lesions are quite common and may involve the temporal bone sometimes before other features are apparent (Tos, 1966). Destruction of the temporal bone may be associated with secondary infection and otorrhoea. Lesions may occur in the scapulae, ribs and long bones, while infiltration may result in hepatosplenomegaly and lymphadenopathy. Systemic manifestations include pyrexia, anorexia, and recurrent upper respiratory tract infections. Perihylar infiltration may be evident on chest X-ray examination.

This disorder is progressive and invariably the outcome is fatal in the young, although spontaneous regression may occur. Low dosage chemotherapy may be employed to control systemic manifestations.
Letterer-Siwe disease

This is a rare disease which may well not be a true histiocytic granuloma, but possibly an unusual form of histiocytic lymphoma. Certainly it has the appearance and behaviour of a malignant tumour of reticulum cells. It occurs in children under 3 years of age and is rapidly fatal. The main clinical features include destructive skeletal lesions especially in the skull, hepatosplenomegaly, lymphadenopathy and widespread replacement of bone marrow which results in a bleeding diathesis and recurrent infections. Lopez-Rios, Benitez and Vivar (1968) described the temporal bone pathology of a typical case.

Apart from the local symptoms due to secondary infection, hearing loss, reduced vestibular function, facial palsy and involvement of cranial nerves in the jugular foramen are commonly seen with larger lesions involving the temporal bone.

Immunology and the temporal bone

Since the turn of the century, the recognition and development of the field of immunology has been one of the most significant advances in medicine. It is, however, only relatively recently that the impact of immunological processes in various aspects of otolaryngology has become apparent. Basic concepts are covered in Volume 1, Chapter 18 and this section will assume a fundamental knowledge of many of these principles.

There are several specific types of immune response which are now recognized. The most useful classification of tissue-damaging hypersensitivity reactions between antigen and antibody is still that devised by Gell and Coombs (19687). They distinguished three types of initiating mechanisms involving humoral antibodies and a further type involving cell-mediated antibodies associated with delayed hypersensitivity reactions.

Clinical experience suggests that the inner ear may be involved in any of these types of immunological reaction. The otological picture is usually one of sudden or rapid bilateral hearing impairment which is frequently fluctuant and often associated with tinnitus. There may be aural pressure or fullness, with variable vestibular symptoms which can frequently be mild and transient but uncommonly acute and severe. The symptomatology may show close similarities to Ménière's disease and indeed, perhaps these disorders are different parts of the same spectrum of cochleovestibular disease. The presence of systemic clinical features depends on the particular mechanisms involved but are invariably conspicuous by their absence.

Types of immune response

Type I

The type I reaction (anaphylactic) described by Gell and Coombs occurs as a result of free antigen interacting in the tissues with cell-bound antibody. Within minutes of exposure to the sensitizing antigen, activation of enzymes in the tissues causes the release of vasoactive substances from mast cells or basophils which increase capillary permeability, alter vascular tone and stimulate smooth muscle contraction. Many allergic reactions take place locally where antibody is bound and do not necessarily induce a severe generalized anaphylactic
response. Allergies, particularly those due to foods or chemicals, are believed to be related to cochleovestibular disorders (Boyles, 1984). Eliminating the offending allergen from the diet in conjunction with antiallergic drug therapy may reverse a long-standing sensorineural loss (Clemis, 1974; Shambaugh, 1981). The importance of allergic processes in otology is, in the authors’ opinion, to be regarded with some degree of scepticism. One of us (GBB) has, however, managed a 36-year-old man with an 18-month history of bilateral Ménière's syndrome, which was undoubtedly initiated or at least aggravated by milk intolerance. Dietary management enabled his 40 dB fluctuant hearing loss to stabilize at a near normal level and he required no further specific treatment.

**Type II**

The type II reaction (cytotoxic) occurs when free circulating antibody interacts with fixed antigen which already forms part of a cell surface or tissue membrane. The invariable result is membrane change and in the case of a cell results in lysis and death. This reaction involves complement fixation and activation. Recent evidence from immunofluorescent studies (Arnold and Gebbers, 1984) suggests that the mechanism may well be important in some types of immune-mediated inner ear disorders, perhaps on occasion in combination with delayed cell-mediated activity (see later).

**Type III**

When both antigen and antibody are freely circulating, the resulting circulating immune complexes are still on occasions able to provoke a tissue response, the type III reaction. Immune complexes are usually rapidly and harmlessly removed from the circulation by the phagocytic cells of the reticuloendothelial system. They can, however, become harmful if they are deposited in body tissues when complement activation enhances local inflammatory processes and cell damage. Immune complex reactions may be related to autoimmunity, or may also occur in response to exogenous antigens such as microorganisms and drugs. Their role in the cause of various disease processes has attracted much attention in recent years. The subject has been well reviewed by Plotz (1982) and Heaney (1982). Recognized clinical disorders which are probably mediated by immune complexes range from the classic anaphylactic serum sickness reaction to disorders which are relevant to otology. These include systemic lupus erythematosus, polymyositis, relapsing polychondritis and the various types of vasculitis, including polyarteritis nodosa, Wegener's granulomatosis, temporal arteritis, Behçet's disease and Cogan's syndrome. These disorders are considered later.

The tissues involved in these type III hypersensitivity reactions depend on the size and specificity of the complexes. Biologically active complexes are of intermediate size and are poorly cleared from the circulation. They may become arrested on the endothelial lining of small blood vessels or in other tissues. Some tissues contain specific receptors for components of the immune complexes and, hence, may become preferentially involved to produce isolated organ or system disorders. Immune complex and complement activation in a vessel wall leads to a local inflammatory reaction, increased vascular permeability and permanent vessel damage.

In the otological context, the vessels of the stria vascularis may be a possible location for immune complex deposition, while the capillaries of the endolymphatic sac are another.
The cochlear capillaries are non-fenestrated (Juhn and Rybar, 1981) and differ from the capillaries of the endolymphatic sac, which are fenestrated (Lundquist, 1976) and arise from the external carotid system. The endolymphatic sac capillaries almost certainly have a filtration function and interference, in this context by antigen-antibody complexes, may lead to inner ear fluid imbalance and secondary hydrops. Leone, Feghali and Linthicum (1984) described the temporal bone features in a patient who died of Wegener's granulomatosis. They found preferential involvement of the endolymphatic sac capillaries, but not those of the cochlea and suggested that a similar pathology in other types of immune complex-mediated autoimmune disease could explain the frequent occurrence of Ménière-like symptoms and underlying hydrops causing sudden or progressive cochlear hearing losses. The recent evidence implicating the endolymphatic sac as the site of the primary immune response of the inner ear may also help to explain these features (see below).

Immunology of syphilis

One disease in which there is mounting evidence to support an immunological basis for the cochleovestibular features in some cases is syphilis. Thus the fluctuant nature of the early auditory symptoms, which are often bilateral and not infrequently associated with underlying endolymphatic hydrops, are also typically seen in other conditions where immune processes are considered aetiologically relevant. Sudden onset or deterioration of symptoms is a feature which is also shared with these other disorders. However, the most cogent support comes from the beneficial symptomatic response, at least temporarily, to systemic steroids even in the absence of bactericidal antibiotic treatment (Hahn, Rosin and Haskins, 1962; Karmody and Schuknecht, 1966; Morrison, 1969).

The general role of circulating immune complexes in the pathology of syphilis has been suspected for many years since their local accumulation was demonstrated in cases with syphilitic nephropathy (Braunstein et al, 1970; Bhorade et al, 1971; Kaplan et al, 1972). More recently, free circulating complexes have been identified in the serum of humans (Sølling et al, 1978; Engel and Diezel, 1980; Wozniczko-Orlowska and Milgrom, 1981) and animals (Baughn, Tung and Musher, 1980) with this disease by various immunological techniques. Thus Engel and Diezel (1980) found elevated immune complexes by a precipitation method in 41% of a series of 51 patients with early syphilis. Moreover, the complexes only decreased to normal limits in about one-half of the cases following treatment. By specific tests using dissolved complexes they were able to show that the complexed antibodies are specific antitreponemal antibodies. This result indicates the persistence of viable Treponema pallidum organisms after treatment, and corroborates the reports of earlier workers who had demonstrated organisms in various sites, such as lymph nodes, aqueous humour and cerebrospinal fluid, under similar circumstances by conventional microbiological techniques (Collart, Borel and Durel, 1964; Smith and Israel, 1967; Goldman and Girard, 1967; Rice, Jones and Wilkinson, 1968; Dunlop, King and Wilkinson, 1969; Mack et al, 1969; Dunlop, 1972). A number of different immunological aberrations have been described following treponemal infection and were reviewed by Sell and Norris (1983). Although the significance of these is not fully understood, it appears that an important phenomenon is the specific activation of suppressor mechanisms. These interfere with the mounting of an adequate cell-mediated immune response and facilitate the survival of the organisms (Leven, Wright and Turk, 1971).
Brookes (1985b) suggested that continuous antigenic stimulation resulting from a persisting low-grade syphilitic infection, either locally in the temporal bone or elsewhere, may lead to continuous and excessive immune complex production with secondary pathological changes including inner ear involvement. Thus two out of 26 patients with 'unexplained' progressive sensorineural hearing loss associated with elevated circulating immune complexes had syphilis. In fact one of these had the highest levels of complexes recorded in the series.

It has been generally accepted for some time that the Herxheimer reaction in response to drug therapy of syphilis is caused by massive destruction of treponemes followed by release of antigen and its reaction with antibodies (Catterall, 1977). Although direct syphilitic infection of the labyrinth undoubtedly occurs, it may well be that a more common pathogenesis for the otological features involves a phenomenon which is somewhat analogous to a chronic Herxheimer-type response. In theory, one might expect that inner ear involvement would thus be confined predominantly to the group of patients with persisting abundant immune complexes. Prospective clinical studies are clearly required to investigate this possible association.

It must be stated, however, that the precise role of immune complexes in the pathogenesis of sensorineural hearing loss remains to be defined. The association was reported by Kanzaki and Ouchi (1981) and Stephens, Luxon and Hinchcliffe (1982). Recently, the current state of knowledge in this field in relation to otological disorders has been comprehensively discussed and illustrated by reference to specific case histories (Brookes, 1985b, 1986). Although circulating immune complexes may effect a final common pathophysiological pathway in various types of cochleovestibular disorder, the possibility that they are merely secondary by-products resulting from local tissue damage in the inner ear, although less likely, cannot be definitely discounted.

**Type IV**

Cell-mediated delayed hypersensitivity reactions (type IV) occur as a result of preliminary sensitization of T lymphocytes in the recirculating pool of immunologically competent cells. These subsequently become arrested and interact at the site of local concentration of antigen liberating chemotactic factors leading to the infiltration of macrophages which cause tissue damage. Some tissue antigens are functionally sequestrated from the blood and reticuloendothelial system and do not produce an antibody response. However, when the tissues are damaged, a cell-mediated response may be induced following antigen release which can result in a secondary immune response in similar tissues, as in sympathetic ophthalmia. In this condition an immune-mediated chronic inflammatory disorder follows trauma or surgery to the contralateral eye. Recently Harris, Low and House (1985) have postulated the likelihood of an analogous otological disease which they termed sympathetic cochleolabyrinthitis. As in sympathetic ophthalmia (Glynn and Holborrow, 1964), humoral antibodies causing immediate type II cytotoxic reactions can probably also occur. In other situations, an inner ear infective condition may prime a cell-mediated otological immune response. Perhaps this is the pathogenesis of 'delayed endolymphatic hydrops', a clinical entity described by Schuknecht (1978).
Autoimmune inner ear disease

Although their role is not fully defined, these immunological mechanisms, either independently or possibly synchronously, may all contribute to the development of autoimmune inner ear disease.

Lehnhardt first postulated the concept of inner ear autoimmunity in 1958, on the basis of clinical observations in cases of recurrent bilateral sudden hearing loss. Various animal studies subsequently documented the model of immunopathological effects on the inner ear (Beickert, 1961; Terrayama and Sasaki, 1968; Quick, 1975; Arnold, Weidauer and Seelig, 1976). More recently Yoo et al (1983a, b) reported the induction of autoimmune sensorineural hearing loss in rats, and later described the development of endolymphatic hydrops in the guinea-pig by stimulating autoimmunity to inner ear collagen.

The possible role of the various parts of the inner ear in such processes is now becoming clearer. Rask-Anderson and Stahle (1980) suggested that the inner ear possessed its own immunodefence system on the basis of experimental work in animals. They described the presence of a rich network of lymphatic capillaries and venules surrounding the endolymphatic sac and duct in guinea-pigs, and the interaction between macrophages and lymphocytes within the sac lumen. From these observations they concluded that the inner ear has the cellular components necessary for generating an immune response, and that the main site of antigen processing may be the endolymphatic sac. Harris (1983, 1984) was able to demonstrate the formation of specific antibody in the perilymph of guinea-pigs following inoculation, and suggested that a blood-labyrinth barrier analogous to the blood-brain barrier existed with respect to immunoglobulin equilibrium. This hypothesis of an inner ear immunodefence system primarily located in the endolymphatic sac was subsequently supported by the studies of Arnold, Altermatt and Gebbers (1984), who observed free and tissue-bound IgA and IgG immunoglobulins restricted to the endolymphatic sac region in human ears. Tomiyama and Harris (1986) have added complementary confirmation by demonstrating a reduced perilymph antibody response to antigen challenge following endolymphatic duct destruction.

McCabe was the first to bring autoimmune inner ear disease to the attention of otologists in 1979. This disorder is now becoming generally accepted as an uncommon, quite well defined, but poorly understood entity. The term may well embrace several different clinical syndromes, which could explain why both cell and humoral mediated pathways appear to be involved in the pathogenesis (Veldman et al, 1984). It may occur as a primary autoimmune disorder or may appear as an occasional local manifestation of a major systemic disorder due to an underlying immune system defect (Tables 15.3 and 15.4). This distinction is certainly not rigid, since systemic features may take several years to develop after the initial otological symptoms.

Otological features

McCabe described 18 patients seen over a 10-year period who presented with a similar clinical course and showed a uniform treatment response. The main features consisted of progressive sensorineural deafness, often bilateral, reduced vestibular responses, symptoms of pressure and tinnitus and very occasionally disruption of soft tissue of the middle and
external ear with facial paralysis. It was a disorder of young people in their 30s and 40s and the deafness progressed over weeks to months. Just under 20% went on to develop autoimmune diseases in other organ systems (McCabe, 1981). The lymphocyte inhibition test, in which the patients’ own lymphocytes are challenged against inner ear antigen, was positive in about 25%. Treatment with steroids and cyclophosphamide either produced sustained hearing improvement or stabilization. The validity of the clinical concept of autoimmune deafness has been supported by some other workers (Shea, 1982; Hughes et al, 1983a, b), although soft tissue destruction and facial paralysis has only rarely been encountered in these reports.

Table 15.3. Otological 'immune' disorders

(1) External ear
   (a) relapsing polychondritis
   (b) necrotizing external otitis
(2) Tympanic membrane and middle ear
   (a) homograft tympanoplasty
   (b) tympanosclerosis
   (c) otosclerosis
   (d) chronic otitis media with effusion
   (e) chronic suppurative otitis media with cholesteatoma
(3) 'Autoimmune' inner ear disease
   (a) localized
   (b) systemic

(After Veldman et al, 1984.)

Table 15.4. Systemic 'immune' diseases which may develop otological involvement

(1) Systemic lupus erythematosus
(2) Vasculitis
   (a) hypersensitivity vasculitis
   (b) polyarteritis nodosa
   (c) Wegener's granulomatosis
   (d) temporal arteritis
   (e) Cogan's syndrome
   (f) Behçet's syndrome
(3) Relapsing polychondritis
(4) Polymyositis and dermatomyositis
(5) Immunodeficiency diseases
   (a) T-cell deficiency
   (b) B-cell deficiency
   (c) disorders of phagocytosis
   (d) complement system disorders

Unfortunately, there are no diagnostic laboratory criteria and often only a beneficial response to treatment has allowed a 'therapeutic' diagnosis to be made. Cell-mediated immunity may be assessed by the lymphocyte migration inhibition test, in which the patient's
blood leucocytes are challenged with an antigenic extract of inner ear membrane (McCabe, 1979), or by a lymphocyte transformation test (Hughes et al, 1983a). However, a negative result does not necessarily exclude the diagnosis. The levels of serum immunoglobulins are of little relevance, but assay of circulating immune complexes and complement may indicate enhanced immune activity perhaps due to an immune complex disease if the levels are persistently raised. In addition, a raised erythrocyte sedimentation rate may reflect systemic disease activity.

**Treatment**

Many, but not all, patients respond to systemic steroids. Recommended regimens suggest prednisolone 20 mg four times daily for 10 days before reducing to a maintenance dosage of 5-10 mg on alternate days for 3-6 months in the face of continuing clinical improvement and lack of toxicity. In the authors' experience much lower dosages can often lead to improvement and reduce the unwanted side-effects, such as increased weight gain and dyspepsia. The figure illustrates the beneficial response to low dose dexamethasone in a 60-year-old man with a 10-year history of bilateral hearing impairment associated with raised circulating immune complexes. The figure shows the efficacy of low-dose prednisolone in a young girl with a 3-year history of immune-complex associated sensorineural hearing loss, who was able to discard her hearing aids completely after treatment.

Failure to respond to steroids may be an indication for immunosuppressant treatment using azathioprine or cyclophosphamide, but each case must be considered on its merit. Certain patients may also show improvement with plasma exchange treatment. This is invariably of a relatively temporary nature, lasting at most 3 months but which may 'buy time' in the management of problem cases (Hamblin, Mufti and Bracewell, 1982; Brookes and Newland, 1986).

**Connective tissue diseases**

Certain of the systemic connective tissue disorders which may produce inner ear involvement are now considered more fully. These may affect many organs and systems and largely, but by no means exclusively, show pathological changes in collagen, namely mucoid degeneration, fibrinoid necrosis and hyalinization. There is a significant female predominance and many of the disorders often commence in young adults in their 20s and 30s. There is now considerable evidence to support the view that many, if not all, are immunologically-mediated disorders, largely on the basis of demonstrable antibodies. However, definitive proof of an autoimmune aetiology is still lacking in most. It should be appreciated that this is a spectrum of disorders and some patients may show features of more than one of the various diseases.

Conditions characterized by immunologically-induced inflammation and necrosis of blood vessels, constitute the hypersensitivity vasculitides; the varies features are dependent on the particular organs and blood vessel sites involved. The specific predilections of involvement enable the group to be divided into several distinct types, the principal ones being systemic lupus erythematosus, polyarteritis nodosa, Wegener's granulomatosis, temporal arteritis, Cogan's syndrome and Behçet's disease. The pathogenesis is multifactorial, although in many instances the lesions are believed to be due to reaction to the deposition of immune complexes in vessel walls (Table 15.5).
Systemic lupus erythematosus

Systemic lupus erythematosus is the archetypal multisystem connective tissue disorder in which an autoimmune aetiology is most certain. The final common pathological process in many organs is immune complex deposition. Typically, lupus erythematosus cells (polymorphs with large engulfed basophilic material) are present and the serum antinuclear factor is positive. The erythrocyte sedimentation rate is very high and anaemia if frequently present. Although well over half the patients have central nervous system involvement, producing cranial neuropathies, otological involvement has only been reported rarely (Sheehy, 1981; Hamblin, Mufti and Bracewell, 1982; Caldarelli, Rejowski and Corey, 1986; Bowman et al, 1986).

Otological features

Sudden sensorineural hearing loss is a common feature in these reports. In the case described by Hamblin, Mufti and Bracewell (1982), a moderately severe cochlear hearing loss had commenced abruptly in a 47-year-old female about 6 weeks after the onset of her systemic symptoms. Treatment with prednisolone 40 mg daily for 2 weeks produced general improvement but the deafness remained. Subsequently plasma exchange treatment effected immediate and complete restoration of hearing, enabling reduction of steroids to a maintenance level of 5 mg daily. A single plasma exchange was repeated at approximately 6-monthly intervals to reverse the recurrent hearing loss which ensued. The dramatic response to plasma exchange infers a vascular mechanism and it was suggested that circulating immune complexes could cause sludging in the microcirculation of the stria vascularis.

Caldarelli, Rejowski and Corey (1986) reported the onset of bilateral profound sensorineural loss associated with mild unsteadiness over a period of 3 weeks. Systemic lupus erythematosus was diagnosed after a full metabolic profile investigation, and despite aggressive treatment with prednisolone initially at 100 mg daily in conjunction with the immunosuppressant drug cyclophosphamide 100 mg 6 hourly, a profound deafness remained. They postulated an underlying mechanism of microinfarction of capillaries or arterioles in the temporal bone, a pathogenesis characteristic of systemic lupus erythematosus in the central nervous system.

More recently, Bowman et al (1986) reported their experience of nine patients with systemic lupus erythematosus and associated hearing loss. It is of interest that the diagnosis was made prior to otological symptoms in four patients and after the onset of the hearing loss in the other five. The same group then carried out a prospective study of 30 further patients who had been hospitalized because of an exacerbation of their systemic lupus erythematosus. They found an 8% incidence of substantial previously undetected hearing loss without attributable cause and strongly suspected a causal association. The hearing loss, however, could not be correlated to age, sex, disease activity, organ system involvement, laboratory test abnormalities or duration of symptoms.

Polyarteritis nodosa

Polyarteritis nodosa is a systemic necrotizing vasculitis of small and medium-sized arteries which demonstrates a 3:1 male:female predominance. There is frequently involvement
of the renal, coronary, hepatic and visceral circulations, while an elevated erythrocyte sedimentation rate, anaemia and leucocytosis are invariably present.

**Otological features**

Deafness is unusual and of the sensorineural type (Druss and Maybaum, 1934; McNeill, Berke and Reingold, 1952; Rose and Spencer, 1957; Welsh and Welsh, 1963; Peitersen and Carlsen, 1966; Wing and Bulteau, 1967; Gussen, 1977; Lake-Bakaar and Gibbs, 1981). In rare instances, it has been the presenting symptom. As with other disorders associated with vasculitis, the onset is often sudden and typically bilateral and symmetrical. Investigations always display cochlear features and fluctuating symptoms may be seen. Exceptionally, middle ear granulation tissue may be present causing a conductive component, although this feature is more typical of Wegener's granulomatosis. This tissue response occurs with involvement of arteries in the middle ear mucosa, a pathological feature. The other histopathological findings are described in Chapter 17. Significant hearing improvement following the administration of systemic steroids (Peiterson and Carlsen, 1966) and steroids combined with the immunosuppressive drug chlorambucil (Wing and Bulteau, 1967) has been reported.

**Wegener's granulomatosis**

Wegener's granulomatosis is a discrete syndrome of necrotizing granulomatosis, vasculitis of the small arteries and veins of the upper and lower respiratory tract and kidney with less frequent involvement of other organs. There may be difficulties in differentiating this disorder from polyarteritis nodosa before the full complex develops. Patients will usually present to the otolaryngologist with persistent epistaxis, and systemic features include pyrexia, weight loss, anaemia, leucocytosis and an elevated erythrocyte sedimentation rate. The average duration of untreated disease is about 6-9 months, and death is usually a result of renal failure.

**Otological features**

Ear involvement has been reported in 15% and 36% of cases in two large series (Blatt et al, 1959; Kornblut et al, 1980) and may be the presenting feature. The higher incidence is probably a more realistic one, because early confusion of the disorder with lethal midline granuloma undoubtedly resulted in the inclusion of cases which were not Wegener's granulomatosis in the former series. The hearing loss seen in most patients is usually conductive. Seromucinous otitis media is an early feature and may lead to frank otorrhoea (Karmody, 1978; Kornblut, Wolff and Fauci, 1982; McDonald and de Remee, 1983). On occasions the tympanic cavity becomes filled with granulomatous tissue in which giant cells may be found, and may be associated with ossicular damage (Blatt and Lawrence, 1961; Densert, Raising and Toremalm, 1969; Friedmann and Bauer, 1973). Clinically, these patients still present as chronic middle ear effusions but, at myringotomy, there is usually excessive bleeding and a middle ear space cannot be identified through the granulation tissue. One of the authors (GBB) has recently managed such a case with a bilateral mixed hearing loss. Systemic steroids produced a significant hearing improvement. However, concomitant sensorineural hearing loss is not common (Blatt and Lawrence, 1961; Cody, 1971). In the case
described by Blatt and Lawrence, direct spread of granulomatous tissue through the round window resulted in destruction of the membranous labyrinth.

Although Wegener's granulomatosis has a sinister reputation, there is growing optimism for survival using combination regimens of steroids and cytotoxic immunosuppressant drugs (see also Chapter 10).

**Temporal arteritis (giant cell arteritis)**

Pyrexia, bitemporal headaches, and tender palpable thickening of the temporal arteries are the main features of this condition which occurs in the older age groups. The underlying vasculitis is primarily confined to the extracranial arteries which may undergo aneurysm formation, stenosis and even occlusion. Blindness occurs in about 30% of untreated cases due to involvement of the ophthalmic artery. Characteristically the erythrocyte sedimentation rate is extremely high and serum globulins are increased.

**Otological features**

Rapidly progressive hearing loss with vertigo has been described, presumably due to involvement of the internal auditory artery (Cody, 1971; Healy and Wilske, 1978). In the case reported by Cody, the cochleovestibular signs were partly reversible with systemic steroids.

**Cogan's syndrome**

Cogan's syndrome is a very rare condition in which a non-syphilitic interstitial keratitis is associated with fluctuant but aggressive cochleovestibular damage (Cogan, 1945). It usually affects young adults and the ocular and otological symptoms commence suddenly and often almost simultaneously.

**Otological features**

The hearing loss is sensory in type and invariably bilateral. It progresses rapidly, although fluctuation may occur and is associated with episodic vertigo, tinnitus and aural pressure, constituting a Ménière's syndrome. Ultimately the deafness becomes profound and may be total. Vestibular assessment reveals significantly reduced or absent responses on caloric stimulation. In contrast, the ophthalmic features consisting of irritation, lacrimation, photophobia and blurred vision typically progress more slowly. Patchy corneal infiltration is associated with neovascularization in the advanced stages.

There is now considerable evidence to support an autoimmune aetiology (McCabe, 1979; Hughes et al, 1983b; Arnold and Gebbers, 1984; Brookes, 1985b). Hughes et al (1983b) described the result of comprehensive immunological testing of two cases and found evidence of cell-mediated autoimmunity. In the two cases reported by Brookes (1985b) very high levels of circulating immune complexes were found. These levels were observed to fluctuate in accordance with temporary systemic improvement induced by active treatment. Thus there could well be a role for immune complex assay in conjunction with erythrocyte sedimentation rate estimation as a useful clinical assessment of disease activity. Finally, Arnold and Gebbers (1984), using indirect immunofluorescent techniques, have recently demonstrated IgG and IgA
antibodies against human cornea and IgG antibodies against human inner ear tissue in the serum of a patient with Cogan's syndrome. The regions of the inner ear where these reactions took place were the stria vascularis, Reissner's membrane, spiral ligament and dark cell areas. This study complements the known main histopathological features in the temporal bone which include endolymphatic hydrops, degeneration of the organ of Corti and severe neuronal loss with infiltration with lymphocytes and plasmacytes in the region of the spiral ligament (Fisher and Hellstrom, 1961; Wolff and Bernard, 1965). Some cases of Cogan's syndrome are associated with systemic involvement consistent with polyarteritis nodosa and it has been suggested that the disorder may be a localized manifestation of the latter type of vasculitis.

Systemic steroids do not usually prevent the relentless progression towards severe cochleovestibular dysfunction. On the basis of the authors' recent experience with two cases, early administration of immunosuppressive drugs is advocated. Indeed, the prognosis is so poor that there could be a place for intermittent plasma exchange therapy early in the natural history (Brookes, 1986).

**Behçet's disease**

Behçet's disease is a very uncommon chronic relapsing inflammatory disorder. The original classic symptom triad of uveitis and orogenital ulceration is now recognized as part of a multisystem vasculitic disorder which is very probably immunologically mediated. A comprehensive review of this condition has recently been published (Lehner and Barnes, 1986) and includes informative reports of contemporary research progress.

**Otological features**

Little attention has been paid to the otological aspects. Brama and Fainaru (1980) investigated 16 consecutive patients and found that 62% had features of inner ear involvement, which typically commenced about a decade after the initial manifestations of the disease. Hearing loss is almost always bilateral and sensory in type, although only slowly progressive. It is frequently associated with vestibular symptoms.

**Relapsing polychondritis**

This disease entity was first described by Jaksch-Wartenhorst in 1923 and is characterized by an inflammatory reaction occurring in the cartilage of several different organs. Other early features include tender swelling of nasal septum and costal cartilages, perhaps associated with an underlying cough and dyspnoea from involvement of the larynx and trachea.

**Otological features**

The auricles are first affected in about 90% of cases (Ödkvist, 1970) resulting in pain, swelling and erythema. They are very tender on palpation and very frequently associated with upper cervical lymphadenopathy.

Chondritis of the cartilage of the eustachian tubes may lead to serous otitis media, while involvement of the external auditory meatus may also contribute to a conductive
Sensorineural hearing impairment can occur independently or in conjunction with the conductive loss (Rabuzzi, 1970; Cody and Sones, 1971; Damiani and Levine, 1979). Eighty per cent of the patients studied by Cody and Sones had a sensory hearing loss which was usually bilateral and either of sudden onset or progressed over a period of a few weeks. Many of the cases also had vestibular symptoms with abnormalities on caloric testing.

The condition has been considered an autoimmune disorder for some years mainly because of the undoubted efficacy of corticosteroids in reducing the inflammatory response. Cody and Sones reported some recovery of hearing in patients with early sensorineural involvement, although relapses tended to occur when this drug was discontinued or when the dosage was markedly reduced. More recently, direct immunofluorescence examination of auricular cartilage, obtained from patients with the disease, has demonstrated deposits of immunoglobulins and the C3 component of complement at the chondrofibrous junction (Valenzuela, 1980).