Chapter 17: Sudden and fluctuant sensorineural hearing loss

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Since this chapter first appeared in the last edition, there have been many contributions on the subject of sudden hearing loss but almost no new forms of treatment. The cause always remains the main challenge and must, therefore, be sought. Adopting an apathetic or nihilistic approach, because many cases improve spontaneously, will not lead to further understanding nor to the finding of new ways of treatment.

Many of the causes are in themselves extremely rare, not only in otological practice, but still more so to the general family practitioner. Many too, are associated with other symptoms which will initially, and quite rightly, command much greater attention even when the patient may have been admitted to hospital. These will often come within the specific causes listed in *Table 17.1*. It should be appreciated at the outset that much of what has been written on this subject contains two ingredients - the case report(s) followed by the theory of causation. Byl (1984) has reported a most helpful prospective study over 8 years of 2225 patients who presented with sudden deafness.

Table 17.1. Some causes of sudden or fluctuating sensorineural hearing loss

Cochlear

(1) Inflammatory - eg, viral, bacterial, spirochaetal
(2) Traumatic
(3) Vascular
(4) Haematological - eg, anaemia, embolism, coagulation disorders
(5) Connective tissue disorders - eg, polyarteritis nodosa, Cogan's syndrome
(6) Endolymphatic hydrops, including Ménière's disease
(7) Metabolic disorders
(8) Ototoxicity
(9) Skeletal system - otic capsule

Retrocochlear and central nervous system

(1) Meningitis - all forms
(2) Multiple sclerosis
(3) Sarcoidosis (see Chapter 15)
(4) Friedreich's ataxia
(5) Amyotrophic lateral sclerosis
(6) Vogt-Koyanagi-Harada syndrome
(7) Xeroderma pigmentosum
(8) Tumours - eg, acoustic neuroma, carcinomatous neuropathy
(9) Central deafness

Idiopathic

For the patient to obtain diagnosis and treatment, he has to present to the doctor either in his local surgery or office, and the family practitioner must then decide to refer him to the specialist immediately if much of the treatment advocated is to be beneficial. Sudden deafness is an emergency but *all* concerned have to realize this. Balanced against the serious cases needing immediate help, come the vast majority never seen by a doctor, yet alone a zealous otologist, and these patients may think that the hearing loss will recover as it did previously when they last 'had a cold'. Fortunately, in many cases of sudden deafness the presentation does show a difference which alerts both doctor and patient. The condition provides a continuing diagnostic and intellectual challenge embracing the whole of sensorineural hearing loss.

It is important to recognize that the classification given in *Table 17.1.* cannot be rigidly applied. Often two or more conditions may coexist in one patient, while some of the diseases listed may damage hearing at more than one anatomical level. The review of *specific causes* which follows must therefore seem somewhat diffuse, and it must include some material which is also mentioned in Chapters 15, 16, 19 and 20.

Specific causes

Many of the cases reported seem to be isolated incidences. What can we learn from these widely varying aetiologies? In many the incidence is statistically no greater than chance, but in some the clinical and audiometric pattern, together with temporal bone findings, are of great importance. It should also be remembered that in several of the causes, hearing loss is but one manifestation of a systemic disease from which the patient may also have a generalized toxaemia, metabolic or other major disturbance. In some of these, the deafness occurs when the disease is at its height and is noticed only later when the patient's health improves sufficiently for him to be aware of his misfortune.

Cochlear cause

Inflammatory

Bacterial

Acute otitis media

While the vast majority of acute otitis media never develop sudden deafness, a small proportion do and this may only become apparent in later life when it is noted that the child is turning the only hearing ear towards the sound source or the patient becomes aware of the fact that he cannot use the telephone on that side.

Typhoid fever

Escajadillo, Alatorre and Zarate (1982) have reported six cases of pathologically confirmed cochleovestibular lesions due to typhoid fever. The lesions occurred between the second and third weeks of the disease, and more often in females. In some of the patients the lesions were reversible. In all but one case the hearing loss was bilateral and slight to

moderate in degree and when associated with reduced labyrinthine function on caloric testing this was unilateral and occurred more often on the left side.

Syphilis

Either in the congenital or the acquired form, this all-invasive disease can cause sudden deafness. Karmody and Schuknecht (1966) reported congenital syphilis as a cause resulting in a profound and usually bilateral loss; especially in younger patients. They also emphasized that the deafness is usually very sudden and may be partially asymmetric, possibly with fluctuation.

In the milder case, the hearing loss may be more marked in the low and high frequencies rather than the more conventional flat pattern. It is frequently accompanied by poor speech discrimination. About 5% of patients with late syphilis of the temporal bone present with sudden deafness, while sudden deteriorations in one or both ears occur at later stages of the disease in a further 15%. Sudden bilateral loss in the patients with acquired disease is unusual (Morrison, 1975).

The otological symptoms of late congenital syphilis may be almost indistinguishable from those of Ménière's disease.

Mycoplasma pneumoniae

While *Mycoplasma pneumoniae* is a common aetiological factor in a variety of respiratory diseases, involvement of the nervous system has only been observed in perhaps 5% of cases. Meningoencephalitis, cerebellitis, myelitis, and cranial nerve palsies have all been described. Reports of this organism as a cause for sudden deafness are few indeed. Rowson, Hinchcliffe, and Gamble (1975) mentioned as a cause in their epidemiological study of patients with acute hearing loss. Jaffe (1975) isolated *M. pneumoniae* in seven patients. More recently Shannon et al (1982) reported a single case in a girl aged 11 years 6 months with left-sided deafness, tinnitus and vertigo, whose investigations indicated a profound hearing loss with reduced labyrinthine activity following caloric stimulation. Brainstem evoked responses showed clear complexes but the transmission time was prolonged and the cochlear microphonic appeared to be abnormal. Three days after commencing treatment with doxycycline, the hearing on the affected side had virtually returned to normal and the discrimination had improved from 40 to 100%.

Nishioka et al (1984) have reported an 11-year-old girl who suffered from infection with *Mycoplasma pneumoniae* with primary atypical pneumonia, complicated first by meningitis followed by a mild bilateral acute otitis media with subsequent severe mixed hearing loss; the final outcome after the middle ear infection had settled, was that she was left with a bilateral high degree sensorineural hearing loss, more marked in the low and middle frequencies. Throughout the course of her serious illness she was treated with a variety of agents including minocycline and steroids. There was no impairment of any of the other cranial nerves and likewise no evidence of labyrinthine involvement.

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Bullous myringitis

The possible pathology and clinical aspects of this condition have been discussed previously (see Chapters 3 and 7). Rarely, it may be associated with a sensorineural hearing loss, often of sudden onset. Merifield (1962) reported two cases. The first was a 22-year-old girl who developed a severe bilateral hearing loss, predominantly sensorineural, associated with tinnitus. It is interesting that she received not only a broad spectrum antibiotic for a 10-day period but also prednisone which was later decreased and discontinued. One month later, she had attained near normal hearing levels but after a further week, that is 5 weeks from the original presentation, she had again developed sudden hearing loss on one side. After a further 2 months, the hearing had again reverted to normal. The second case was a 31-year-old female with a unilateral, predominantly sensorineural loss, which returned to its probable earlier near normal level in just over 2 weeks. Wetmore and Abramson (1979) reported three cases, all unilateral (two male) with moderate to severe mixed hearing losses, although predominantly sensorineural, all of which were untreated and whose subsequent audiograms showed normal hearing.

More recently, a prospective study has been reported by Hoffman and Shepsman (1983) on 15 patients with 21 ears diagnosed as bullous myringitis, seen over a 2-year period. Seven ears demonstrated a sensorineural hearing loss and seven a mixed loss. Recovery of hearing was complete in eight of the 14 years. Five of the 14 ears experienced persistent high frequency loss but this study demonstrated a much higher incidence of hearing problems in this condition than had previously been thought to occur.

An excellent review of the aetiology of this condition and the possible role of mycoplasmas was reported by Roberts (1980). He could find evidence of only one positive culture of *M. pneumoniae* and he stressed the considerable difficulties of obtaining uncontaminated specimens in this condition.

Finally, it should not be forgotten that two types of non-suppurative complication may occur in this condition: single or multiple cranial nerve lesions and/or meningoencephalitis. The former may be transient or permanent and most commonly the facial and auditory nerves are affected; typically a lower motor neuron paralysis results from facial nerve involvement and either division of the auditory nerve may be affected individually or together. Two types of meningoencephalitis may occur. The first appears close to the onset of the bullous lesion and the second post-infectious' type, 3 weeks later.

Chlamydia

The genus Chlamydiaceae comprises two species - *C. trachomatis* and *C. psittaci*. The first is well known and causes a variety of ocular and genital infections in man, the best known being trachoma. The second is less often encountered in man but causes several infections in animals, for example psitaccosis, ornithosis. In recent years, *C. psittaci* has been shown to cause endocarditis in man and is well recognized although infrequently as a cause of ocular infections.

Darougar et al (1978) have reported a case with long-standing interstitial keratitis and uveitis associated with a marked otological syndrome and fatal cardiovascular lesions. The

girl had a sudden bilateral hearing loss, tinnitus and imbalance. The deafness was initially moderate, sensorineural and symmetrical, with poor speech discrimination. Treatment with prednisolone failed to improve the hearing loss which fluctuated, but always relapsed leading ultimately to almost total loss. Later *C. psittaci* was isolated from the eye and the patient received two course of doxycycline, which helped the kerato-uveitis, but otherwise after treatment, there was a definite increase in the intensity of the clinical signs and the number of recurrences.

Hearing loss due to middle ear infections, in association with eye infections with Chlamydia have been reported previously (in adults) (Gow, Ostler and Schachter, 1974). More recently the use of direct fluorescent antibody tests for *C. trachomatis,* previously used in examining cervical and urethral specimens, enabled Banks, Vanden Driesen and Stark (1985) to test the fluid from the middle ear in children with otitis media with effusion (glue ear) in central Australia, which is an area endemic for trachoma, and showed an apparent 67% positive result. However, these results have been challenged and appear atypical (Retting, 1985).

Viral

Mumps

Patients with mumps infection may have a benign, complicated or even lethal course. The disease is usually more severe in adults. Hearing loss is uncommon, occurring in less than 0.1% of cases, but adolescents and adults are more likely to be affected. Although encephalitis occurs in less than 0.1% of patients, up to 23% are said to develop clinical meningitis. Most reported cases (80%) of sensorineural hearing loss are unilateral (Davis and Johnsson, 1983).

Murakami and Muzushima (1985) reported 53 cases seen over a 10-year period. The hearing loss in their patients was exclusively unilateral, profound or total and permanent, and more than 45% of the patients developed disequilibrium of vestibular origin. As might be expected, two-thirds of the patients were under 10 years of age, with an equal sex ratio. They considered that the haematogenous infection 'theory' was the most valid, causing inflammatory changes in the stria vascularis of the cochlea, resulting in severe impairment of the endolymphatic system. They proposed 'viral endolymphatic labyrinthitis' as the possible pathogenesis of the deafness.

By an unusual combination of events, Westmore, Pickard and Stern (1979) were able to obtain a specimen of perilymph from a patient with mumps who had developed sudden deafness. This 26-year-old woman with bilateral otosclerosis had previously undergone a right stapedectomy with an excellent result. One year later she developed sudden symptoms of mumps and within 2 days over a period of 4 hours developed total deafness on the operated side. She was seen 3 days later, but as it was thought that a perilymph leak might have developed and in the hope that this could be restored by surgery, the ear was re-explored. At operation there was no evidence of fistula formation and after the Teflon piston was removed, a sample of perilymph was aspirated and sent for culture, subsequently growing mumps virus.

Measles (rubeola)

It has long been known that measles can cause inner-ear deafness and estimates vary widely but in post-war years it seems to be between 5 and 10% of cases. Measles is an important cause of acquired deafness. Before the introduction of rubeola vaccine, 3-10% of acquired deafness in children was secondary to measles. The incidence of deafness following rubeola has been reduced dramatically since the introduction of the vaccine and is now less than one per 1000 cases.

Children with labyrinthine involvement usually develop abrupt bilateral hearing loss along with the measles rash. However, some children develop only unilateral deafness retaining normal hearing in the opposite ear. The characteristic audiogram is an asymmetric, bilateral hearing loss affecting hearing at higher more than lower frequencies which is usually permanent. Tinnitus and vertigo may accompany the hearing loss and up to 72% of patients have absent or diminished caloric responses in one or both ears (Davis and Johnsson, 1983).

Measles has also been reported as producing congenital deafness in a child whose mother had the disease in pregnancy; immunization against measles in pregnancy has been implicated in two congenital cases.

Chickenpox (varicella)

Nervous system complications of chickenpox are relatively infrequent and include cerebellar ataxia, aseptic meningitis, acute transverse myelitis, chicken-pox-Reye syndrome and less commonly, aphasia, hemiplegia and seventh cranial nerve palsy.

Bhandari and Steinman (1983) reported the case of a 14-month-old infant who developed bilateral sudden deafness. Brainstem auditory responses could not be evoked and there was no subsequent improvement.

Varicella zoster virus

Herpes zoster oticus is well known by all otologists, and sudden deafness with facial palsy forms part of the Ramsay Hunt syndrome. From a clinical standpoint, many patients afflicted by this virus present early because of their symptoms. In zoster deafness the site is sometimes neural, sometimes sensory but most often mixed. This is confirmed by a recent study by Abramovich and Prasher (1986) who investigated 13 patients with Ramsay Hunt syndrome. Electrocochleography in five showed a normal action potential (AP) and the summating potential (SP) was not enhanced. (SP/AP ratio 21%). Brainstem auditory evoked potentials on the affected side were clearly abnormal in seven. The latencies of waves III and V were prolonged, including one who had a normal pure-tone audiogram and in one case deranged. Four of the seven patients were re-tested 6 months after clinical recovery of their vesicular eruption and found to have normal brainstem evoked potentials. A slight tendency for greater abnormalities was noted in patients with complete facial paralysis.

Steroid therapy has been tried in this condition with excellent results and the risks of disseminating the virus seem to be more theoretical than real. However, it would seem that this form of medication may have been superseded by the use of acyclovir (9-2

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hydroxyethoxy-methyl-guanine); this antiviral agent is a DNA nucleoside analogue which inhibits virus DNA replication, thus halting the cell cycle. Acyclovir is relatively insoluble in water and crystalizes in the renal tubules. As a result, it is essential to ascertain that the patient has good renal function throughout therapy and the agent itself is better given intravenously (5 mg/kg three times per day). Hall and Kerr (1985) reported successful treatment of seven patients, using acyclovir therapy, producing a striking improvement in the toxaemia associated with this condition. Of the six patients who had total facial paralysis, four recovered completely, one almost completely and one showed no recovery at 3 months. Of three patients with sensorineural hearing loss, two regained their hearing and their associated vertigo resolved rapidly. The patient with residual deafness and a total facial paralysis had brainstem involvement.

Stafford and Welch (1986) have reported the successful treatment of five patients using a different regimen. The acyclovir was initially administered intravenously for a minimum of 3 days accompanied by high dose oral steroids for 5 days. Treatment with acyclovir was continued orally for a further 2-week period.

Infectious mononucleosis

The nervous system may become involved in some 1% of cases of infectious mononucleosis and such complications as lymphocytic meningitis, encephalomyelitis, polyneuritis and mononeuritis have been described (Gautier-Smith, 1965). Considerable difficulty in diagnosis may occur when several cranial nerves are affected at different intervals during the illness, as similar combinations may be found in other neurological syndromes such as the Guillain-Barré syndrome (Owen, 1952; Fiese, Cheu and Radding, 1953).

Schnell et al (1966) reviewed 1285 patients seen at the Mayo Clinic over a 14-year period and concluded that 12 fulfilled their criteria. Of these, one (the only female), showed a temporary bilateral hearing loss on the fourteenth day, 7 days after admission; the audiogram showed a 60 dB hearing loss at 2000 Hz which gradually improved and was normal one year later. In their cases with neurological complications, the process was self-limiting and of relatively short duration; the average total duration of illness was 25 days. The authors were particularly interested in the electroencephalographic findings but these showed no specific diagnostic features. However, the consistent presence of abnormalities in the EEG during the acute phase of the illness corroborates the other evidence of cerebral involvement. They emphasized that the neurological manifestations of infectious mononucleosis alone were indistinguishable from certain other viral and non-viral encephalomyelopathies and neuropathies.

Taylor and Parsons-Smith (1969) reported a patient who developed other cranial nerve signs; Petheram (1976) described a patient whose infection was characterized by a severe autoimmune haemolytic anaemia with autoantibody of anti-i specificity. Further cases have been documented by Gregg and Schaeffer (1964), Jaffe (1967) and most recently by Beg (1981). Site of lesion tests in these cases have indicated cochlear damage and in the two cases reported by Beg, brainstem evoked responses were normal as were caloric tests. Only the first and last cases mentioned have been bilateral and all but one have occurred in females! As also might be expected in this condition, the patients are young, only one being just over 30 years of age.

Traumatic

Electricity

It is generally considered that individuals unlucky enough to be struck by lightning are either killed or suffer no untoward effects. While reports are few, lightning may affect the ears. Most occur while the individuals are conversing on the telephone during a thunderstorm (Weiss, 1980) and Kristensen and Tveteras (1985) reported two patients who received injuries simultaneously while telephoning each other a few hundred metres apart. This possibility is now so well recognized that advice is given by the telephone companies themselves not to make calls during this period, particularly when the thunderstorm is overhead.

The most frequent damage is acoustic rupture of the tympanic membrane caused by the sonic shock wave emanating from the access of the lightning channel. This can occur whether the lightning strikes the person himself or the ground nearby. Burning of the skin surrounding the ear may be seen and an exit burn on the feet may also occur when the skin is wet. Although the perforation is usually unilateral, bilateral rupture has been reported (Wright and Silk, 1974). Sensorineural hearing loss may also occur and this too may be bilateral; the loss is usually transient but may last for a longer period, although it is seldom permanent. Ipsilateral peripheral facial nerve palsy, which recovered spontaneously, has been reported (Weiss, 1980). Bergstrom et al (1974) reported the temporal bone pathology of one of their four cases who dies 5 days after being struck. This showed tympanic membrane rupture, middle ear and mastoid effusion of pus and blood, total rupture of Reissner's membrane, degeneration of the stria vascularis and organ of Corti, oedema of the intracanalicular portion of the facial nerve and herniation of portion of the cerebellum into the internal auditory meatus. More recently, Poulsen and Knudstrup (1986) reported a case where lightning had caused inner ear damage and an intracranial haematoma which was subsequently successfully treated by surgery.

Radiotherapy

Radiotherapy given to head and neck tumours regularly involves its application to the ear and organ of Corti. For many years it was considered that the cochlea was resistant to radiotherapeutic injury. This was strongly challenged first by Leach (1965) and later by Moretti (1976). Further details will be found in Chapters 4 and 7.

Postoperative

Several cases of deafness following surgery have been reported. It seems most generally accepted that these are due to microembolism involving the cochlear division of the internal auditory artery (Jaffe, 1967). Brownson, Stroud and Carver (1971) carried out audiograms in a series of 50 patients before and after cardiopulmonary bypass surgery but none of the patients showed any postoperative loss. Single cases following bypass surgery were reported by Arenberg, Allen and De Boer (1972), and Wright and Saunders (1975). In neither case did the hearing recover and in both it was the left ear that was affected. More recently Plasse et al (1980) reported seven cases of sensorineural deafness from a series of 7000 patients who underwent cardiopulmonary bypass surgery. Again the hearing loss was in one ear only and developed immediately after the operation. Four of the seven patients

showed improvement in hearing after the initial loss, although in no case did the hearing return completely to normal. There was no predilection as to which ear was affected.

Millen, Toohill and Lehman (1982) reported five further cases of sudden sensorineural hearing loss following non-otological surgery. Two of these were bypass procedures both producing hearing problems in their left ear.

Other neurological complications of coronary artery bypass surgery have recently come under scrutiny in several centres and those in Newcastle reported earlier by Shaw et al (1985) have been compared with studies elsewhere (Shaw, 1986). The two major aetiological factors cited in the causation of neurological damage in heart surgery are hypoperfusion of the central nervous system, and embolization. A whole series of factors are now under scrutiny such as the study of membrane versus bubble oxygenators.

Perhaps it may be added as an interesting footnote that the effect of hypothermia upon the electrocochleogram and auditory evoked responses was investigated by Kusakari et al (1984) in 10 children undergoing open heart surgery. The latencies of N1, waves III and V were prolonged. The summating potential was increased by hypothermia and never disappeared; on rewarming the summating potential appeared first, followed by N1, and finally waves III and V. Conversely, raising the body temperature by 1°C in nine subjects significantly shortened the latency of wave V, while there were similar though less consistent changes in other waves (Bridger and Graham, 1985).

Other operations of widely differing nature have on occasions been reported as being followed by sudden hearing loss; one case followed a spinal anaesthetic. The cases are mentioned usually only by title and no details are published to allow any real comparison.

Postoperative vestibular dysfunction following head and neck surgery was investigated by Johnson et al (1985); 80 patients had normal vestibulo-ocular responses preoperatively, but on their first test after operation 58% had significant vestibulo-ocular response abnormalities and even at one year after surgery, 20 (43%) continued to demonstrate vestibular abnormality.

Transient hearing loss, occasionally associated with vestibular symptoms, has been reported on a few occasions following the use of water-soluble contrast media for lumbar myelography. Two cases have been reported following the use of metrizamide (Grant et al, 1985). The low frequency sensorineural hearing loss was considered to be the result of increased stiffness of one or both of the inner ear membranes. Nelson and Lamb (1985) reported hearing impairment in one case. They subsequently investigated 10 patients, five of whom received iohexol and five iopamidol, but the audiograms remained normal and showed no change after lumbar myelography. It was noted that the course of the hearing impairment in these patients was similar to that of the cortical absorption of contrast medium after myelography and of the associated electroencephalographic changes. It may be remembered that for a period the use of meglumine diatrozoate (Hypaque) was advocated in the treatment of sudden sensorineural hearing loss as it acted in a similar way to glycerol (Emmett and Shea, 1979).

Hammar (1981) noted that the side-effects of intrathecally-injected contrast media were more frequent in patients with reflux and stasis of the contrast substance in the ventricular

system combined with a damaged ependyma. The cause of the side-effects was the penetration of the contrast agent into the brain parenchyma.

Anaesthesia

Much has been written in recent years about the effect caused by nitrous oxide on the middle ear pressure during general anaesthesia and as to whether the gas is given by inhalation or ventilation. Richards, O'Neill and Wilson (1982) emphasized that there is a large degree of variation between the studies, between children and adults and of course in the concentration of nitrous oxide in the inspired gas. However, even if the same concentrations of nitrous oxide are used, different rates of pressure increase occur in different individuals and this may be related not only to variations in perfusion of the middle ear mucosa but also the volume to area ratio of the tympanomastoid air spaces; indeed the four highest values they recorded were in those whose mastoids were radiologically sclerotic!

Patterson and Bartlett (1976) reported four cases of hearing impairment after anaesthesia, three receiving ear surgery and a fourth who underwent an orthopaedic operation but was already suspected of having a perilymph leak from a previous stapedectomy (which was subsequently confirmed at operation and closed). In all four, the hearing returned.

Davis, Moore and Lahiri (1979) reported the case of a patient who one year previously had undergone a successful left stapedectomy with complete closure of the air bone gap and who subsequently underwent a hysterectomy operation. This was followed by a 20-25 dB conductive hearing loss which persisted thereafter.

An occasional complication of nitrous oxide anaesthesia may be either a tympanic membrane perforation or haemotympanum; these are more likely to occur where an old perforation has healed with a neomembrane (Perreault et al, 1982). Owens, Gustave and Sclaroff (1978) reported two cases both of whom had previous anaesthetics for ear surgery whose tympanic membranes ruptured on the opposite side when a further intervention was required (one for abdominal pain and the second for a urethroplasty); both ruptures healed spontaneously.

Marsh et al (1985) carried out a study of auditory and vestibular function and hyperbaric oxygen on 11 normal adult men exposed to 100% oxygen at 303 kPa (3 atm) absolute. No alterations in either function were detected although there was some elevation of the pure-tone thresholds at that pressure level which appeared to reflect in large part the effects of the pressure rather than the oxygen itself; there was no worsening of hearing over the 3 hour exposure.

The use of hyperbaric oxygen therapy has been investigated in soldiers following acute acoustic trauma and reported by Pilgramm and Schumann (1985).

It should be remembered that the inhalation of pure oxygen causes cerebral vasoconstriction.

Vascular

While vascular disease or its effect are frequently proposed as the principal cause of cochlear-type sudden hearing loss, the number of occasions when they have definitely been implicated is relatively few. It is therefore perhaps worth examining some of the conditions or factors which may be related.

Hypertension

An early study between sensorineural hearing loss and arterial hypertension by Hansen (1968) was uncontrolled and unconvincing. Drettner et al (1975) looked at a series of cardiovascular risk factors including blood pressure and heart rate but could find no significant correlation between these and sensorineural hearing loss when assessing 1000, 50-year-old men. Studies of the cochlear and vestibular arteries, as well as the labyrinthine arteries, showed that they remain patent at all ages (Fisch, Dobozi and Greig, 1972). No close relationship between the changes in the inner ear and the supplying vessels has been found, nor in patients dying of hypertensive disease. Similarly there is no evidence of atherosclerosis occurring in any of the smaller vessels supplying the ear.

Earlier there was considerable interest in the work of Rosen (Rosen et al, 1962; Rosen and Olin, 1965; Rosen, Olin and Rosen, 1970), who investigated the Mabaan tribe in south-east Sudan and was impressed by their superior hearing, compared with those living in industrial areas of the USA; their blood pressure remained constant throughout life and coronary heart disease is unknown. A similar study on the inhabitants of Easter Island has recently been reported (Goycoolea et al, 1986). The median hearing thresholds of natives who had always lived on the island were similar to those of female citizens in the USA.

Recently a single patient, a young man, has been reported who developed a sudden loss of hearing in one ear and in whom investigations revealed a total deafness and failure of the vestibular system on the affected side. This was attributed to a sudden rise in blood pressure in a man with secondary hypertension of renal origin due to polycystic kidneys (Nofal, 1985).

Inflammation of the vessels as in cranial arteritis may present to the otolaryngologist as headache, facial palsy, hearing loss, dysphagia, jaw claudication, lingual Raynaud's phenomenon, and tongue infarction. Sensorineural hearing loss with vertigo has been described but no case of sudden deafness has yet been reported (Sofferman, 1980). Occlusion of the vertebral and basilar arteries has been reported in a single case associated with marked atherosclerotic changes in the vessel walls and an aneurysm of the left vertebral artery (Kitamura and Berreby, 1983). Ectasia of the basilar artery is a rare cause of sensorineural loss and this is usually unilateral and progressive, accompanied by vestibular symptoms and other neurological abnormalities. Vertebral arteriography and other invasive studies have now been replaced by computerized tomographic (CT) scanning in making the diagnosis. Plain radiology of the internal auditory meatus may be normal.

The secondary effects of vascular obstruction to the inner ear in experimental animals is well known. A study of seven patients with sudden unilateral partial vestibular loss has been described by Lindsay and Hemenway (1956). The findings in a 57-year-old man who

had sudden onset of dizziness and unilateral deafness 2 months prior to death have been reported by Gussen (1976). More recently, Sando, Ogawa and Jafek (1982) have reported the inner ear pathology including temporal bone findings following injury to the eighth cranial nerve and the labyrinthine artery. The first case, in which both the nerve and the artery were surgically severed, revealed severe pathological changes in the cochlea including complete loss of the organ of Corti and moderate pathological changes in the fairly well-preserved vestibular end-organs. In the second case, in which the nerve only was sectioned but the artery preserved, the organ of Corti and vestibular end-organs appeared to be well preserved and normal. These findings suggest that the blood supply from the labyrinthine artery plays a major role in maintaining most of the structures in the inner ear except for the endolymphatic sac and that the vestibular end-organs are more resistant than the organ of Corti, to the effects of damage to the labyrinthine artery.

Buerger's disease (thromboangiitis obliterans cerebri)

Cerebral involvement in patients with Buerger's disease is rare. It has been estimated as less than 0.5%. Kirikae et al (1962) have reported a single case. A moderate smoker, after developing intermittent claudication, noted a hearing loss on the same side. While an injection of vasodilator drugs improved the leg, there was no improvement in the hearing loss. Five years later the radial artery of the opposite side became slowly occluded over 2 months. At surgery, part of the artery was excised and the diagnosis was confirmed histologically. Seven months after the operation, the patient became suddenly deaf on the same side (that is the opposite side to the earlier loss). Both sides showed a sensorineural loss with absence of recruitment (see also Polyarteritis nodosa).

Hypercoagulation

In addition to the clinical syndromes with known haematological characteristics, a further, less well-defined group exists whose common feature can best be described as 'hypercoagulation'. The clinical diagnosis of hypercoagulation is characterized by recurring episodes of thrombophlebitis and sometimes pulmonary embolism. The work of Jaffe (1975) showed that the two-stage prothrombin technique measuring the prothrombin consumption rate was the most accurate test.

It is known that the stria vascularis has a slow blood flow with a high haematocrit value. It has therefore been suggested that stasis of blood flow and accelerated coagulation may be the twin interrelated factors responsible. However, at this stage almost no other further work in this field has been carried out, and it should be noted that while viral diseases may cause haematological conditions, for example haemolytic anaemia, there is no evidence of hypercoagulability in such patients except perhaps when their illness is at its most extreme.

Fibrinolytic activity and capacity were studied by Bomholt, Bak-Pedersen and Gormsen (1979) in a group of 18 patients with sudden sensorineural hearing loss and were found to be reduced in 12. Five of the patients had associated triglyceridaemia; similarly, five patients with decreased fibrinolytic activity later went on to develop Ménière's disease (Bomholt, 1980).

Noda et al (1985) investigated 16 patients with vertigo (no mention is made of hearing loss or audiological tests) in whom no significant difference could be found in the fibrinogen, or plasminogen content nor the fibrin-degradation product level and healthy adult controls. Similarly, no difference could be found in the alpha 2-macroglobulin content, alpha 1-antitrypsin or C1-inactivator content between the two groups. However, there was a significant difference in the antiplasmin activity and antithrombin activity and between the ADP- and collagen- induced platelet aggregations which were decreased in the patients with vertigo.

Viscosity

Ischaemia is not only determined by vascular disease but also by blood viscosity and it has been suggested that particularly in patients with sudden deafness increased blood viscosity may play a role, but this has never been proven. Recently, Browning, Gatehouse and Lowe (1986) investigated the relationship between hearing threshold and blood viscosity, plasma viscosity, and haematocrit in 49 patients with idiopathic hearing loss. They established that hearing thresholds were unrelated to haematocrit or low shear blood viscosity but hearing impairment at high frequencies was directly related to high-shear blood viscosity and inversely related to high-shear blood viscosity and inversely related to plasma viscosity. The derived measure of red cell rigidity was significantly related to hearing thresholds at all frequencies. The significant negative relationship between plasma viscosity and pure-tone hearing thresholds is perhaps contrary to expectations, but of even more interest is their finding that the greater the high shear blood viscosity, the poorer the sensorineural thresholds. High-shear blood viscosity, once corrected for the haematocrit and divided by plasma viscosity (relative viscosity), is a measure of red-cell rigidity or lack of deformability under shear. It is unknown whether this lack of red-cell deformability is a primary or secondary phenomenon. Conversely, the high-shear viscosity values were all within the normal range and in conditions such as haemolytic anaemia, in which red cells are less deformable, there is no known association with hearing impairment. This situation is not dissimilar from the finding of fluctuating hearing in some patients with secondary hyperlipoproteinaemia, whereas so far hearing loss has never been reported in association with the primary condition.

The influence of blood viscosity on cochlear action potentials and oxygenation has been investigated in the guinea-pig (Hildesheimer et al, 1982). Perfusion of the ear with high viscosity blood showed a rise in the action potential threshold in 56% of animals and in one-third there was a significant fluctuation of the action potential response.

Haematological

Haemopoietic system

Anaemia, as such, has rarely been reported as being associated with deafness, sensorineural or otherwise. Morrison and Booth (1970) reported two patients with profound anaemia (haemoglobin levels of 0.62 µmol/L) associated with iron deficiency - both had a sudden bilateral total loss and neither showed any improved following transfusion.

More recently, Morrison (1978) has reported a 58-year-old woman who awoke with sudden total bilateral deafness whose electrocochleogram confirmed that there was no action potential or cochlear microphonic on either side. She was found to have some megaloblastic

change in the bone marrow and a plentiful supply of iron; she had a moderate anaemia due to folic acid deficiency. No recovery has taken place in the hearing.

Deafness may be associated with Fanconi's anaemia - constitutional aplastic anaemia (Harada et al, 1980). Tinnitus has recently been reported as the presenting symptom in a case of pernicious anaemia, with normal hearing, which resolved with treatment (Cochran and Kosmicki, 1979).

Polycythaemia vera

In polycythaemia vera, the viscosity of the blood is increased five to eight times normal; the total red cell count becomes elevates by 20-50% and the total blood volume is increased to two to three times normal. These alterations affect the peripheral blood by causing engorgement of the capillaries, venules and arterioles with high viscosity, slowly circulating oxygen-deficient blood. When Vaquez first described polycythaemia in 1892, he noticed tinnitus and vertigo among the primary symptoms.

It had been indicated in an earlier report on two patients with a bilateral sensorineural hearing loss, that the hearing fluctuated in relation to the viscosity of the peripheral blood and that the level improved after phlebotomy. However, Kenyon, Booth and Newland (unpublished data, 1984), in a small series of patients with this condition treated by the same procedure and a separate group with Waldenstrom's macroglobulinaemia, treated by cell separation, showed that while the viscosity changed after 'treatment', there was no observable change or improvement either in the pure-tone audiogram, or in the susceptance or conductance on otoadmittance measurements (220 and 660 Hz).

Cerebral blood flow in polycythaemia is significantly reduced. In a study on 15 patients, lowering of the haematocrit by venesection increased the cerebral blood flow and reduced whole blood viscosity at all shear rates, the effect being greatest at low shear rates; plasma viscosity was also reduced but the changes were less striking (Thomas et al, 1977). Brown and Marshall (1982) investigated the effect of plasma exchange on blood viscosity and cerebral blood flow in eight normal subjects. The exchange resulted in significant reductions in plasma viscosity, whole blood viscosity, globulin and fibrinogen concentration without affected packed cell volume. Reduction in whole blood viscosity was more pronounced at low shear rates but, despite the fall in viscosity, there was no significant change in cerebral blood flow. Within the circulation, blood is subjected to continuously varying shear rates and because the viscosity of blood varies with the shear rate a single measurement of viscosity cannot be applied to blood throughout the circulation. Within the microcirculation however, shear rates are mostly very high. The apparent viscosity of the blood in very narrow tubes decreases as the diameter of the tube is reduced as an axial migration of the red cells occurs. In the study by Brown and Marshall, changes in blood viscosity without changes in arterial oxygen content did not alter the cerebral blood flow.

Sickle-cell disease

While sickle-cell disease is not generally considered as a cause of deafness, it has been shown by Todd, Serjeant and Larson (1973) that sensorineural hearing loss of apparently gradual onset can occur. This loss is only reported in the homozygous disease (abnormal

haemoglobin S-SS disease). Both ends of the audiometric range may be affected but more often the higher tones. The sickling phenomena occur and crisis develops when certain intermolecular hydrophobic bonds form with subsequent polymerization. Any decrease in the PO_2 with associated hypoxaemia can initiate the process and the concomitant stasis, hyperviscosity, or acidosis significantly increases the likelihood of sickling. The end effect is tissue hypoxia. In the inner ear it is considered that the sickling and impaired blood flow in the cochlear venous system with secondary anoxia of the hair cells and stria vascularis are the most likely causes of the sensorineural hearing loss. Todd, Serjeant and Larson (1973) found a sensorineural loss in 22% of their 83 patients. They considered two possible pathological causes - anaemia and thrombosis. The haemoglobin level in SS disease was considered unlikely to reflect the oxygen carrying capacity since the decreased oxygen affinity of haemoglobin S allows greater oxygen release/gram haemoglobin than in haemoglobin A. Furthermore, the oxygen affinity is lower in cases with lower haemoglobin levels. The pattern of hearing loss in SS disease is similar to that in certain animal studies which show a low-grade continuous venous thrombotic process. However, they were unable to find a correlation between the irreversibly sickled cells and the hearing loss in their small group.

The haemolytic process characteristic of sickle-cell disease is associated with increase of bone-marrow activity. Active bone marrow is present in the petrous temporal bone in SS disease but Serjeant, Norman and Todd (1975) failed to find evidence that this caused any narrowing of the internal auditory meatus or compression of the eighth cranial nerve. In this condition the hearing loss may be gradually progressive, fluctuant or sudden in onset; in the last, partial or almost total recovery may occur (Morgenstein and Mannace, 1969; Urban, 1973; Orchik and Dunn, 1977). There is some dispute as to whether the number and frequency of the haemolytic crises may be a factor (Berry, 1975; Friedman et al, 1980). Sensorineural hearing loss in patients with sickle cell disease may also be related to the increased susceptibility to bacterial meningitis. Neurological involvement is a common complication of sickle cell disease and vestibular dysfunction may occur. Morrison and Booth (1970) reported one case of bilateral deafness in sickle cell trait (haemoglobin S and C) which they presumed to be thrombotic.

Sickle cell thalassaemia has been described in two out of a family of four sisters, another of whom had sickle cell trait and the fourth was normal. The two sisters with sickle cell thalassaemia showed symptoms of vertigo or hearing involvement, and vertigo after strenuous exercise. One sister with unilateral hearing loss subsequently developed a sudden, almost identical loss in the other ear, but unfortunately follow-up was impossible (Marcus and Lee, 1976).

Waldenstrom's macroglobulinaemia

This condition, which tends to occur in elderly males, is characterized by retinal changes, an abnormal bleeding tendency from mucous membranes, generalized weakness and dyspnoea. Fundamental to the diagnosis is a raised sedimentation rate and marked increase of serum globulin level, in the form of a narrow, dense band in the $\beta 2$ region. The abnormal macroglobulin coats the platelets and reduces their adhesiveness; it also interferes with fibrin polymerization.

It is most often met in otolaryngological practice as a cause of epistaxis or bleeding from the gums, but a few cases of sudden deafness have been recorded, although vertigo may be the earliest symptom (Coyle et al, 1961; Afifi and Tawfeek, 1971). Immediate diagnosis is essential if the patient is to be prevented from probable permanent bilateral deafness. The optic fundus must be examined and may reveal gross retinal haemorrhages or central vein thrombosis. Ruben et al (1969) reported a case developing first in one ear and 10 months later in the other. Subsequently both ears deteriorated to an almost total loss and, while vestibular function was lost in the second ear, that on the original side remained normal. Wilkinson, Davidson and Sommaripa (1966) reported another bilateral case.

In 1963, Solomon and Fahey reported 10 patients and their treatment by plasmapheresis. Vertigo and nystagmus were reported in two patients while audiometry showed some degree of bilateral hearing loss, especially in the high frequencies, in five. Additional information is given on two; the first complained of progressive deafness and tinnitus but, after intensive plasmapheresis, her auditory acuity improved and tinnitus diminished. The second patient developed horizontal and vertical nystagmus and progressive vertigo but, after plasmapheresis, the vertigo and nystagmus gradually disappeared.

Cryoglobulinaemia

Cryoglobulins are proteins which precipitate in the cold and redissolve on warming. They may occur in small amount in systemic lupus erythematosus and other 'connective tissue' disorders and may be associated with multiple myeloma or macroglobulinaemia. Almost two-thirds are mixtures of IgG and IgM molecules, while a further one-quarter are G myeloma proteins and less than 10% are macroglobulins.

The characteristic clinical signs are purpura, arthralgia and a Raynaud-like phenomenon in the lower extremities. Patients with progressive sensorineural deafness, tinnitus and vestibular problems have been reported but neurological involvement is infrequent (Nomura et al, 1982).

Leukaemia

The first account of leukaemia of the inner ear was presented by Politzer in 1884; the patient experienced bilateral, severe deafness one year before death. The various forms of leukaemia may affect the ear but it is usually the middle ear that is involved. Otological complications occur almost invariably in those patients with the acute forms, particularly acute lymphocytic leukaemia. The changes seen in the temporal bone fall into three categories: leukaemic infiltration, haemorrhage, and infection.

Leukaemic infiltration may occur in the mucoperiosteum of the middle ear following the mucous membrane folds but this may extend on to the ossicles and the sheaths of the tendons of the intratympanic muscles. Infiltration into the bone marrow spaces of the petrous apex frequently occurs and also, to a lesser extent, within the ossicles. Infiltration into the inner ear is uncommon. Haemorrhage into the inner ear is also uncommon.

Sudden deafness and/or vertigo is reported in acute leukaemia and seems to occur most often in the acute stem-cell type. As a general rule, the otological symptoms appear to be more associated with infiltration and seem to be based on the degree.

Haemorrhagic changes in the temporal bone are more frequently seen in patients with acute lymphocytic leukaemia than the other forms. Patients with acute leukaemia suffer a bone-marrow failure with a resultant thrombocytopenia and other coagulation defects such as hypofibrinogenaemia may occur. Disseminated intravascular coagulation and secondary fibrinolysis may also occur.

Connective tissue disorders

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a multi-system disease associated with high tires of circulating autoantibodies, most commonly the antinuclear factor and the antibody to double-stranded DNA. Joint and skin involvement are the most common presenting features (see Chapter 15).

Polyarteritis nodosa

Polyarteritis nodosa is a systemic vasculitis of unknown aetiology, involving mainly small and middle calibre arteries. The lesions are segmental with a predilection for the bifurcation of the vessels. The disease process spreads longitudinally along the arterioles and eventually involves accompanying venules. In the later stages, the vessels undergo fibrinoid necrosis, mainly in the media layer, with loss of elastic fibres in the elastic membrane of the arterial wall. In the classical form of polyarteritis, all three stages may occur simultaneously. Typically the distribution of the disease in the body spares the small vessels of the lung and spleen.

Deafness in this condition is itself unusual and only on rare occasions has it been the presenting symptom. The deafness is sensorineural. Late-Bakaar and Gibbs (1978) reported a case with profound bilateral deafness and sudden tinnitus; electrocochleography pointed to an end-organ impairment. Before treatment, the patient's hearing improved to within normal limits. Subsequently her polyarteritis nodosa was treated with prednisolone and there has been no recurrence of the deafness. Peiterson and Carlson (1966) reported a case, also with bilateral, and almost symmetrical, gradually deteriorating hearing loss. Subsequently the hearing fluctuated. After an interval of more than 6 months, polyarteritis nodosa seemed the most likely diagnosis and she was treated with prednisolone which brought about a considerable hearing improvement. The remaining reported cases totalled only approximately a dozen. The only common feature would seem to be that deafness is sensorineural and bilateral. In most of the earlier reports, minimal details are available. Later in the disease, or perhaps already present, other lesions of polyarteritis nodosa will be found in the body and it is by these that the diagnosis is made.

Gussen (1977) examined the temporal bone of a 66-year-old woman with polyarteritis nodosa who became deaf 7 months before death. Polyarteritis nodosa of the left internal auditory artery was demonstrated with fibrosis and bone formation involving the cochlear and

vestibular systems. Jenkins, Pollak and Fisch (1981) reported a 48-year-old man in whom the onset of sudden unilateral deafness and vertigo occurred 7 months prior to death as one of the earlier manifestations of the disease. Audiometric studies showed complete deafness on the left side together with a non-functioning labyrinth on caloric testing; there was a mild mixed hearing loss on the right. Subsequent examination of the temporal bones showed small vessel arteritis in the dural and subarcuate vessels on both sides.

A third case with temporal bone studies has now been reported (Adkins and Ward, 1986). They described the findings in a 60-year-old man with well documented hearing loss who had rheumatoid arthritis, polyarteritis nodosa and otosclerosis. Polyarteritis nodosa extensively involved the subarcuate arteries on the left side and the arteries in the facial canal in its vertical and horizontal portions; the changes were especially prominent in the region of the geniculate ganglion and also involved the superficial petrosal artery.

In 1974, Sergent and Christian reported an interesting series of seven adult patients who developed a sudden hearing loss (bilateral in three, unilateral in four) due to serous otitis media. Clinically these patients resembled others with vasculitis - neurological signs, renal disease and systemic symptoms were the dominating features. It is important therefore for the otologist to realize such a combination of symptoms in these circumstances and to look further than the end of a ventilation tube. More recently Hill, Graham and Gikas (1980) reported a case of a female who earlier had presented with nasal and pharyngeal symptoms associated with decreased auditory acuity and bilaterally thickened hypomobile tympanic membranes. Four years later, a right myringotomy revealed the middle ear space to be completely obliterated by fibrous tissue. On the left side there was thick fibrous hypertrophic mucosa filling the middle ear space. Histologically these changes were interpreted as being consistent with leucocytoclastic vasculitis.

Wegener's granulomatosis

While pathologically there may be difficulties in differentiating this from polyarteritis nodosa, clinically the two conditions are usually quite different in their presentation. Cases of polyarteritis nodosa seldom present to an otolaryngologist, while most will see Wegener's granulomatosis in their career and it will frequently present because of nasal symptoms. Similarly, while clinically it is different from lethal midline granuloma, pathologically these two may also present problems; the latter is considered by some to be another variant of polyarteritis nodosa. Indeed Wegener himself in 1939, stated that polyarteritis nodosa was a common finding in patients with lethal granulomata of the midline facial tissues (quoted by Duvall, Nelms and Williams, 1969).

Wegener's granulomatosis has three principal components:

(1) necrotizing granulomatosis lesions in the upper or lower respiratory tract or both

(2) generalized focal necrotizing vasculitis involving both arteries and veins, almost always present in the lungs and more or less widely disseminated in other sites

(3) glomerulitis, characterized by necrosis and thrombosis of loops or lobes of the capillary tuft, capsular adhesions, and evolution as a granulomatous lesion.

Wegener discovered the necrotizing granulomata in post-mortem tissue studies of three patients who had died of fulminant sepsis. Although the pathology predominantly involved the upper and lower respiratory tracts, a generalized vasculitis was also found, as well as evidence of end-stage glomerulonephritis. The disseminated vasculitis may involve both small arteries and veins and any organ system may be involved with granulomatous changes as disease progresses.

DeRemee et al (1976) reported a series of 50 patients over a 10-year period in which the ear was the most frequently involved site (37 patients), followed by the lung (35 patients) and kidney (23 patients). Karmody (1978) reported five patients seen over a 7-year period in which the ear was the presenting site. Illum and Thorling (1982) reported a series of 17 patients of whom 10 exhibited otological symptoms and in seven of whom it was the presenting sign.

Cogan's syndrome

In 1945, Cogan reported four cases of non-syphilitic keratitis characterized by vestibular and auditory disorders. He noted that in syphilitic keratitis only 4% of the patients developed deafness, and that this did not occur until months or even years after the keratitis. he saw his first four cases all within one year and was impressed that while the corneal changes progressed relatively little, the vertigo became incapacitating and the deafness progressive and ultimately profound. Norton and Cogan reviewed the cases again in 1959. They confirmed the ocular signs of patchy, deep corneal infiltrates which tend to fluctuate in intensity and distribution, usually located in the periphery, and accompanied by deep corneal vascularization if they persist long enough. No evidence of syphilitic infection, by the tests then available, could be found. However, the sensorineural hearing loss is progressive, often sudden in onset, and always associated with tinnitus and vertigo. Very occasionally, the vestibular/auditory symptoms have preceded the eye changes but only by a few weeks or a month or so in all reported cases. More than three-quarters of the cases have occurred in patients under 30; two have been associated with pregnancy.

Haynes et al (1980) carried out detailed investigations into 13 of Cogan's original series of 30 patients and also reviewed 111 patients from the literature. They again confirmed that while vestibular/auditory symptoms may appear before or after the onset of interstitial keratitis, they usually occur within 1-6 months of the onset of eye symptoms and progress to deafness over a period of 1-3 months. In their own series an elevated erythrocyte sedimentation rate was the most common abnormal laboratory finding (100%) followed by raised serum cryoglobulins (23%). Studies during flares of the disease showed C3 and C4 levels were normal and circulating immune complexes by the C1Q-binding assay failed to be demonstrated. Haynes et al (1981) prospectively followed six patients with Cogan's syndrome who were treated within 4 weeks of the acute onset of the hearing loss. Within 1-2 weeks after the initiation of corticosteroid therapy, all six demonstrated improved hearing thresholds for pure tones and suprathreshold speech discrimination results which have since been maintained. No retrocochlear abnormalities were found in any patient. Hughes et al (1981) reported cellular immune testing on two patients; lymphocyte migration inhibition tests on stimulation with inner ear membrane antigen were positive in both.

McDonald, Vollerstein and Younge (1985) reviewed their experience of 18 patients with Cogan's syndrome. Thirteen showed a typical presentation with audiovestibular symptoms quickly followed by the ocular findings. Five patients had an atypical presentation, two of whom had severe bilateral audiovestibular dysfunction 2 years before the onset of the classic ocular symptoms and signs. Reviewing 78 previously published cases, they noted that one-third of the patients had abdominal findings, most commonly gastrointestinal haemorrhage; one-quarter of the patients had cardiac involvement (aortic insufficiency was the most significant lesion) and there are several reports of such patients undergoing cardiac surgery. A number of patients are on record as developing systemic vasculitis in the course of their disease and in a few cases it has led to their death.

Bicknell and Holland (1978) reported two patients in whom neurological problems were prominent and a review of 79 cases in the literature showed that more than one-half had involvement of the nervous system. Clinical syndromes of acute inferior cerebellar artery occlusion have also occurred on two occasions. It remains undecided whether Cogan's syndrome is a separate entity. Cases of systemic involvement tend to be labelled as polyarteritis nodosa.

Treatment with steroids remains the recommended treatment supplemented in the more progressive case by immunosuppressive drugs for example azathioprine, cyclophosphamide, or chlorambucil. Plasma exchange has been successfully used on two occasions when other treatment has failed to halt the progress of the condition (Brookes and Newland, 1986). Serial audiometry in many cases has proved to be a satisfactory barometer for increasing or decreasing medication (McDonald, Vollerstein and Younge, 1985).

Veldmann (1986) has reported a case of immune-mediated sensorineural hearing loss which presented with sudden deafness - case 2, a 23-year-old female who was later found to have a rare complement deficiency.

Endolymphatic hydrops

Hallberg (1956) thought that not more than 5% of all cases of sudden hearing loss eventually developed Ménière's disease. He found only 57 such cases in his review of 1270 patients. Two cases of sudden hearing loss which showed endolymphatic hydrops at autopsy have now been reported (Takahara et al, 1974; Sando et al, 1977). Ménière's disease due to endolymphatic hydrops, as opposed to conditions producing a Ménière-like disorder, displays a characteristic pattern (see also Chapter 19). It is well known that it may fail to oblige by producing its principal symptoms simultaneously and the fluctuant hearing associated with this condition has become a subject of particular interest.

Recent investigations have shown the possibility that Ménière's disease may have an autoimmune basis. HLA typing in a series of 41 patients with Ménière's disease, showed that 75% on class I typing were found to have the HLA-Cw7 antigen. No differences were found between males and females, unilateral or bilateral disease or the side affected. The very close association with Cw7 and to a lesser extent with A1 and B8 antigens suggests that an autoimmune reactivity could be involved in the pathogenesis of this disease (Xenellis et al, 1986). Leone, Feghali and Linthicum (1984) have suggested that the endolymphatic sac with its fenestrated capillaries might be damaged by immune complexes, whereas the capillaries

of the cochlea being non-fenestrated would be better protected. An isolated defect of the complement system could also be the initiating cause of the disease. It is also known that stress can affect the immunological system and lead to exacerbation of symptoms in autoimmune disease.

Brookes (1986) investigated circulating immune complexes in Ménière's disease. He studied 66 patients in whom 36 were found to have significantly raised levels; the incidence was 57.1% in the group with active Ménière's disease, 50% in the group in which it was quiescent and 40% in the group where it was inactive, but these differences were not statistically significant. In 20 of the 36 patients, IgM alone was the complex that was raised. In the same group of 36, 83% also had increased C1Q complement levels in the complexes. However, there was no correlation at all between the presence of serum autoantibodies and raised circulating immune complexes.

Glycerol dehydration test

When this test was originally introduced by Klockhoff and Lindblom in 1966, it was hoped by this means to select those case of Ménière's disease whose hearing and other symptoms would be improved by diuretic therapy - the drug chosen was chlorthalidone which promotes sodium excretion without great potassium loss. Later, they took as significant, a rise of at least 10 dB in three adjacent octave bands or speech discrimination improvement exceeding 12%. No effect was seen in more advanced cases of Ménière's disease where a non-fluctuating hearing loss was present or in sensorineural loss of less specific types. Snyder (1974) felt that a pure tone threshold improvement of 15 dB was more likely to be significant; he also noticed that the changes were more marked in the low tones and the significant change was in the speech discrimination score. This test combined with transtympanic electrocochleography (Gibson, Moffat and Ramsden, 1977; Moffat et al, 1978) has extended its diagnostic usefulness and provided much information about the electrophysiological changes occurring in the cochlea. They found that in some 65% of patients with Ménière's disease, a large DC potential is present which causes an apparent widening of the summating potential/action potential (SP/AP) wave form. This potential is thought to be a summating potential which has been enhanced relative to the action potential component and is directly related to the presence of endolymphatic hydrops. During glycerol dehydration, the marked negative summating potential is seen to decrease. The positive result to glycerol testing can only occur if the patient has a fluctuating hearing loss due to endolymphatic hydrops and the hearing is impaired at its lower level at the time of testing. Gibson, Moffat and Ramsden (1977) suggested that the enhanced negative summating potential was related to an increased production of non-linear electrical activity due to the endolymphatic hydrops affecting the symmetry of the basilar membrane vibration. The glycerol is administered orally (1.5 mg/kg body weight) in the fasting state and the test can only be considered positive if there is an increase in serum osmolality of at least 10 mOs/kg to verify the effectiveness of the dehydration. The figure (Gibson and Morrison, 1983) shows the changes after one hour where the amplitude of the action potential appeared to diminish by 12%; in this case a large summating potential was present. A 'negative' glycerol dehydration test (no significant change in pure-tone threshold or speech discrimination) is meaningless if there has been less than 10 mOsm/kg increase in plasma osmolality; a 'negative' result coupled with a greater than 10 mOsm/kg change is meaningful.

Studies on inner ear impedance in patients undergoing the glycerol dehydration test have indicated that the pure-tone audiogram (the average threshold levels at 250, 500 and 1000 Hz) in Ménière's disease has shown changes which can be correlated with the maximal conductance. The conductance at 660 Hz represents the measure at which the least opposition to sound waves through the middle ear occurs and the frequency most likely to change with changes in inner ear impedance. In normal ears and in hydroptic ears in the absence of adequate dehydration, there is no change in the maximal conductance. However, there is a significant relationship between the improvement in mean speech discrimination score and the increase in conductance in hydroptic ears and proportionately in the low tone hearing improvement. With this technique it has been found that for every 1 mmol of change in maximal conductance there will be a 16.2% improvement in the mean speech discrimination score (Morrison, Moffat and O'Connor, 1980). Studies in another patient combined audiometry and the results of the glycerol dehydration test with those of surgery, one month, 6 months and 8 months postoperatively (Moffat, 1979).

Other substances that raise the serum osmolality and that diffuse and spread rapidly in the inner ear fluids, such as ethanol or mannitol, do not result in hearing gains in patients with endolymphatic hydrops. While glycerol has been found to increase the cochlear blood flow, ethanol and mannitol have no such effect. Likewise following the oral administration of urea (20 g) in humans, there is a modest elevation of plasma osmolality (7.7 mmol/kg), but neither the urea test nor that which frusemide (furosemide) has found popularity except in certain centres (Imoto and Stahle, 1983).

Isosorbide

Kitahara et al (1982) have reported the use of isosorbide, a dehydric alcohol formed by the abstraction of two molecules of water from one of sorbitol, which is known for its effect as an osmotic expanding agent. The endolymphatic pressure was reduced by its administration in guinea-pigs with hydrops while in a controlled trial of 102 patients with Ménière's disease, it produced an improvement in dizziness and tinnitus, but no mention was made of any effect upon the hearing levels.

Acetazolamide test

Acetazolamide is a water soluble sulphonamide derivative and a specific inhibitor of the widely distributed enzyme carbonic anhydrase. This reaction is fundamental to the production of either acid or alkaline secretions, and a high concentration of carbonic anhydrase is found in various secretory cells. Work by Erulkar and Maren (1961) in the cat, led to the surprising finding that the tissues of the cochlear partition possess the highest known concentrations of carbonic anhydrase of any organ assayed. The highest concentrations were found in the apical turn of the cochlea and saccus endolymphaticus, progressively lower concentrations in the middle and basal turns, and the lowest in the vestibule. It was noted that after the administration of intravenous acetazolamide the volumes and pressures of the perilymph and endolymph appeared considerably reduced. A dose of 5 mg/kg of intravenous acetazolamide caused enzyme saturation which was sufficient to produce a metabolic acidosis and mild diuresis (Maren, 1963). It was considered, therefore, that this drug might have a diagnostic use in the investigation of patients with Ménière's disease but without the side-effects of glycerol. Acetazolamide 500 mg in aqueous solution is injected intravenously over

one minute (dose range 5.1-11.9 mg/kg) and the electrocochleogram monitored continuously for 45 minutes. Pure-tone and speech thresholds are also carried out before and after the test; plasma osmolality measurements before and after the test are also made. There is usually an initial fall in osmolality with subsequent recovery. It is though that these variations in osmolality may produce osmotic gradients which lead to secondary endolymph volume changes inducing a transient increase in the endolymphatic hydrops. Electrocohleographic recordings showed an enhanced negative summating potential commencing within 10-15 minutes of drug infusion, reversing towards the pre-infusion base line level at 45-60 minutes. No change was seen in normal subjects or in those with other cochleovestibular pathology. The additional advantage of the test is that it may be carried out in those patients whose Ménière's disease is in remission, producing a small drop in the pure tone and speech thresholds which subsequently returns to normal and thereby helps to confirm the diagnosis (Brookes, Morrison and Booth, 1982; Brookes et al, 1982).

Maren and Robinson (1960) studied the cerebrospinal fluid pressure changes in hydrocephalics following intravenous acetazolamide. The temporal relationship between the transient cerebrospinal fluid pressure rise and drug infusion found in those patients is almost identical to the relationships observed with the electrocochleographic summating potential amplitude changes. However, a trial of oral acetazolamide concluded that there was no place for its use in the medical treatment of Ménière's disease (Brookes and Booth, 1984).

Watanabe and Ogawa (1984) demonstrated carbonic anhydrase activity in the dark cells of the vestibular labyrinth and in the stria vascularis of the guinea-pig. Localization of the enzyme was very similar between the dark cells and the intermediate cells but the marginal cells had a different localization pattern. In the marginal cells, carbonic anhydrase activity was observed on the lateral plasma membrane of the apical area and a few apical vesicles, in the cytoplasm of capillary endothelial cells and the fibrocytes of the spiral ligament. They considered that carbonic anhydrase may play a major role in water and electrolyte transport in both the dark cells and stria vascularis.

Inhalation of carbon dioxide

It has been known for many years that carbon dioxide is a potent cerebral vasodilator, but for this to be achieved it is usual to use a mixture containing at least 10% CO_2 (Pollock et al, 1974). Prazma (Prazma, 1978; Prazma et al, 1979) showed, in guinea-pigs, that extreme hypercapnia caused an increase of the endocochlear potential; as the latter increased, so the cochlear microphonic decreased. They concluded that the enzyme carbonic anhydrase may participate in the generation of the endocochlear potential. However, inhalations of 10% CO_2 in man may cause a dangerous increase in arterial blood pressure. Using inhalations of 5% CO_2 and 95% O_2 for a period of 20 minutes in a small series of patients with Ménière's disease, the cochlear microphonic increased in some but there was no change in the summating potential and no obvious decrease in the width of the action potential (Booth, 1980).

Metabolic disorders

Renal failure

The analogy between the nephron and the organ of Corti is one which has become more frequent particularly with the increasing numbers of patients with renal failure who may be treated by haemodialysis or transplantation. It must be remembered that many of such patients have of necessity received ototoxic drugs, either to control their infection or to promote diuresis. Certain studies therefore, are not only of interest but helpful to the otologist, who is now more frequently involved with the management of such cases.

Yassin, Badry and Fatt-Hi (1970) found that the degree of hearing loss was directly related to the degree of hyponatraemia irrespective of the level of the blood urea. Urea by itself was non-toxic to the cochlear end-organs and the cochlear affections were greatly improved by correcting the renal failure and restoring the serum sodium. Eighty per cent of the cases with acute renal failure were improved by treatment, but only 52.4% in those with chronic forms.

Oda et al (1974) have shown that in a study of 290 patients with chronic renal failure, 43 developed a significant hearing loss which could be attributed to the therapy of the kidney problem. None of the patients were complaining of hearing impairment before the kidney treatment was started. Five patients treated with less than 60 haemodialyses showed no subjective hearing loss; three who had received more than 260 haemodialyses and multiple transplants complained of hearing and vestibular difficulties. During haemodialysis frequent and intense osmotic changes occur. Johnson and Mathog (1976) noted fluctuations in hearing in a single dialysis period, but could find no correlation with corresponding changes in blood urea nitrogen, creatinine, Na, K, Ca, glucose, mean blood pressure level or weight.

Quick (1976), in a prospective study of a large series of patients receiving dialysis and/or transplantation, found that a hearing loss occurs quite frequently and while one factor might trigger off the loss, it was a combination effect of many factors, but this was not a simple addition of effects, more a potentiation. In his series, one in six had some form of hearing disorder. Six patients experienced sudden hearing loss and while a hypercoagulative state was evident in one patient, when the loss followed bilateral nephrectomy and splenectomy, there was no apparent cause in the others.

Kligerman et al (1981), in a prospective study of 67 patients with chronic end-stage renal failure, noted a trend which appeared to suggest an association between haemodialysis and high frequency impairment, the degree of hearing loss did not vary with the length of treatment. Likewise, there was a striking similarity between the audiological findings obtained for all subjects with high frequency impairment, irrespective of medical treatment.

More recently, Hutchinson and Klodd (1982) assessed a series of 15 patients under the age of 60, suffering from chronic renal failure who were being treated by haemodialysis. They eliminated from their study any patient who was diabetic or in whom the cause of renal failure was considered to be congenital. Each patient was tested once when the effects of the renal failure were most severe and they were about to undergo dialysis. They were tested using pure-tone audiometry, acoustic reflex thresholds and reflex decay tests,

electronystagmography and brainstem auditory evoked responses. They concluded that when ototoxic drugs, noise exposure, diabetes, congenital nephritis, and age above 60 years are eliminated, that although individual abnormalities will occur, chronic renal failure does not in itself produce a clinically significant hearing loss; neither does it produce an abnormality of the peripheral or central vestibular function that is clinically significant; nor did it produce an abnormality within the brainstem that affects the auditory or vestibular brainstem function from the clinical standpoint.

Finally, perhaps a cautionary note should be introduced for those who acquire iron overload due to severe anaemia and frequent transfusion requirements associated with haemodialysis. Long-term desferrioxamine was given at each dialysis (40 mg/kg) to a 26-year-old woman to reduce her serum ferritin (Guerin et al, 1985). As this fell to normal after 7 months' medication, she complained of decreased hearing and an audiogram revealed a sensorineural hearing deficit with raised threshold in the mid-high frequency range. As medication continued, her hearing worsened and it was therefore decided to discontinue this. Within 3 weeks her hearing and the audiogram improved; the hearing returned to normal within 5 weeks. Continued use of desferrioxamine when the serum ferritin has reached normal levels therefore seems unwise and serial audiometry would seem prudent. Desferrioxamine is now widely used in patients with chronic renal failure to treat aluminium osteodystrophy.

Alport's syndrome

Occasionally Alport's syndrome has been mentioned in relation to sudden hearing loss. Alport (1927) himself reported a relationship between nephritis and deafness and noted a familial occurrence. The aetiology of the hearing loss has never been clearly defined. Characteristically it varies in severity with the family, is slowly progressive and the high frequencies are those most severely affected. Myers and Tyler (1972) suggested that there may be as many as five variants - renal disease with organ of Corti damage, renal disease with spiral ganglion cochlear neuron loss, renal disease and deafness but no histological ear lesion, renal disease without deafness, and finally deafness without renal disease. Hearing loss with normal or only mild renal changes is especially typical of female members of affected families.

The commonest presenting signs are hypertension, proteinuria, and haematuria. Gubler et al (1981) reported a series of 58 cases in one of whom, a male child, deafness was the presenting symptom. Some degree of hearing loss may be present by the time the renal lesion is diagnosed and in their series, 37 patients showed a hearing loss, in 22 of whom the defect was diagnosed by audiometry and in 15 there was an apparent hearing impairment. In eight of their patients the first audiogram was normal! The hearing loss is of the slowly progressive symmetrical sensorineural type which is often not significant until the second decade, appears to affect the male much more than the female, and is always bilateral. The rate of progression of the hearing loss is no greater in those receiving haemodialysis or showing hypertension. Three types of pure tone audiometric pattern have been described - trough-shaped, sloping and flat (Rintelmann, 1976). Gleeson (1984) noted unequal recruitment throughout the auditory range with a trend to it being greater in the middle frequencies, producing dynamic compression at 2 kHz. Speech reception thresholds are in agreement with pure tone averages and speech discrimination scores are consistent with the audiometric configuration. Brainstem auditory evoked responses were normal. Gleeson (1984) reported a series of 11 patients (from

nine families) including seven with functioning transplants, one on regular haemodialysis, another on continuous ambulatory peritoneal dialysis and two (both female) still with functioning kidneys.

Renal transplantation

Hearing improvement in sensorineural deafness has been reported in two papers. Mitschke et al (1975) noted this in eight out of 10 patients with a cochlear loss; the two who had Alport's syndrome failed to improve. Paradoxically McDonald et al (1978) have reported six cases with this syndrome who have undergone transplantation; of these, one patient who received a cadaver kidney had a substantial improvement, the remainder (two received allograft kidneys from living, related donors) obtained stabilization of hearing (follow-up period - 3 years).

Quick (1976) reported a hearing loss in four patients after transplantation. Occasionally hearing loss was noted during transplantation and consideration was given as to whether this was due to the administration of frusemide (furosemide) but it was felt that the irrigation of the wound and peritoneal cavity prior to wound closure with neomycin was more likely; as a result this practice was discontinued.

More recently Jordan et al (1984) have reported on seven patients with Alport's syndrome, four of whom underwent transplantation and three who were treated by dialysis; (as might be expected all those undergoing transplant had previously been on dialysis, three for 2 years and one for 3 months). One patient with a mild pre-transplant deficit had a slight improvement in hearing 2 years later; a second patient with a mild hearing loss had no change after 18 months; the patient with a severe deficit has not exhibited any change in the hearing 10 years after surgery and the patient with the moderate hearing loss showed significant deterioration 2 years after transplantation. Of the three patients with Alport's syndrome in the dialysis group, it was only a boy who was diagnosed at the age of 4 years, had his first audiogram at the age of 11 and who commenced dialysis at the age of 20, whose hearing showed a mild loss over a 9-year period. The two other patients revealed a moderate hearing loss which was not progressive.

In the series reported by Gubler, three patients underwent transplantation of whom one was observed to have a hearing improvement (see also Duvall, Nelms and Williams, 1969).

So far, liver transplantation in children, which now has a one-year survival rate of over 70% using the immunosuppressive regimen of cyclosporin and prednisone, has not been associated with known inner ear problems, although middle ear effusion has been noted (Reilly et al, 1984).

Renal tubular acidosis

In some patients with renal tubular acidosis there is an association with nerve deafness. This condition is one of disordered tubular function, characterized by a sustained metabolic acidosis and hyperchloraemia and an inappropriately high urinary pH. Classical renal tubular acidosis (type I) is a distal tubular defect, while type II is characterized by defective bicarbonate reabsorption in the proximal tubules. It is classical (type I) renal tubular acidosis

which may be associated with deafness. While the condition may be sporadic there are many incidences of familial occurrence showing an autosomal dominant mode of transmission (Dunger, Brenton and Cain, 1980). There is also an association between renal tubular acidosis and enzymatically inactive red cell carbonic anhydrase B. Studies indicate that the synthesis of the two major isoenzymes, carbonic anhydrase B and C are controlled by a separate locus. Carbonic anhydrase B has less enzymatic activity and lower affinity for acetazolamide than type C. Families exhibiting renal tubular acidosis and the carbonic anhydrase B inactivity also exhibit nerve deafness (Shapira et al, 1974).

Diabetes mellitus

A relationship between diabetes and sensorineural hearing loss was first reported by Jordao in 1857. An excellent review by Taylor and Irwin (1978) endeavoured to put this into perspective and made the following points from their own initial survey and from the literature. The incidence of sensorineural hearing loss in diabetes will very largely depend on the limits of 'normality' and therein the statistical methodology. Second, nearly all the work has naturally been carried out in the group of diabetics most likely to be affected, that is those on insulin. They were careful to limit their upper age range to 50 years, thereby reducing the effect of presbyacusis. They noted that a diabetic with a family history had significantly better hearing thresholds than those without. They found that the diabetics, as a whole, were deafer particularly in the lower frequencies, than the controls and gradually approached each other in the middle range (1-4 kHz) and were similar at 8 kHz.

Peripheral and central neuropathies are well known in diabetes mellitus and the vestibular neurons may also be affected.

Friedman and Schulman (1975) studied 20 diabetic patients with peripheral neuropathy; 55% had a symmetrical hearing loss of the sensorineural type, involving at least one frequency, although none gave a history of hearing loss or ear disease. The hearing loss was unrelated to age, and the impairment was similar at low and high frequencies, with maximum deficiency between 750 and 2000 Hz.

Sieger et al (1983) reported a study in children but found no statistically significant differences in auditory function between insulin-dependent diabetics and normal controls, between the diabetics in good or poor control, or between diabetics with or without neurological or vascular complications. Brainstem responses also showed no difference between the two groups.

A small group of patients suffering idiopathic sudden hearing loss was investigated by Wilson et al (1982) to find out if there was a possible relationship to diabetes but no correlation could be found in the audiological pattern; a similar incidence of recovery was noticed in the two groups through the middle frequencies; however, the diabetic patients failed to recover as well in the high frequencies. Brainstem evoked responses also showed no abnormality and no evidence of retrocochlear dysfunction or pathology.

Mehra et al (1985) investigated a series of 102 patients with diabetes and peripheral neuropathy to see if such patients were prone to dysfunction of the inner ear. Only 26 gave a history of hearing loss of mild degree, while 17 had tinnitus, and 18 complained of vague

giddiness. Investigations showed that one-half demonstrated some sensorineural hearing loss but when corrected for ageing, only 24 showed a mild loss (20-30 dB). Eleven out of 91 showed markedly diminished caloric responses but all of these were in the older age group and had long-standing diabetes. Brainstem auditory evoked responses were carried out in 20 diabetic patients and a matched group of normal controls; there was a no difference in the latency of wave V and wave II, although waves III, IV and V were delayed in the diabetic patients.

Almost all studies on diabetic patients have been on those who are insulin-dependent, but Piras et al (1985) have reported a series of 30 diabetics of whom 27 were insulin-independent. Eight of the total group showed vascular lesions inherent to diabetics. They carried out auditory and vestibular studies both on the diabetic group and a similar number of normal controls and found that the influence of the disease was almost non-existent and the cochleovestibular response was similar in both groups.

Two centres in the UK (Nottingham and Cardiff) have combined in recent years. Gibbin and Davis (1981) investigated 50 diabetic subjects, 22 of whom were insulin-dependent, the remainder being managed by other regimens and 50 control subjects. No significant differences were found between the two groups on pure-tone audiometry or speech testing, nor between those who were insulin-dependent and those on different treatments.

Miller et al (1983) from the same two centres investigated hearing loss in patients with diabetic retinopathy. They found that the hearing thresholds of patients with known diabetic retinopathy did not differ significantly from those of a control population. However, using a more subtle psychoacoustic test - filtered speech task - a definite difference in hearing acuity between the two groups was demonstrated. The patient sample was made up of 15 women and 18 men of whom 18 had adult onset and 15 juvenile onset diabetes. The psychoacoustic test 0 four-alternative auditory feature speech identification test - could not be applied to all patients because of the reduction in their visual acuity. Sixteen patient completed the full-spectrum speech test and there was no significant difference between these results and those from the normal population. However, use of the filtered four-alternative auditory feature test showed significantly poorer speech perception in the diabetic group. The filtered test removes the normally important mid-frequencies emphasizing reliance on high frequencies; the filtered form of the test is expressly designed to try to exclude possible damage specific to the basal end of the cochlea. Perhaps somewhat perversely the hearing thresholds at the high frequencies were actually greater in the controls than in the diabetic patients! It has been suggested from these two studies that it is possible that there is a subpopulation of diabetic patients who suffer from subtle retrocochlear losses. However, as has already been pointed out above, brainstem auditory evoked responses have hitherto shown no difference between diabetic and non-diabetic subjects.

It should be remembered that there is a wide variation in the instance of diabetes mellitus and it is evident that this is related to the prevalence of obesity. Basal insulin secretion is directly related to relative body weight in both diabetics and non-diabetics. Maintaining ideal body weight reduces plasma insulin requirements and improves the metabolism of all tissues; high levels of circulating insulin may have a role in the development of atherosclerosis.

Hyperlipidaemia (hyperlipoproteinaemia)

When considering this condition as a cause of fluctuating hearing loss, it is important to stress at the outset, the difference between primary and secondary hyperlipidaemia (Chait, 1974). There is a large number of conditions causing secondary hyperlipidaemia, the most common of which are diabetes, alcoholism, chronic renal failure and gout. Pregnancy may also be a cause and oral contraceptives have been shown to elevate the plasma triglyceride in most subjects taking them. It is therefore essential to exclude these secondary causes, if not at the time of the original sampling, at least when the fasting lipids are being checked.

The next factor to be taken into account is the incidence of hyperlipidaemia, not in populations elsewhere in the world, but in the same part of the same country. Cholesterol levels have been shown to vary widely between countries and between different parts of the same country, for example Finland and Yugoslavia. A survey in the north-east of London of 276 carefully screened men and women, aged 20-69 years, showed that 4.3% of men and 4.8% of women (aged 40-69) had serum cholesterol values exceeding 7.8 mmol/L (300 mg/100 mL); 14% of men and 3% of women had triglyceride levels greater than 2.0 mmol/litre (180 mg/100 mL). By these definitions, 18% of men and 8% of women had hyperlipidaemia (Lewis et al, 1974).

It cannot be stressed enough that great care is required in carrying out these investigations and relating them to statistics of 'normal controls' in the same geographical area and to the normal levels for the individual laboratory and the methods adopted.

Booth (1977) investigated 44 patients with premature bilateral sensorineural hearing loss, without vertigo, and failed to find any incidence greater than in the local general population and no patient requiring treatment other than by a modification of their diet. Further cases have confirmed this finding and none so far has shown any significant improvement in hearing; conversely there has also been no progression apart from age-related changes.

Drettner et al (1975) in a study of 1000, 50-year-old men investigated a number of cardiovascular risk factors to see if they might be of importance in the development of sensorineural hearing loss. No significant correlations were found and included among the risk factors which were studied were serum cholesterol, serum triglycerides, uric acid and glucose tolerance. Spencer (1981) has now carried out the largest series associating abnormal lipids and inner ear symptoms. Of his 1419 patients, 18.4% were classified as having type IIA or pure hypercholesterolaemia with normal triglycerides; 6.3% had type IIB primary hypercholesterolaemia associated with lesser hypertriglyceridaemia, while by far the largest part showed a type IV primary hypertriglyceridaemia with a lesser elevation of the cholesterol level. However, the incidence of obesity in these patients has varied from 72 to 100% depending upon the type of disorder and whether it was associated with an elevated glucose tolerance. In his patients, by reversing their dietary habits by cutting out refined carbohydrates, reducing the intake of saturated fats and by increasing the amount of dietary fibre, avoidance of additional salt and sugar, and obtaining ideal body weight, he has reported improvements in hearing and has found similar therapy of value in treating patients with Ménière's disease. Moffat, Booth and Morrison (1979) carried out detailed investigations including metabolic studies into 27 patients with Ménière's disease, but found no increased

abnormality on glucose tolerance testing, fasting serum cholesterol and triglyceride levels, or estimations of thyroid stimulating hormone. A similar evaluation was carried out by Kinney (1980) in 134 patients showing a high correlation of abnormal carbohydrate metabolism (Shaur test) and hyperlipidaemia. Pullen et al (1985) in a study on 30 patients with migraine and 15 with Ménière's disease reported what they believe is an association between hyperinsulinism and these conditions.

Recently Karjalainen et al (1986) carried out oral glucose (75 g) tolerance tests and measured plasma insulin levels in 74 patients with Ménière's disease and 74 control subjects. They could find no significant difference in fasting and 2-hour blood glucose or insulin levels between the two groups.

Hypothyroidism

Schuknecht (1974) found the literature up to that time unconvincing on the relationship between acquired idiopathic hypothyroidism and sensorineural hearing loss, although commented that clinicians seemed to have the impression that there probably was such an association. Post (1964) investigated 42 patients - seven with spontaneous primary hypothyroidism and 35 hypothyroid patients with treated carcinoma of the thyroid. He noted that slow mentation while hypothyroid may be interpreted by the patient as a subjective hearing loss. None of the patients with sensorineural loss attained entirely normal hearing when euthyroid. He was unable to demonstrate any specific correlation between age, degree of hypothyroidism and resulting deafness. He was also unable to determine the time required for patients to remain hypothyroid before experiencing a hearing loss. Stephens and Hinchcliffe (1968) found a significant correlation between the diagnosis of myxoedema, and fatigue or temporary threshold drift measured at 8000 Hz by the Carhart technique. Stephens (1970) later confirmed that this was not an artefact relating to age, but a true finding. He suggested that the sensorineural lesion in myxoedema lies proximal to the hair cells. Meyerhoff (1976) reviewed the possible relationship between all forms of reduced thyroid function and hearing loss; under the heading 'non-genetic acquired' he reiterated the claims made up to that time, that is there was no definite association.

Two more recent papers continue to highlight the conflicting evidence. van't Hoff and Stuart (1979) have reported an incidence of deafness of 85% in a consecutive series of 48 patients with myxoedema. The more severe the disease, the higher was the incidence of deafness; there was no difference between the effect on the high or low frequencies and in some cases the loss was unilateral. Testing after the patients became euthyroid showed improved hearing in 73% of ears. The percentage returning to normal (23%) showed no significant difference in the proportion of severe (20%) to mild myxoedema (26%). Repeat testing after becoming euthyroid, failed to show any further improvement. Age did not appear to be a factor in the cause of deafness in myxoedema. While severity of myxoedema was associated with a higher instance of deafness, no other relationship could be found between severity in myxoedema and a variety of other neurophysiological measurements. van't Hoff and Stuart were in no doubt that the deafness was sensorineural.

Parving, Parving and Lyngsøe (1983) in a series of 15 patients with confirmed myxoedema, median age 76 years, demonstrated a bilateral symmetrical or nearly symmetrical sensorineural hearing loss in all patients before treatment. Treatment with L-thyroxine in this

group of elderly patients showed no improvement in hearing sensitivity and the group demonstrated neither more nor less hearing loss than other hearing-impaired patients of the same age group.

An interesting study comparing the hearing of otherwise normal schoolchildren, in a province in China (Yan-You and Shu-Hua, 1985) in a known area of endemic iodine deficiency, showed the mean hearing level was significantly lower than that of children in a non-endemic control area and that after 2 years of taking iodized salt the mean hearing level approached that of the controls; prior to prophylaxis the mean hearing level was 17.4 dB, after one year it had been improved to 13.9 dB and after the second year to 7.6 dB.

Recently, Hall et al (1985) reported a prospective study undertaken to compare the auditory acuity in hypothyroid patients and to assess the effect of thyroxine on these thresholds, for a mean period of 5.7 months (range 2-24 months). Auditory thresholds were reduced over all frequencies but the difference being significant only at 2000 and 4000 Hz. Speech discrimination was also significantly reduced in both ears. With thyroxine there was a small improvement in pure-tone thresholds and speech discrimination; this was only significant at 4000 Hz in both ears.

More recently Parving et al (1986) have reported the audiological and temporal bone findings in myxoedema. They investigated 15 patients with confirmed myxoedema with a median age of 48 years before and after treatment with L-thyroxine. No improvement in hearing sensitivity could be demonstrated either in the younger patients (age 32-60 years) or in the older group (64-95 years). When compared to an age and sex-matched unscreened population, the myxoedematous patients did not demonstrate any different degree of hearing loss. Histological investigation of the temporal bones from an 83-year-old woman with myxoedema, however, showed no morphological changes or deposition of glycosaminoglycans, changes which were compatible with true age-related hearing loss. They concluded that those series which had previously indicated a hearing improvement after restoring the patients to a euthyroid state had been carried out on only a very limited number of patients and when the sample was larger no abnormal hearing levels could be found either before or after treatment in myxoedema.

Crifo et al (1980) in a retrospective survey of 46 congenital hypothyroid cases found severe and profound hearing loss in the five cases with dyshormonogenesis whereas the one-third of patients with thyroid agenesis presented with only a mild or moderate hearing loss.

Vanderschueren-Lodeweyckx et al (1983) and Debruyne, Vandershueren-Lodeweyckx and Bastijns (1983) reported a series of 45 children with thyroid agenesis, hypogenesis or dyshormogenesis with adequate substitution therapy; the majority (80%) had normal auditory thresholds while the remainder exhibited a sensorineural loss of differing degree in half of whom this was important. No relationship between the hearing acuity and bone age at diagnosis of hypothyroidism or the aetiology of thyroid function could be found. The first case of sensorineural deafness in congenital hypopituitarism with severe hypothyroidism in an 18-year-old boy has been reported but in spite of satisfactory replacement therapy there was no improvement in his audiological function (DeLuca et al, 1985).

Himelfarb et al (1981) have attempted to correlate changes in the brainstem electric responses of patients with thyroid dysfunction (six hyperthyroid; six hypothyroid). A good correlation was observed between the brainstem conduction time and level of serum tetraiodothyronine (T4; thyroxine). In untreated hyperthyroidism, the brainstem conduction time was decreased and in some patients the brainstem electric response was characterized by high amplitude waves, sharp peaks and jittery contours becoming smoother in pattern and more well-defined after treatment.

In untreated hypothyroidism, the brainstem electric response was generally characterized by prolonged conduction time, diminished amplitudes, flattened peaks and poor synchronization; in the older patients the changes in wave pattern were more pronounced. Brainstem conduction time appears to be a sensitive index of the thyroxine-dependent cellular status in the neural pathways of the brainstem.

Lolas et al (1977) found low amplitudes of the brain potentials evoked by visual stimuli in hypothyroid subjects.

Experimental work by Meyerhoff (1979) on the guinea-pig after induced hypothyroidism, measuring the interwave intervals for the N_1 and N_2 response at the round window and vertex identified elevated auditory thresholds. The interwave intervals for the N_1N_2 response at the round window as well as the interwave intervals for the brainstem response were normal once threshold had been achieved. Meyerhoff concluded from this that the lower central auditory pathways were functioning normally and this eliminated the delayed conduction of auditory response to the brainstem as a possible mechanism and identified the cochlea as the site for the hearing loss associated with hypothyroidism. He was able to support this as the site of the lesion for the sensorineural hearing loss by morphological and biochemical findings. It should perhaps be emphasized that these animals were rendered experimentally hypothyroid during gestation with radioactive iodine-131 or propylthiouracil (both methods produced the same auditory results). More recently Ben-Tovim et al (1985) induced myxoedema in adult albino rats using oral propylthiouracil. They found minor changes in the amplitudes of all auditory brainstem response waves without any correlation with the serum T4 levels. They measured a conspicuous, dynamic, and reversible change in the amplitude of the third wave which correlated directly with the T4 (thyroxine) level in the rats' blood. Their findings in the rat indicate a lesion in the auditory tracts in the brainstem but mainly in the superior olivary complex in the central auditory pathway.

Propylthiouracil

A single case is on record of a young girl who developed hyperthyroidism with a diffuse goitre. She received propylthiouracil for 10 months before complaining of tinnitus and a fluctuating hearing in the left ear (cochlea). After discontinuing medication, she underwent a subtotal thyroidectomy followed by a complete return of the hearing to normal after 2 weeks, but the mild tinnitus persisted (Smith and Spaulding, 1972).

Ototoxicity

This subject is discussed more fully in Chapter 20. It is well known that several types of medication particularly certain groups of antibiotics can cause sudden hearing loss, and likewise some diuretic agents.

However, here certain other 'drugs' - alcohol, tobacco, marijuana - are included for the sake of completeness.

Alcohol

Under ordinary circumstances, plasma osmolality is determined primarily by the concentration of inorganic ions; other substances contribute to it and, in certain pathological states, may cause appreciable elevation of the plasma osmolality over that contributed by inorganic ions alone, for example diabetes mellitus and uraemia. The elevation of plasma glucose and urea levels is well recognized as capable of causing notable changes. Ethyl alcohol by virtue of its low molecular weight (46) might be expected to have a marked osmotic effect per unit mass present in plasma. Ethyl alcohol is ingested in quantities amounting to many grams at a time and is rapidly absorbed from the stomach, and like urea but unlike glucose, has ready access to intracellular water, causing pronounced changes in intracellular osmolality. Alcohol is therefore probably the commonest cause of the hyperosmolar state (Robinson and Loeb, 1971). Other alcohols, for example glycerol (a trivalent alcohol) and isosorbide (a dihydric alcohol) are used either diagnostically or therapeutically as hyperosmolar agents.

Spitzer and Ventry (1980) showed significant differences between alcoholic subjects and controls for acoustic reflex measurements, and tests of central auditory dysfunction (staggered spondaic word test, synthetic sentence identification). Approximately half of the alcoholics yielded results consistent with brainstem pathological features. However, there was no difference between the two groups in respect of pure-tone hearing loss or discrimination loss.

Tobacco poisoning (cigarette smoking)

Zelman (1973) found that at all frequencies the percentage of hearing loss was greater for smokers, being most apparent in the higher frequencies, in his investigation of 1000 consecutive candidates for audiometry; the tone frequency pattern of hearing loss did not differ between smokers and non-smokers. Drettner et al (1975) investigated a number of cardiovascular risk factors, included among which was the smoking habit. They compared 509 smokers with 276 patients who had never smoked, but could find no significant differences in hearing loss related to smoking habits *per se*. Marston, Sterrett and McLennan (1980) investigated the effect of cigarette smoking on tympanic membrane otoadmittance characteristics; they could find no significant difference between the two groups. Experimental work by Maffei and Miani (1962) on the guinea-pig showed that chronically intoxicated animals always showed degeneration of the neurosensory epithelia and of some specific cochlear structures besides the tubal mucosa.

Marijuana *(Cannabis sativa l.)*

Marijuana minimally affects the sensory acuity (Caldwell et al, 1969) but in chronic users significantly changes vestibular functions (Spector, 1974). The first only occurs while under the influence of the drug, and so far there is no evidence that either produces a long-term effect.

Skeletal system and otic capsule

Conditions under this heading are considered more fully in Chapter 15 but may rarely cause sudden cochlear hearing loss. Metastatic carcinoma may also occasionally occur in the ear producing such an effect and should not be overlooked.

Relapsing polychondritis

Ocular inflammatory lesions, hearing loss, and dizziness are frequent manifestations of this condition. While the hearing loss may be secondary to a middle ear problem resulting from involvement of the eustachian tube cartilage, sensorineural deafness may also occur. In several of the reported cases the hearing loss has accompanied either an abrupt cessation of steroid therapy or a drastic reduction in the level of medication. Specialized audiometric tests show the loss to be of the cochlear type. The condition is dealt with more fully in Chapter 15.

Hoshino et al (1978, 1980) have described a single case of a 56-year old female who suffered sudden deafness during the course of relapsing polychondritis. Audiometry showed a complete hearing loss in both ears and caloric testing did not elicit any responses. The patient was treated continuously with steroids which were supplemented over the last 6 years of her life with azathioprine before she died of gastrointestinal haemorrhage. They reported the temporal bone changes including scanning electron microscopy in this patient and described findings similar to those of viral deafness with endolymphatic labyrinthitis.

Hydralazine-induced relapsing polychondritis has been recorded as an adverse reaction to this drug, developing almost exclusively in patients who are slow acetylators (females who are also slow acetylators and are HLA-DR4 positive, when treated with hydralazine, are at serious risk of contracting systemic lupus erythematosus syndrome).

Retrocochlear (eighth nerve) and central nervous system

Meningitis

Leptomeningitis still causes a few cases of sudden deafness - it is typically bilateral, and total or subtotal. It may occur as a complication of acute otitis media, and is usually pneumococcal in origin. Tuberculous meningitis may still rarely be encountered and the cranial nerves may be involved by the arachnoiditis and adhesions in spite of modern therapy; as in other bacterial forms of meningitis both the cochlear and vestibular nerves may be affected (McCabe, 1975).

Acute meningovascular syphilis still occurs and may present to the otologist.

Viral disease may also cause meningitis, although it is infrequently the cause of sudden deafness.

Multiple sclerosis

Deafness in multiple sclerosis seems more likely to occur during the first 4 years of the presentation of the condition, but thereafter there is no relationship between the hearing loss and the duration of the disease. It has been estimated that some 3% of patients have a hearing problem but a higher percentage, perhaps 25%, are troubled by vertigo at some stage during the disease. The disparity between the pure tone result which may be good and speech discrimination scores which are often poor is well recognized.

Luxon (1980) in a retrospective analysis of 309 unselected patients with brainstem disorders found 52 (16.8%) with multiple sclerosis. However, only two patients complained of deafness at the time of presentation. Forty per cent of the group suffered a unilateral deficit and in common with other brainstem lesions, the frequency distribution revealed a loss in the high frequency range in 60% of the patients. No characteristic audiometric pattern was found but in both bilateral and unilateral deafness 'island loss' occurred most commonly.

It will be remembered that Dix (1965) in a series of 31 cases of multiple sclerosis of unilateral deafness paid particular emphasis to the phenomenon of loudness reversal and illustrated this in a case which showed recovery of the loudness function after its original absence.

Quine et al (1984) have shown that patients with multiple sclerosis experience hearing loss specifically for shifts of tone frequency. Tests of central auditory dysfunction may be helpful, for example binaural fusion, dichotic sentences. Hausler, Colburn and Marr (1983) reported a series of 26 patients with multiple sclerosis with normal audiograms and good speech discrimination, but they often performed abnormally on the spatial and lateralization discrimination tests. They found that patients with clearly abnormal interaural time just-noticeable differences also have abnormal brainstem evoked potentials on at least one side.

Recently Jerger et al (1986) have examined the morphology of the acoustic reflex in 122 patients with 'definite' multiple sclerosis. They found an abnormality in some dimension in 75%, most commonly in one or more of the three relative amplitude indices (afferent, efferent or central pathway). The mean average pure-tone hearing threshold (500, 1000 and 2000 Hz) was 11 dB for the poorer and 7 dB for the better ear; 80% had a mean hearing threshold for the poorer ear no worse than 20 dB. The mean value for the frequencies 1000, 2000 and 4000 Hz, were 15 dB for the poorer and 10 dB for the better side; 77% had a mean hearing threshold for these frequencies of no worse than 20 dB in the poorer ear.

Grénman (1985) has carried out a detailed neuro-otological and audiological study of the involvement of the audiovestibular system in multiple sclerosis. He examined 70 patients and found a good correlation between his results and the clinical findings of cerebellar and brainstem lesions, and this was most apparent in the vestibular tests (smooth pursuit, saccadic eye movements and optokinetic nystagmus).

Because by definition multiple sclerosis is a disease characterized by multiple areas of demyelination of the central nervous system, the clinical diagnosis depends on the demonstration of two or more lesions. For this reason, non-invasive techniques of investigation are of particular value and brainstem auditory evoked potentials have proved most welcome to the neurologists who have traditionally used binaural stimulation (Robinson and Rudge, 1977). The benefit of auditory monaural stimulation in this condition has been emphasized by several authors (Prasher and Gibson, 1980). The binaural technique produces a greater amplitude response with greater inter-test consistency but this is only true in eliciting brainstem electric response abnormalities in cases with clinically definite criteria. In the group of patients with possible multiple sclerosis, abnormally late waves may be seen on ipsilateral or contralateral stimulation.

Unlike normal subjects, there is no increase in wave V amplitude on binaural stimulation in a large majority of patients with multiple sclerosis who have no hearing deficit. The first stage of bilateral innervation occurs at the level of the superior olivary complex. Binaural stimulation may be incomplete at this level, so that only the subsequent waves originating from the brainstem nuclei caudal to the superior olivary complex will result in increased amplitude on binaural stimulation. Prasher, Sainz and Gibson (1982) showed that the mean amplitude of wave V in patients with multiple sclerosis did not alter significantly when stimulation was changed from one ear to the other or even when both ears were stimulated simultaneously; the majority of their patients showed a decrease in amplitude on binaural stimulation. In patients with chronic disease, the amplitude of wave V was small and was not affected by changing from monaural to binaural stimulation. Their studies showed that the brainstem potentials in patients with multiple sclerosis who have no hearing deficit, did not increase in amplitude on binaural stimulation.

Daugherty et al (1983) reported nine cases of multiple sclerosis all of whom included hearing loss as a prominent complaint. Seven of these underwent brainstem electric response testing. The hearing loss was unilateral in seven and bilateral in two and was a feature of the initial attack in four patients and occurred within one year of onset in a further two. In two, clinical remission was accompanied by improvement in the brainstem response. Tinnitus and/or vertigo accompanied the hearing loss in five of the nine and all had some other concurrent neurological symptoms or signs. Seven patients underwent electrophysiological studies, only one of whom had a normal brainstem response. There is no single characteristic pattern either in this or other series but prolongation of wave V latency appears to be the most consistent finding. By contrast, Chiappa et al (1980) reported brainstem auditory evoked responses in 202 patients with 'definite', 'probable', or 'possible' multiple sclerosis, but no patient presented with hearing difficulties. Only a few patients in their series had formal audiograms and all of these were normal. Using *monaural* stimulation, 68% had normal brainstem responses. In those showing abnormal responses, there was no significant correlation between the multiple sclerosis classification and the abnormality in brainstem response. In the abnormal group, 13% had only interwave latency abnormalities, 55% had only wave V amplitude abnormalities, and 33% had abnormalities of both interwave latency and wave V amplitude.

Only relatively few patients are reported as developing acute hearing loss and two recent reports of such patients undergoing brainstem auditory evoked responses are of interest. Jabbari, Marsh and Gunderson (1982) reported two cases of acute unilateral deafness whose

responses showed an absence of waves II and V in the first and the presence of only wave I in the second. Fischer et al (1985) reported 12 patients with definite multiple sclerosis who experienced an acute hearing loss during a relapse of the demyelinating disease, in a series of 705 patients. Responses were recorded in all 12 patients, during the relapse with acute hearing loss in four and after the relapse with hearing loss in the remaining eight. During the relapse with hearing loss, brainstem electric responses abnormalities were present in four, wave I being absent in two. Responses were also noted to improve substantially when recorded after the relapse in two of the three patients in whom such records were made. Brainstem electric response recordings were abnormal on the side of the earlier hearing loss in five of the eight patient investigated after the relapse. Fischer et al considered that the lesion causing unilateral hearing loss in multiple sclerosis could be situated in the cochlear nerve or close to its entry zone in the brainstem. In the classical case of a predominant, if not exclusive, central demyelination in multiple sclerosis, peak 1 remains present, well-shaped and of normal latency in most patients who have not experienced an acute episode of hearing loss in the course of their disease. Fischer et al reported an absence of wave I in only five cases in a series of 340 patients without a history of hearing loss. Arnold and Bender (1983) reported a case of particular interest in whom hearing tests were carried out over a 6-year period prior to the apparent development of multiple sclerosis. In spite of the subjective left-sided hearing loss, all the patient's investigations including specialized tests showed no abnormality. Brainstem auditory evoked responses using monaural stimulation showed that the latencies beyond wave II were delayed, particularly wave V. One month after the investigations, the patient was struck and killed by lightning. Histopathological examination of the brainstem showed extensive demyelination with specific sites of involvement in the superior olive, lateral lemniscus, and inferior colliculus.

Recently, Ferguson, Ramsden and Lythgoe (1985) sought to determine whether the combination of brainstem auditory evoked potentials and the blink reflex would yield a higher rate of abnormality than each test performed separately. In a series of 50 patients with multiple sclerosis (definite - 30, probable - 10, possible - 10) using monaural stimulation, they found that 64% had abnormal responses. The blink reflex was elicited using electrical stimulation to the supraorbital nerve. Fifty-two per cent had an abnormal blink reflex, but when the results were combined with the brainstem electric response, 76% were abnormal. In this series, symptomatic deafness was present in 20%.

Recently, magnetic resonance imaging (MR) has been shown to be of particular value in demonstrating plaques of demyelination including those in the brainstem. Cortical deafness in multiple sclerosis is a particularly rare event. Tabira et al (1981) reported such a case with complete recovery from total deafness following stages of auditory agnosia and pure word deafness. The otological and neurophysiological studies suggested lesions in the subcortical white matter.

Friedreich's ataxia

In Friedreich's ataxia there is no relationship between the progressive clinical involvement and the degenerative changes affecting the peripheral nerves. Pelosi et al (1984) investigated a series of 15 patients of whom only five had a hearing difficulty (three mild, one moderate and one severe). However brainstem electric responses were completely dissociated from the hearing disorder, being normal in one patient and abnormal in the

remaining 12 investigated. Five showed severe abnormalities and there were mild to moderate abnormalities in the remaining seven, but wave I was present in all of this group. Patients without clinical acoustic disturbances showed abnormalities in brainstem response to the same degree or even greater than those who had a mild or moderate sensorineural hearing difficulty. However, the findings were significantly correlated with the level of clinical disability generally.

Visual evoked potentials showed abnormalities which corresponded to the severity of the clinical ophthalmological disturbance but were unrelated to the duration or severity of the clinical condition. Somatosensory evoked potentials showed findings which were also unrelated to either the duration or severity of the clinical conditions. Jabbari et al (1983) studied five children in an effort to find out the primary site of auditory dysfunction in classic Friedreich's ataxia; none of the children had any hearing complaints and all were tested soon after the onset of symptoms. The brainstem evoked potentials indicated dysfunction of the auditory system in the pontomesencephalic region. Acoustic reflex studies on two of the patients also suggested involvement of the brainstem auditory pathways. Wave I was retained in all patients and they thought it unlikely therefore that there was significant dysfunction of the spiral ganglia.

Amyotrophic lateral sclerosis (van Laere's disease)

Cristovao et al (1985) have reported a family with this condition showing cochleovestibular involvement. This is an uncommon pattern of the disease and in the non-familial type such involvement has not been reported. The older two members of the family, aged 19 and 15 years, reported hearing loss as the first manifestation and on testing the eldest showed a severe bilateral sensorineural hearing loss with very poor discrimination scores, pathological decay of the stapedius reflex bilaterally, asymmetry of the horizontal optokinetic nystagmus and bilateral absent responses in rotatory and caloric vestibular tests. The younger member (aged 12) had no complaints and normal hearing but pathological decay of the stapedius reflex at one frequency in one ear was noted. Only the eldest member showed other neurological involvement which was severe by that time.

Vogt-Koyanagi-Harada syndrome

In 1926, Harada described what he believed to be a distinct entity comprising bilateral detachment of the retina, uveitis, mild meningeal irritation and 'dysacousia'. It is now generally considered that this 'disease' forms part of the now combined syndrome. Vogt in 1906, noted the association between bilateral uveitis, alopecia, vitiligo, poliosis (whitening of the hair) and 'dysacousia'. (Koyanagi described his variant in 1929 - this brought vitiligo and the deafness together.) Most of the reported cases have occurred in people of pigmented race. The principal feature is the prolonged bilateral uveitis, causing blindness. The hearing loss develops at or near the time the blindness occurs; it is also usually bilateral, of varying degree, frequently associated with tinnitus and vertigo. The ear symptoms begin to improve after 1-3 weeks as the tinnitus and vertigo subside, gradually returning to normal. Vision often returns to normal in 2-6 months, but glaucoma and cataract may continue as complications. The vitiligo, poliosis and alopecia usually appear when the uveitic begins to improve. Rosen (1945) reported one case and reviewed those then in the literature - a total of 45; Maxwell has reported another (1963). Schuknecht 91974) noted that ordinarily three stages may be

recognized in the disease: the meningeal, the ophthalmic and the convalescent. The meningeal stage is present in at least 50% of the patients and may last from 2-4 weeks. The hearing loss may occasionally be unilateral and need not always recover. The cause remains unknown.

Xeroderma pigmentosum

Xeroderma pigmentosum is a rare autosomal recessive condition first described by Kaposi in 1874. Clinically the patients present with an abnormal sensitivity to sunlight, this is characterized by the appearance of a delayed yet marked erythema of skin exposed to ultraviolet light. Subsequently pigmented macules appear together with telangiectasia and skin atrophy and, in time, multiple cutaneous neoplasms develop. The condition is associated with abnormalities of excision and repair of DNA segments damaged by ultraviolet light. Complementation studies have shown seven different types of the condition, all of whom have an excision repair defect; there are still others known as xeroderma pigmentosum variants, in which no such defect is evident, but in whom synthesis of DNA is still abnormal with slow maturation of new DNA chains. Neurological abnormalities have also been described, particularly peripheral neuropathy and changes in the central nervous system may also occur. deafness has also become recognized as being associated with this disease.

Longridge (1976) studied a pair of siblings and came to the conclusion that the disorder was central and not cochlear in origin. He based this opinion on absent stapedial reflexes, and absence of tone decay and a speech audiogram which he considered to be worse than would have been anticipated from the pure tone audiogram. More recently, Kenyon et al (1985) reported three cases in whom detailed neuro-otological investigations had been carried out. These patients had widely differing ages (16, 46 and 57 years) and two showed a high and one a low tone recruiting hearing loss; brainstem auditory evoked responses obtained in one patient were completely normal and only mildly deranged in another strongly suggesting the origin of the deafness to be more peripheral than the brainstem. Although the deafness was bilateral, in none of the patients was it entirely symmetrical. The vestibular pathways appear to be involved, but apparently to a lesser extent than the auditory ones and vestibulo-ocular reflex suppression is abnormal. The two older patients showed evidence of a mild supranuclear palsy that was only apparent on volitional movement.

Tumours

Acoustic neuroma

Few would regard this as a common tumour and in relation to the vast number of cases of all forms of unilateral sensorineural hearing loss investigated in clinics, the number of confirmed cases is infinitesimal. However, its clinical interest makes every clinician feel this effort to be well worthwhile and the satisfactory surgical removal rewarding, thereby entirely vindicating the investigative time involved. Those who see these tumours but infrequently or rarely, may be surprised to learn that they can present as sudden deafness. It is of the greatest importance that this should be thoroughly understood and, even though the deafness may no longer seem worth treating, it is always worth investigating as thoroughly as circumstances allow.

It is interesting to note that Cushing in 1914 mentioned that two cases had sudden hearing loss as a manifestation of cerebellopontine angle tumour, but it was not described as the presenting symptom in the English literature until 1956 by Hallberg (see also Hallberg, Uihlein and Siekert, 1959). In addition, Edwards and Paterson (1951) mentioned five patients whose hearing loss was described as abrupt in their review of 157 cases. Higgs (1973) reported that 10% in his series of 44 patients presented with sudden deafness. Morrison (1975) showed that no less than 17% of his patients presented in this way. More recently several papers have appeared reporting cases which have presented with sudden deafness. Pensac et al (1985) in a retrospective analysis of 506 patients with surgically proven cerebellopontine angle lesions seen over a period of 14 years, found 77 (15.2%) who presented in this way (69 acoustic neuromata, seven meningiomata and one malignant cholesteatoma). They could find no characteristics which distinguished these cases from the remainder. Twenty-four were small lesions (up to 1.5 cm); 28 were medium-sized (1.6-2.9 cm) and 25 were large (3.0 cm or greater). The hearing patterns were in the same proportions as those for acoustic tumours generally; several had hearing losses which improved before they could be tested. Eleven had reasonably normal audiometric findings (tumour size 1-4.5 cm); the patient with the largest tumour (4.5 cm) had a pure tone threshold of 50 dB with 100% speech discrimination! Chow and Garcia (1985) reported a patient with sudden hearing loss whose hearing returned to normal 2 weeks later only to fall again 4 weeks later, with normal caloric responses and speech discrimination at that time of 24%, then recovering within 6 weeks to 76%. A CT scan showed a 1.5 cm mass and the patient refused surgical treatment.

If only this were all! Berg et al (1986) reviewed patients with 133 tumours seen over a 10-year period, of whom 17 (13%) had presented with sudden hearing loss. Of these, four (23%) had recovered auditory function before surgery - three spontaneously and one after steroid therapy. One case, in addition to the sudden deafness, had a progressive facial palsy, which was treated with steroids leading to almost complete return of facial motor function (tumour 1.5 cm); the tinnitus and vertigo also resolved. Another patient in their series had three episodes of sudden hearing loss over one year, plus tinnitus, but no vertigo; the first two episodes resolved within 72 hours (tumour 1.5 cm). However, no bilateral tumours have yet been reported as presenting in this way. Of the 16 cases who presented with sudden idiopathic deafness reported by Morrison (1975) and who proceeded to advanced meatal studies, five were found to have slight enlargement of the internal meatus but no tumour!

Conversely, in the series of more than 1200 cases of sudden deafness reported by Shaia and Sheehy (1976) almost 1% had an acoustic tumour. They found nothing to distinguish these cases from the group as a whole, other than the fact that 50% had a profound or total loss of hearing; 70% had a reduced vestibular response and all had an enlarged internal auditory meatus.

Finally, Clemis, Mastricola and Schuler-Vogler (1982) reported three cases of sudden hearing loss postoperatively in the contralateral ear of patients with an acoustic tumour.

Metastases in cerebellopontine angle

Secondary deposits may occur in the cerebellopontine angle from primary disease in the breast, bronchus and prostate.

Carcinomatous neuropathy

Peripheral neuropathy caused by malignant disease ranks second to the Guillain-Barré syndrome. Conversely, unexplained peripheral neuropathy should be the signal to search for malignant disease.

The highest incidence of this condition has been found in patients with carcinoma of the lung, ovary and stomach, and lowest in the rectum, cervix and uterus. Other malignant diseases may also have an associated involvement - progressive multifocal leucoencephalopathy is linked with Hodgkin's disease, lymphosarcoma and some other reticuloses. There is also an unusual form of encephalomyelitis nearly always associated with oat-cell bronchial carcinoma.

No particular association with either branch of the eighth nerve has so far been shown (Henson and Urich, 1982). Hearing loss has been reported in carcinomatous meningitis and five such cases have been seen in which the hearing loss was the presenting symptom (Alberts and Terrence, 1978).

Central deafness

'Central' deafness may be unilateral or bilateral but it is the latter type that seems to yield the most helpful information so far. It should be stressed that cases are rare, autopsy reports are few and that there is no uniform pattern of hearing loss. However, certain features appear to give some diagnostic and investigative guide.

Jerger et al (1969) and Jerger, Lovering and Wertz (1972) have reported two cases in great detail. Both were cases of bilateral temporal lobe damage, both males. Both experienced transient aphasia but no hearing problems after the first side (left) episode. Both reported severe hearing loss after the second (right) episode. In both, the presumed sensitivity loss had essentially recovered within 3 months of the second episode; both showed marked inability to recognize either single words or sentences. However, there was one significant difference and that was in their ability to localize sound; in the younger case this was impaired but not in the older.

In the first (younger) patient, it was concluded that he had experienced occlusion of the terminal branches of the middle cerebral artery on each side at different points in time, resulting in bilateral partial cerebral hemisphere infarction, maximal in the temporal lobes, and producing the clinical picture of cortical deafness. In the second case, at his second admission, angiography showed occlusion of the major middle cerebral trunk with anastomotic filling in a retrograde manner from the parieto-occipital branch of the right posterior cerebral artery. This patient had a third and final admission, 6 months later for acute cerebral infarction with right hemiplegia and aphasia; he died one week later of an acute myocardial infarct. Examination of the brain revealed bilateral and symmetrical areas of softening of the posterior segments of the superior temporal gyri, these were caused by cystic infarcts; the major arteries displayed moderate atherosclerosis but there was no evidence of embolism.

More recently, Earnest, Monroe and Yarnell (1977) have reported a case of a man (left-handed) who subsequently had bilateral cerebral infarcts that caused a non-fluent aphasia,

oral apraxia, and deafness and who, at the age of 27, had a mitral valve prosthesis fitted and received subsequent anticoagulation. They expressed the view that the cortical clinical syndrome of pure word deafness in many cases is probably a less severe form of cortical deafness and is due to less extensive bilateral temporal grey matter lesions. Strictly white matter lesions may produce cases of either syndrome.

Graham, Greenwood and Lecky (1980) carried out brainstem evoked responses on a 47-year-old woman (right-handed) who 3 years before had a mitral valve replacement. She was thought to have suffered three separate embolic lesions of cardiac origin, the first to the left temporal cortex producing dysphasia, 6 months after operation, (an isotope scan at that time showed a left homonymous hemianopia) and the third to the right temporal lobe, resulting in total deafness. The first and third events represent left and right middle cerebral artery embolism and the second, right posterior cerebral artery embolism. She also suffered a series of epileptic fits. A CT scan and isotope scan showed bilateral temporal infarction and a right occipital infarct. Galvanic responses were negative. No cortical electrical response activity could be obtained but stapedius (acoustic) and postauricular myogenic responses were both present. A similar diagnosis to the other cases reported has been made, that is bilateral temporal lobe infarction of embolic origin. In addition to reporting their own case, Graham, Greenwood and Lecky (1980) gave an excellent review of the earlier literature and of the four cases published since 1969 making a total of 12 in all prior to their own study.

Cortical encephalitis

Diffuse cortical encephalitis causes an auditory aphasia when both temporal lobes are involved; the patients have normal pure-tone audiograms but no understanding of speech. The diagnosis is confirmed by EEG and the condition may develop over weeks or months with periods of fluctuation and acute episodes. Morrison (1975) reported three cases, all adult females, in all of whom the sudden hearing loss occurred relatively late in the disease but all made good recoveries after treatment with steroids followed by ACTH. However, one has continued to have occasional episodes of auditory aphasia.

Recently, it would appear that a new syndrome has been described which afflicts women in the third or fourth decade of life, is characterized by a subacute encephalopathy with sensorineural hearing loss and retinal artery branch occlusions, and shows no clinical or laboratory evidence of visceral lesions. It is associated with sclerosis of the media and adventitia of small pial and cortical vessels. Monteiro et al (1985) have recorded two cases and reviewed the four reported previously. Hearing loss was present in all patients and was the first symptom in two and bilateral in all but one; tinnitus was described in three. Pure-tone audiometry showed bilateral asymmetric sensorineural hearing loss with a preferential loss in the low and middle frequencies. Speech discrimination was poor in the ear on the more involved side. Brainstem auditory evoked responses were normal in the three patients tested. They felt it unlikely, therefore, that the deafness was of eighth nerve origin but was more attributable to cochlear damage. Magnetic resonance imaging was obtained in only one patient but this showed changes compatible with a small brain infarct in the white matter, as suspected clinically. Treatment with prednisone was given to all patients, but in three, progression of symptoms led to additional therapy with cyclophosphamide; it is noteworthy that none of the three patients receiving cyclophosphamide developed new symptoms. None

of the patients had recurrence of symptoms after the disease subsided. However, treatment brought about no improvement in any of the six patients.

Alzheimer's disease

Central auditory function has been investigated by Grimes et al (1985) in 38 patients with Alzheimer's disease (36 right-handed). Significant relationships were observed between the dichotic scores and intelligence quotient, cortical atrophy in the temporal lobes, and cerebral glucose metabolism in the left temporal lobe. Specifically it was impairment in dichotic performance that was related to cerebral atrophy, not a general deficit in ability to hear. The presence of dysfunction was related to the severity of atrophy and hypometabolism in the temporal lobes. The contralateral ear effect for dichotic performance was consistent with dichotic speech recognition in patients with other temporal lobe lesions.

Idiopathic

Pathogenesis

There have been two 'rival' theories as to the causation of the idiopathic case - *viral* and *vascular.* It has been known for a long time that certain viruses, for example mumps, measles, rubella, can cause sensorineural deafness, that the finding of a preceding 'viral' infection in many cases of sudden loss, varying in incidence from 30-40% according to the author, made the association of ideas, if not facts, irresistible (for example van Dishoeck and Bierman, 1957). Conversely, the suddenness of onset made the analogy with similar events in the cardiovascular system equally attractive to the opposing school (for example Hallberg, 1956). As many of the cases occurred in patients over 40 years of age, the association looked even more tempting. Attempts have been made to reconcile these view points. The theory of *membrane breaks or ruptures* has also been put forward.

It is traditional in otology to try to match the clinical picture with the findings from the temporal bone laboratory, wherever possible. As in many other otological conditions, few patients die of their disease, so the interval between the event, in this case sudden deafness, and autopsy may be long, and reparative processes will have been at work. Alternatively, the end may come very rapidly from overwhelming disease, which in itself may complicate the histological picture. However, all this is familiar and expected by temporal bone experts.

Membrane breaks

In an effort to understand the causation of sudden hearing loss, Simmons in 1968, considered the history and clinical findings in patients with this problem. He noted that all but two were under 45 years of age and that many could date their sudden onset to a particular day and time and he was struck by the association of a 'popping', 'clicking' preceding the hearing loss or of the sudden development of a marked roaring tinnitus. He also asked whether the patient's physical activity at the time could have caused any increase in the intrathoracic or intracranial venous or cerebrospinal fluid pressure, or if more than a modest amount of alcohol had been drunk beforehand. He postulated that perhaps there was a disruption to the cochlear membranes which subsequently healed, in a similar manner to that in experimental animals exposed to intense sound. He reported a series of 15 patients and

commented in this, and in a later paper discussing 56 patients (Simmons, 1973), that very few noticed vestibular symptoms at the time, but on questioning transient unsteady feelings were present in one-third; a few were frankly vertiginous. He observed that untreated, there appeared to be an improvement in the hearing, sometimes quite suddenly, even after quite long intervals. He therefore advocated that nothing which would raise the pressure in the inner ear or might otherwise injure it further, for example high intensity audiometry, should occur in order to facilitate healing of the cochlear membranes.

Reports of three temporal bone studies have now been published, all by Gussen (1981, 1983), showing cochlear membrane rupture in patients with sudden hearing loss. In the first report, she demonstrated the ruptures occurring in the left temporal bones of two patients, one as a result of barotrauma associated with sudden deafness, tinnitus and some vertigo and the second in a patient with profound deafness in a previously normal hearing ear. Both occurred as ruptures of Reissner's membrane at the junction of the ductus reuniens with the caecum vestibulare portion of the cochlear duct. With healing, a balloon-like structure formed from the rupture site into the adjacent vestibule, resulting in a secondary ruptured saccule duct in one case and in collapse of the saccule in the second. Gussen stressed the left-sided preponderance of such ruptures and the vulnerability of the ductus reuniens junction with the cochlea. The third patient also showed rupture of the cochlear membrane in the left ear following episodes of vertigo, but later by sudden loss of the hearing on that side. Because of continuing unsteadiness, the patient subsequently underwent a left labyrinthectomy, but 2 months later had a sudden loss of hearing in the right only hearing ear. She was considered to have vertebrobasilar arteriosclerosis and died of a massive stroke 4 years later. Two healed ruptures were demonstrated on the right side, and one in the area of the promontory. The latter was adherent to the saccule, distorting it inferiorly. In the left temporal bone, a healed rupture was demonstrated at approximately 5 mm distal to the labyrinthectomy obliteration.

Koskas, Linthicum and House (1983) described membranous ruptures which they found only in patients with Ménière's disease and occurred more frequently in Reissner's membrane than in the vestibular membrane. Of the 12 bones from patients with Ménière's disease which they examined, two had no hydrops and were therefore excluded. Hydrops in Reissner's membrane as a result of congenital syphilis was found in two bones. They described three different types of rupture, the most common of which, found in nine bones, was in the shape of a balloon and the connective tissue had formed to seal off Reissner's membrane.

Symptomatology

'Sudden hearing loss is a symptom in search of a diagnosis' (Simmons, 1973). It will be readily apparent that many of the causes of sudden hearing loss are in themselves rare. Many of them are discussed in other chapters. The preceding section is devoted to excluding the specific causes, thereby leaving the so-called 'idiopathic' losses - still the largest single group and constituting the everyday case - for treatment according to 'site-of-loss'.

For the purist, 'sudden' hearing loss means an instantaneous event; 'rapid' hearing loss means deafness occurring over a short period of time, for example hours. If the loss subsequently improves, either spontaneously or as a result of treatment, then some would label this 'fluctuant'! It should be appreciated that cases may present in any of these ways and

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the distinction between them from a diagnostic viewpoint is frequently somewhat artificial. It will become apparent that such divisions should not be interpreted too rigidly.

Age and sex distribution

In the 1220 cases reported by Shaia and Sheehy (1976), age at onset of the symptoms was as follows:

Under 30	13%
30-39	13%
40-49	21%
50-59	22%
60-69	18%
70 years +	13%

Three-quarters of the patients therefore were over the age of 40, but 1.4% dated the onset of their sudden hearing loss below the age of 10. Four per cent had a sudden bilateral loss, and one-half of these were simultaneous. Only one-quarter of the 1220 patients were seen within one month of onset. As all series show that the best results are obtained in those receiving their treatment within 15 days of onset, it will be immediately appreciated how vast is the wastage of untreated cases. in all series, the sex distribution is approximately equal at all age groups.

Precipitating factors

Many published series state an incidence of a preceding viral infection in 30-40%.

Almost every virus has been reported or implicated as a causative factor in a proportion of these cases, but certain facts should be considered before such an aetiology is too readily accepted.

The viruses which have been suggested as causing sudden hearing loss may be divided into three groups. The first of these consists of viruses causing acute respiratory diseases such as influenza, parainfluenza and rhinoviruses. Such infections are very common. Adults suffer on average four to five respiratory infections a year, so that about one-third of any group of adults will give a history of a respiratory infection within the preceding 4 weeks. There is no confirmed evidence of a seasonal incidence as might be expected for the respiratory viruses and none following an epidemic such as might be expected after influenza. Although a high incidence might be expected in children because they sustain more infections than adults none such has been reported (Rowson, Hinchcliffe and Gamble, 1976).

The second group includes poliovirus, coxsackie virus, rubella, Epstein-Barr virus, adenovirus type 3 and herpes simplex virus. Following such infections, occasional cases of sudden hearing loss have been reported, but they are very uncommon. The third group comprises three viruses - mumps, measles and varicella zoster, all of which are known to produce sudden deafness.

Other symptoms

Many patients with sudden hearing loss can state the day, date and time that it occurred, or that they awoke with it. Others may recall severe physical effort at the time of onset. Nearly always it is a dramatic, well-remembered event. *Pain* or a feeling of pressure may be present in the affected ear, but so far no particular prognostic significance has been found to be attached to this. *Tinnitus* occurs in approximately 80% of cases usually starting with, and alarmingly as, the deafness. In approximately 25% the tinnitus may precede the deafness by minutes or hours, very occasionally by some days. *Vertigo* is commonest in those with a probable vascular aetiology. It carries a poorer prognosis for hearing recovery, while tinnitus apparently does not affect the outcome. Danino et al (1984) found tinnitus to be a favourable prognostic sign and felt that its presence seemed to indicate that cells were still functioning and therefore may recover. Tinnitus was present in 71% of the patients who recovered compared with 39% who did not. Conversely they agreed that vertigo is a bad prognostic factor (24% in the recovery and 54% in the non-recovery group).

In the series of Shaia and Sheehy (1976), 60% of patients had no vestibular symptoms, 22% had them initially, and 18% persistently.

Vertigo of any duration associated with the hearing loss is an indication to investigate the patient very thoroughly, and the possibility of an acoustic neuroma should never be overlooked.

There is a series of reports of patients who after developing sudden deafness, subsequently go on to develop episodic vertigo characteristic of endolymphatic hydrops. Wolfson and Leiberman (1975) recorded five such cases. The interval in their cases ranges from 6-10 years. After long observation, destruction labyrinthectomy was carried out with complete relief of the vertigo. Nadol, Weiss and Parker (1975) reported 12 cases, with vertigo developing from 1 to 68 years later! They found the long interval particularly puzzling. Few of the 12 had any coincidental vestibular symptoms at the time of onset of the sudden deafness. Again labyrinthectomy was curative. Both groups of authors question whether the cause could be Ménière's disease.

Investigation of sudden or fluctuant sensorineural hearing loss may require:

Haematology

Haemoglobin, full blood count, erythrocyte sedimentation rate, prothrombin time
Paul Bunnell screening test and titre (Epstein-Barr virus)
(Blood for viral studies - repeat specimen will be required after 2-3 weeks to assess change in titre)
Syphilis serology (full - including fluorescent treponemal antibody-absorption (FTA-ABS) test and *Treponema pallidum* haemagglutination (TPHA) test)
Sickle-cell test (if appropriate and haemoglobin electrophoresis)
Fasting serum lipids (after 12-14 hours complete fast and 45 minutes total body rest; no stasis during blood withdrawal, that is no sphygmomanometer or other occluding cuff)
Glucose tolerance test
Serum electrolytes including urea, calcium, phosphorus, phosphate, uric acid, etc.

Electrocardiogram

Radiology

Chest X-ray
Mastoids (plain films)
Internal auditory meatus (tomography, preferably hypocycloidal polytomography)
CT scan (air CT studies)
Magnetic resonance imaging

Audiometry

Pure-tone audiogram
Tone decay test (Carhart)
Speech audiometry
Acoustic impedance measurements including stapedius reflex thresholds and decay
Fistula test (electronystagmography + impedance) if appropriate
Electrocochleography
Brainstem electric response audiometry
Promontory stimulation (if no hearing present)

Lumbar puncture

For routine cerebrospinal fluid examination, serology, Lange curve and immunoglobulins.

It must be remembered that when a patient with sudden hearing loss presents within the early stages, that is under 15 days, everyone carrying out investigations wants to help simultaneously. At the receiving end of this investigative enthusiasm and energy, lies a patient! Many of these investigations are time-consuming (for example glucose tolerance tests) and as they yield the least urgent information they should be left until last. Those conditions encompassed by the taking of blood on a rested, fasted patient can all be accomplished in a single venepuncture the morning after admission. 'Lumbar puncture if considered necessary (which is seldom now the case) should be left until last, as after this the patient may have much discomfort in the back and the head. To follow this with any procedure requiring mobility, mental attention and cooperation or the maintenance of a prolonged position is cruel.

Audiometry

A patient with sudden hearing loss needs first the simplest tests, of pure-tone thresholds, acoustic impedance measurements (except in cases of suspected oval or round window rupture or perilymph fistula); stapedius (acoustic) reflex thresholds and tone decay (Carhart). Tests of longer duration can be more conveniently carried out later on. It should be remembered that tones above 85 dB can cause temporary threshold shift even in a normal ear. In an already damaged cochlea, the possibility of further damage by test tones at high intensities is very real (Simmons, 1973).

From the simple pure-tone test, two most interesting prognostic factors have been reported (Mattox and Simmons, 1977). First, the less obvious, is the significance of the test frequency of 8 kHz, and the second is the shape of the audiogram. In their series they noted that all but one patient with an upward-sloping auiogram had complete or good recovery. Conversely all but two patients with a severe downward slope had a fair or poor recovery. Flat and less severe down-sloping patterns fell between the two extremes. Expressed in another way, if the threshold loss, going from the apex to the base of the cochlea was either improving or stable at 8 kHz, the prognosis for a good or complete recovery was 78%. If there was no hearing at 8 kHz, regardless of the hearing at other frequencies, the same prognosis was only 29%. Recovery was always better at the apex of the cochlea, than at the base. This seemed independent of the contour of the severity of the loss on the initial threshold audiogram. It should be remembered that these findings were noted on *untreated* patients.

In the series reported by Shaia and Sheehy (1976), 12% showed a low-tone loss, 32% a flat loss and 31% a high-tone loss. However, 25% showed a profound or total loss. It is this last group which deserves special mention and again they may be subdivided - first into those with a severe loss and second those with a total loss.

In the same series, of the 10 patients who were found to have acoustic tumours, five had a total loss. Those with severe losses may show some hearing at both low and high frequencies but none in the mid-range.

Audiometry in sudden hearing loss serves two purposes - first, to assess the day-to-day level of the loss by the level of the pure-tone threshold, and second to determine the site of the lesion. The site is of particular importance in determining the treatment. Many of the patients showing a retrocochlear pattern have the contour shown and frequently they will be in the younger age group, that is below 40.

In the group with a total loss, the primary audiometric tests will be of no avail in helping the worried clinician or patient, but electrocochleography has a useful part to play. Graham et al (1978), used transtympanic electrocochleography to test 70 patients with sudden hearing loss. Of particular interest are the 24% where threshold audiometry was impossible. Of these 17 patients, a result was obtained indicating a retrocochlear pattern in seven. In the remaining 10 patients, neither a cochlear microphonic nor an action potential was found, suggesting a cochlear loss, with or without retrocochlear involvement. In two of these patients, the promontory electrode was used to provide direct stimulation to the cochlea and this evoked a subjective sensation of sound, suggesting that the cochlear nerve was intact to some extent (House and Brackmann, 1974; Graham and Hazell, 1977).

Tonndorf (1980) believed that the combination of hearing loss, recruitment, poor speech discrimination and tinnitus, which is characteristic of acute cochlear disorders can be accounted for on the basis of decoupling of hair cells from their drive system, the tectorial membrane; the magnitude of the hearing loss depends on the degree and number of hair cells involved.

Vestibular tests

These have a particular place in those patients with sudden hearing loss which has been accompanied by vertigo, but in most instances such tests can be deferred until all the necessary audiometric tests have been completed, and the patient's morale is beginning to improve. They are never urgent.

Electronystagmography is often helpful; it is of special benefit in diagnosing vertebrobasilar insufficiency or other possible vascular causes of positional nystagmus.

It may be combined with impedance testing to demonstrate a possible perilymph fistula (see Chapter 14 on otosclerosis).

Management

Three unfavourable prognostic factors are known - the shape of the audiogram, especially the degree of involvement at 8 kHz, the severity of the hearing loss, and the presence of vertigo. It is also known that in the idiopathic case, there will be spontaneous improvement within 15 days in 50-60% of cases. However, failure to investigate patients will inevitably lead to a missed diagnosis and a missed opportunity for treatment.

Patients with a cochlear (sensory) loss should have a daily pure-tone threshold audiogram under identical test conditions and ideally speech audiometry and discrimination scores should also be carried out on a daily basis. Those who fail to show spontaneous improvement under observation by the tenth or twelfth day should be offered treatment. On occasions, the pattern of hearing loss has been shown to change from neural to sensory as 'improvement' occurs (Stephens, Swisher and Novotny, 1967).

Increasing cochlear blood flow

Vasodilators

There is little or no evidence that these are of proven value. The difference between the autoregulatory mechanisms in the circulation of the brain and of the inner ear have often been ignored; the cerebral circulation is practically unaffected by variations in the systemic blood pressure. Experimental work in animals (the cat) has shown that vasoconstrictor drugs such as angiotensin produce, with some delay, a moderate increase in perilymphatic PO_2. drugs inducing vasodilatation, such as histamine, are followed by the opposite effect. The changes observed in the perilymphatic PO_2 after injection of vasoactive drugs indicate that there is a direct correlation between the systemic blood pressure and inner ear oxygenation. The evidence therefore implies that vasodilator drugs should be abandoned (Yagi, Fisch and Murata, 1978).

Glycerol has been found to increase the cochlear and cerebral blood flow significantly after intravenous administration experimentally in the rabbit (Larsen, Angelborg and Hultcrantz, 1982).

Low molecular weight dextran (Rheomacrodex)

Among the aetiological factors proposed in sudden hearing loss is hypercoagulability of the blood. Low molecular weight dextran by intravenous infusion has therefore been recommended. This preparation with a molecular weight of 40.000 is available as a 10% solution, either in 5% dextrose or in normal saline. It is contraindicated in patients with cardiac failure and bleeding disorders and has on rare occasions proven fatal (Zaytoun, Schuknecht and Farmer, 1983). Dextran forte increases capillary blood flow in general by hypervolaemic haemodilution and by decreasing factor VIII; this decreased blood viscosity results in increased cardiac output and tissue blood flow. Dextran forte has a half-life of 5 hours in the circulation. Experiments in guinea-pigs, by Hultcrantz et al (1985), showed an increase in the cochlear blood flow of 75%, but this soon reached a steady state and fell as soon as the infusion was ended. The compound action potentials were initially improved during the haemodilution. In practice, in human patients with sudden hearing loss, it has so far proved disappointing.

Stellate ganglion block

This induces an increase in blood flow by ceasing the action of the cervical sympathetic nervous system. The vasodilatation produces an immediate response but has not been found to be of benefit after 2 weeks of the onset of sudden deafness. Of the several methods of estimating cochlear blood flow in animals, only one appears to have any practical application in man. The ultrasonic Doppler method has been used to demonstrate the vertebral artery blood flow but this gives no direct indication of the perfusion of the inner ear. Using this method, the vertebral blood flow in 10 patients with sudden deafness was estimated before and after stellate ganglion block (Sano et al, 1985). Using the blood flow index it was found that the flow in the vertebral artery on the 'blocked' side was greatly increased but with little change on the 'unblocked' side.

Inhalation of 5% carbon dioxide: 95% oxygen (carbogen)

Using the polarographic technique, Nagahara, Fisch and Yagi (1983) and Fisch (1983), measured the oxygen tension in human perilymph. Following the inhalation of carbogen (5% CO_2 : 95% O_2) they demonstrated two different patterns of disturbed perilymphatic oxygenation; in sudden deafness and sudden cochleovestibular loss of inner ear function, there were low initial values but a normal response to inhalation, while patients with a slowly progressive sensorineural hearing loss showed normal initial values but a low response to carbogen. In a group of seven patients who presented with sudden deafness with or without vertigo but normal caloric responses, there was an initial value of perilymphatic oxygenation of 8.6 mmHg which rose after 13 minutes to an average of 14.8 mmHg (an increase of 175%). No significant correlation could be found between the hearing loss, or the initial value and maximal response to carbogen inhalation. Likewise there was no significant correlation between the initial value of oxygenation and the time interval between the onset of deafness and the measurement, that is the duration of the disease. In four patients with some cochleovestibular loss, the carbogen response started after 45 seconds and reached a maximum of 20.7 mmHg (an increase of 215%) 15 minutes after the onset of inhalation. The mean initial values of perilymphatic oxygenation were below the normal range obtained in cats, and in otosclerotic patients. In patients with sudden cochleovestibular loss, a significant correlation

was found between the initial value of perilymphatic oxygenation and the duration of the disease.

Fisch, Nagahara and Pollak (1984) have emphasized that the arterial PCO_2 has a stronger effect on the oxygenation of the perilymph than the arterial PO_2. Similarly hypoventilation induces an increase of the perilymphatic oxygen, while hyperventilation is followed by the opposite effect. Hypoventilation causes the arterial PO_2 to drop, while the $PaCO_2$ increases. The combination of 5% CO_2 and 95% O_2 gives a fourfold increase in perilymphatic oxygen compared with pure oxygen alone or the inhalation of CO_2 in air. The recommended regimen, therefore, is the inhalation by mask of 95% O_2 and 5% CO_2 for 30 minutes eight times per day at intervals of one hour. Baghat and Shenoi (1982), using this regimen in four patients who were carefully monitored, achieved a good hearing improvement in three who received the treatment within a fortnight of the onset of deafness, but in the remaining patient, after an interval of 4 months, there was no change. It was originally Shea and Kitabchi (1971, 1973) who advocated inhalations of 5% CO_2 and 95% O_2 for 30 minutes four times a day, but this earlier work seems to have been largely overlooked.

Hyperbaric oxygen

Pilgramm, Lenders and Schumann (1985) reported the use of this treatment for one hour at 250 kPa (2.5 bar) in 37 patients with sudden deafness of acute onset and a further 51 non-acute cases. In a controlled trial, they concluded that patients with sudden deafness of acute onset fared better in terms of hearing gain and tinnitus reduction and that hyperbaric oxygen therapy was therefore an effective adjunct where it was available.

Anticoagulants

There no longer seems any indication to give these unless indicated by the haematological investigations or other disease within the cardiovascular system. Heparin may be chosen in the initial stages and has an effect in reducing the serum lipid level and by stimulating lipoprotein lipase formation; it also binds with histamine.

Steroid therapy

Treatment of a vascular cause by trying to improve the local circulation within the cochlea appears entirely reasonable, as has been outlined above. In all other branches of otology great stress is placed upon the tests designed to diagnose the site of the lesion. In our present state of knowledge therefore it appears illogical, having carried out such tests, to jettison the results in favour of a single treatment modality particularly when it involves the use of a group of potent drugs - steroids. It has been the experience of Morrison and Booth (1970), and remains so, that steroids are the treatment of choice when the loss is retrocochlear, and are the only effective treatment in the severe case of this type. It should be remembered that some two-thirds of cases with idiopathic sudden hearing loss may be expected to recover completely, or partially, particularly if the loss is moderate. Wilson, Byl and Laird (1980) carried out a double-blind clinical trial on the efficacy of steroids and concluded that they had a statistically significant effect on the recovery of hearing in patients with moderate hearing losses. However, in so doing, they assumed that a substantial proportion were of viral origin, but made no attempt to correlate this with the probable site

of the lesion. It cannot be emphasized enough that such tests are required and may well need to be repeated as more hearing is recovered, thereby allowing more detailed testing (Kumar, Maudelonde and Mafee, 1986).

All forms of steroids have been used and selection should probably depend on personal experience. Patients receiving these drugs should be examined at regular intervals for side-effects including checks on blood pressure, serum electrolytes and if appropriate, electrocardiography. For clinicians without an established or familiar scheme, prednisone may be recommended, 60 mg on the first day in divided doses (every 6 hours), 50 mg on the second day, 40 mg daily for 3 days, 30 mg daily for 3 days and then the regimen may be tailed off, so that the patient ends medication after approximately 3 weeks.

Bed rest

If there is the possibility of a membrane rupture, rest in bed may be indicated. Certainly, strenuous exertion should be avoided.