SENSORINEURAL HEARING LOSS

A Ciba Foundation Symposium

Edited by
G. E. W. WOLSTENHOLME
and
JULIE KNIGHT

J. & A. CHURCHILL
104 GLOUCESTER PLACE, LONDON
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Preface

In October 1968 Mr Jack Ashley, MP, wrote to enquire whether the Ciba Foundation would consider calling together an international group of otologists, pathologists, epidemiologists, biochemists, physicists, electronic engineers, and any others who might conceivably contribute to a discussion of the way in which future research on perceptive deafness might be more effectively organized. At the time we had a full programme for a year or two ahead and I sent a regretful reply.

I felt unhappy about denying this opportunity to a victim of total deafness, who with the aid of his wife was courageously turning this personal disaster, through his public life in parliament and on television, into a drive for better recognition of the needs of the deaf everywhere for improved care and research. A note from Mr Ashley courteously not accepting defeat was more than enough to persuade me to add this further symposium to our commitments in 1969.

It is doubtful whether any symposium on Sensorineural Hearing Loss could be satisfactory but we hope that the members who contributed so cooperatively and concernedly to this one, and to the preparation of these proceedings, will be encouraged to persevere with current lines of research and be prompted to discover others. Any improvement in outlook for the deaf will be a rich reward to Jack and Pauline Ashley and their many friends.

Illness prevented Professor S. Rauch from taking part in the symposium and we were grateful to Dr Phyllis Stopp and Dr S. K. Bosher who stepped in at very short notice with papers on the labyrinthine fluids. Dr F. B. Simmons was also unable to come but sent his paper after the meeting.

All who were involved in the symposium are much indebted to Dr I. C. Whitfield for the eager and friendly way in which he directed these multidisciplinary discussions.

G. E. W. Wolstenholme
The Ciba Foundation

The Ciba Foundation was opened in 1949 to promote international cooperation in medical and chemical research. It owes its existence to the generosity of CIBA Ltd, Basle, who, recognizing the obstacles to scientific communication created by war, man's natural secretiveness, disciplinary divisions, academic prejudices, distance, and differences of language, decided to set up a philanthropic institution whose aim would be to overcome such barriers. London was chosen as its site for reasons dictated by the special advantages of English charitable trust law (ensuring the independence of its actions), as well as those of language and geography.

The Foundation's house at 41 Portland Place, London, has become well known to workers in many fields of science. Every year the Foundation organizes six to ten three-day symposia and three or four shorter study groups, all of which are published in book form. Many other scientific meetings are held, organized either by the Foundation or by other groups in need of a meeting place. Accommodation is also provided for scientists visiting London, whether or not they are attending a meeting in the house.

The Foundation's many activities are controlled by a small group of distinguished trustees. Within the general framework of biological science, interpreted in its broadest sense, these activities are well summed up by the motto of the Ciba Foundation: *Conscient Gentes*—let the peoples come together.
The deaf world will be profoundly grateful to Dr Wolstenholme and the Ciba Foundation for establishing this symposium. It is an event which can have far-reaching effects on the lives of deaf people all over the world because it is a constructive attempt to shed light on the intractable problem of sensorineural deafness.

Exactly two years ago today to the day my hearing was reasonable. But after a myringoplasty and what the surgeon described as "it's what they call a virus" I was shunted from a life of normal hearing into a new world of total deafness.

The most shattering feature of sensorineural deafness is its finality. We live in an age when men are given new hearts and promised new genes, but the totally deaf are denied hope. Why? Is it because the problems are too complex for modern medical science? Or because the deaf rank too low in the order of medical and financial priorities?

In medicine, as in politics, there are fashionable subjects, and I believe deafness is regarded as one of the least glamorous. If this was merely a manifestation of professional snobbery it could be disregarded. But if it results in lack of resources, shortage of skill and inadequate finance it must have serious effects on future research.

But how far are otologists themselves responsible for the lack of fundamental research? You wouldn't wish me to be less than frank as your appreciative guest. And I must say that I detect among some of your colleagues an enthusiasm for middle ear surgery and a pessimism amounting to despair about sensorineural deafness. That made sense in the 1950s but it is inadequate for the 1970s.

It is an attitude typified by the reaction to tinnitus whenever that unhappy subject is raised. There is a regretful head shaking and a muttering of the ancient incantation that "you must learn to live with it". No politician could give such an answer when confronted with serious problems. Why should otologists?
I suspect that no concerted effort is made to tackle the hidden but serious problem of tinnitus because its disabling effects are little appreciated except by those who suffer from it.

This is one of the major difficulties of sensorineural deafness. No disability presents a greater challenge to the imagination. It is invisible. It cannot be simulated. It is an unseen individual cage.

The onset of total deafness can be a shattering experience which devastates and sometimes drowns a man in a sea of silence. Yet, what Dr Johnson called "the most desperate of human calamities" drifts belatedly in the medical backwaters.

It's not surprising that some of your colleagues are disheartened. Yet they are wrong, because there is an increasing awareness of the problems and a new attitude developing towards sensorineural deafness. A growing number of men are seeking to apply modern tools of medical science in new methods of research. They realize that fragmented and duplicated efforts are wasteful and that the different strands of research must be woven into a coherent pattern.

It is an attitude which underlies the growing demand for national research institutes and for an international agency which can plan the pattern of future research. I hope that from your deliberations will emerge constructive ideas for planning in the future. I believe that the planning, like the composition of this symposium, should be multidisciplinary. Because although it is widely recognized that otologists alone cannot solve the problems of sensorineural deafness, I know of no plans to integrate the many medical disciplines necessary for a concerted effort.

The members of this symposium can give a lead. There is no shortage of historical reviews and we can learn from the past. But the past is dead. We now require a careful assessment of future needs and specific recommendations for research projects to be fostered in the future.

One day the forbidding Everest of sensorineural deafness will be scaled. It will not be done without a determined assault requiring far-sighted planning and international cooperation. But I am convinced that it will be done. And the group of men who scale the heights will not only carve their niche in history; they will rescue men, women and children from a tomb of silence. There can be no nobler achievement than that.
CHAIRMAN’S INTRODUCTION

I. C. WHITFIELD

In introducing this symposium I want first to take up Mr Ashley’s point of the very serious nature of the disability we shall be discussing. Man is a gregarious animal who lives by communication with the world around him, and loss of hearing is probably the most psychologically traumatic of the sensory losses that he can undergo. We are quite accustomed to not being able to see half of what goes on around us—we can look only one way at a time—but hearing takes in all our surroundings; it lets us know what goes on behind our backs—and most of us like to know what is going on behind our backs! Absence of hearing raises problems of verbal communication too, not only in learning the sheer mechanics of exchanging information by speech, but because such communication has a strong emotive content and one that can only be shadowed in print, where it has nothing like the same force.

Deafness, whether brought about by accident or disease, has always been with us, but it is a problem that is growing. Not only is the hearing mechanism subject to direct local attack, but it is also peculiarly susceptible to attack by extraneous chemical substances, whether they be from systemic diseases or from systemically administered drugs. We can in some cases do quite as much damage in trying to cure the diseases as the diseases caused in the first place, so that we may not gain on the situation unless we have a thorough understanding of events in the inner ear and what damage we may inadvertently do. A more serious problem, in that it is more widespread, is the increase in deafness due to industrial noise. The susceptibility of the ear to over-stimulation has been known for many years as a hazard of certain occupations, but only recently have the noise levels to which the general population is exposed become so great that they are liable to reach damaging proportions.

The central nervous system has been popularly compared to a computer. It has at least one thing in common with the modern miniaturized computer, namely that if it goes wrong you can’t mend it! In the case of the computer we can pull out the appropriate card with the offending element, throw it away and put in another one. We don’t yet know how to do this with the nervous system, and in spite of some successful organ transplants it seems
very doubtful whether we ever shall. We have two courses open to us: one is to try to prevent the breakdown occurring, and the other is to provide a substitute—a prosthesis—for the damaged part of the mechanism. Both of these solutions require a thorough understanding of how the mechanism of the inner ear works, and this understanding we have at the moment only in part—a very small part. In this symposium our task will be to look at the present state of the art, to see where we stand, and particularly to map out what are likely to be the profitable paths for the future. We can't go everywhere, but we must understand where the main risks lie and what are the possibilities of minimizing them.
THE CAUSES OF PROFOUND DEAFNESS IN CHILDHOOD

G. R. Fraser

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SCOPE OF THE SURVEY

Over the past 12 years I have been studying a total of 3534 individuals who have been profoundly deaf from childhood. An additional 34 persons were misclassified as deaf and owed their difficulties with speech, which led to their original inclusion in the survey, to other causes. A small further series of 21 cases was studied in whom the deafness was only unilateral and due to malformations of the auditory apparatus.

For the purposes of this study profound deafness in childhood is defined, with minor exceptions discussed below, as hearing loss of sufficient severity and of sufficiently early onset to necessitate the use of special educational methods for the acquisition of speech or alternative methods of communication. It should be emphasized that this definition, based as it is on educational criteria, is a pragmatic one adopted for convenience of ascertainment. It does not correspond to any simple biological basis, involving, for example, the distinction between forms of deafness which are congenital and those which are of later onset (in so far as this distinction can be accurately made) or involving any particular objective range of hearing loss. These questions of ascertainment of childhood deafness are of considerable complexity and in this series, as in any other, the criteria of selection should be clearly borne in mind.

Nevertheless, although this definition is not a biological one, there is reasonably good correspondence between the degree of hearing loss and the presence of educational handicap, so that this series includes in the main the more severe forms of deafness of childhood onset, almost invariably perceptive in type. It contains very few cases of the mild deafness due to recurrent infectious disease which is so common in childhood, and does not include persons with otosclerosis and with the perceptive hearing losses of adult life which become increasingly frequent with advancing age.
Table I gives an indication of the ascertainment of these individuals. The figures in the table have to be adjusted to allow for the double ascertainment of 47 individuals in two separate sub-groups during different phases of the study. It will be seen that the main part of the survey concerns 2355 deaf children in special schools in the British Isles, including the Republic of Eire, and that two other substantial studies were done of populations—one in the English counties of Oxfordshire and Berkshire and one in South Australia. In these studies an attempt was made to ascertain all persons in

Table I

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<th></th>
<th>Males</th>
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<td></td>
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<tr>
<td>The school study</td>
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<td>1064</td>
<td>2355</td>
</tr>
<tr>
<td>Oxfordshire and Berkshire study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>87</td>
<td>93</td>
<td>180</td>
</tr>
<tr>
<td>Children</td>
<td>139</td>
<td>113</td>
<td>252</td>
</tr>
<tr>
<td>Deaf with visual handicap</td>
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<td></td>
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</tr>
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</tr>
<tr>
<td>Children</td>
<td>9</td>
<td>14</td>
<td>23</td>
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<tr>
<td>Mentally subnormal deaf</td>
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<tr>
<td>Adults</td>
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<td>Children</td>
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<tr>
<td>Adult females living in a protected environment in Dublin, Eire</td>
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<tr>
<td>Families referred specially</td>
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<tr>
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<td>72</td>
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<tr>
<td>Children</td>
<td>80</td>
<td>96</td>
<td>176</td>
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<tr>
<td><strong>South Australia</strong></td>
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<td></td>
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<tr>
<td>Adults</td>
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<td>154</td>
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<tr>
<td>Children</td>
<td>113</td>
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<tr>
<td><strong>Total</strong></td>
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<td>3636</td>
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</table>

the area who suffered from profound childhood deafness by working with educational and welfare authorities, but this aim could not be achieved in the case of the adults in Oxfordshire and Berkshire. Among these, inclusion in the survey was voluntary and only about half chose to collaborate. Among the children in these two counties, ascertainment was on a wider basis in that the cooperation of medical, as well as social and educational, authorities was sought, and thus many children were included whose hearing loss was milder than in the other sub-groups studied.

Small series of persons who were mentally subnormal or who had severe visual handicap as well as deafness were also studied. In addition, a group of 72 women living in a sheltered environment in a home connected with a school for deaf children in Dublin collaborated in the survey.
Lastly, the 176 persons referred specially belonged to families in which the clinical features or accompaniments of the deafness were of particular interest. These persons were referred by medical, social and educational authorities all over the British Isles; a few were referred by deaf friends, and a further small number responded to advertisements in journals for the deaf.

IDENTIFICATION OF THE CAUSE OF DEAFNESS

It is no easy matter to identify the proximate cause of hearing loss in each of a large group of deaf people. Various methods were used in an attempt to achieve this aim. Firstly, particular attention was paid to the alleged cause of hearing loss as reported by the index cases or their parents. In the case of acquired causes, an attempt was made to verify from medical sources details of illnesses in the perinatal period, in infancy, and in childhood which may have contributed to the deafness.

Secondly, an examination of each deaf person was undertaken, including inspection of the head and neck region to detect obvious malformations, and a more detailed clinical examination was made if warranted. In addition, palpation of the neck to evaluate thyroid size, and ophthalmoscopy were performed on each person surveyed. Lastly, electrocardiographic tracings, using one lead only, were taken of a large proportion of the propositi.

Thirdly, genetical information about the family, together with records about deafness and other diseases in relatives, was collected either by questionnaire or by personal visit where this was geographically convenient or where the answers to the questionnaire indicated some special reason for further investigation. The results of these family studies were used in the evaluation of the cause of deafness in each case as well as for statistical analyses pertaining to the material as a whole.

Each of these three main methods of enquiry will now be discussed in some detail in the context of the light which it throws on aetiological aspects of profound deafness in childhood.

Identification of cause on the basis of anamnestic evidence

In the simplest case, a child may have been known to have been hearing normally before an attack of meningitis or some other severe illness but deafness may have been noted immediately after recovery. In such cases, it is often not possible to determine whether the deafness is due to the effect of the illness, to drugs such as streptomycin given as treatment or to a combination of the two. In some cases, it is clear that only the drug is responsible,
as, for example, when streptomycin is given for the management of pulmonary tuberculosis. In either case, whether the illness or its treatment is responsible, a firm diagnosis of acquired deafness may be made. Unfortunately, however, it is only in a proportion of cases that the acquired cause of deafness as determined in this way can be accepted without reservation. This is because the crucial evidence that the child was hearing normally before the illness may be lacking, and the proportion of cases where this evidence is missing increases with decreasing age of the child at the time the alleged causative illness occurred. Thus, when the illness occurred in the perinatal period, such evidence is lacking altogether and, even when the child is older, there is an understandable tendency on the part of parents to rationalize and to claim that the child heard normally beforehand when in fact there can be no doubt that the hearing loss antecedent the disease in question. This tendency can be seen particularly well with common diseases such as measles and whooping cough through which a majority of infants passed until recently, and there can be no doubt that today these diseases are not as common causes of the profound type of deafness discussed here as might be gauged from the parents' accounts. Parents are anxious to avoid the supposed stigma of having a child who is deaf through an "unknown" cause and they are aided in their rationalizations by the very variable pattern of speech acquisition which leads to deafness often being explained away as "slow development".

Thus, certainly if the alleged onset of deafness due to disease is before the age of two years and in many cases even later, the cause as given by the parents cannot be accepted unreservedly, and such caution is even more necessary where the parents are dead or cannot be contacted and only the account of the deaf person or hearsay evidence is available. Thus, I have made it a practice to accept disease occurring before the age of three years as a cause of profound deafness only if there is a firm indication that the child heard normally previously and, usually, only if there is evidence that the disease was a serious one, such as meningitis, pyogenic or tuberculous, or if there is evidence that an ototoxic drug such as streptomycin was used. Exceptions do occur, in that measles and whooping cough do occasionally give rise to deafness of sufficient severity to cause educational handicap, and a few such cases were accepted. Middle ear disease is now very rarely a cause of profound deafness in children but may give rise to so-called "partial" deafness; it is more important in adults in whom permanent damage may have occurred when they were children, at a time when antibiotics were not available.

Injury of the skull may give rise to deafness occasionally and other rare
acquired causes acting in infancy and childhood are mumps (usually responsible for unilateral rather than bilateral deafness), poliomyelitis, encephalitis due to a number of viruses, including those of measles, mumps and poliomyelitis, and scarlet fever. Other diseases which can be associated with the causes of deafness, either because of involvement of the brain in the infectious process or because streptomycin and other ototoxic drugs are used in treatment, are pneumonia, especially if it is recurrent over many months, and gastro-enteritis. In a few cases in the present survey such diseases or their treatment were accepted as the proximate causes of deafness, but the vast majority of persons in whom acquired causes were accepted were deaf due to various types of meningitis. Lastly, in a small number of persons, deafness followed apparently trivial illnesses. Sudden losses of hearing of this type are well-documented and are assumed to be due to mild viral infections which may not even cause clinical symptoms; fortunately, such hearing loss is usually unilateral.

Anamnestic medical evidence, therefore, cannot be regarded as a definitive guide to the aetiological basis of deafness in the individual case and there is often a subjective decision involved. Thus, sometimes a spurious cause adduced by the parents may be wrongly accepted; on the other hand, misdiagnoses may occur in the opposite direction also, in that illnesses are erroneously rejected as causes of hearing loss. This difficulty recurs with every single cause of deafness and it is to be hoped that in an analysis involving the whole material rather than individual cases these two opposing tendencies will balance each other.

Identification of cause is even more difficult in the case of deafness due to illnesses and other events which take place at birth, in the neonatal period, and in the first few months of life, since at this time no cause and effect relationship can be established by direct evidence between any particular untoward incident and the onset of hearing loss. Nevertheless, there can be no doubt from both my own data and those of other investigators that there is an association of prematurity with deafness (as is the case with almost every other type of childhood handicap), or rather an association between deafness and types of traumatic episodes in early life (especially in the neonatal period) which occur with increased frequency in premature children. What precisely leads to deafness during these episodes is still an open question. It may be anoxia, it may be profound neonatal jaundice, it may be the administration of streptomycin, either to sick neonates or prophylactically, its effects aggravated by the immature excretory system of the infant of low birth weight, or it may be a number of other factors either alone or in combination. Certainly, jaundice and kernicterus can be
incriminated as a cause of deafness in neonatal disease due to rhesus incompatibility, and there are good a priori grounds for supposing that streptomycin can cause deafness when administered in early life. Anoxia may be associated with cerebral haemorrhages at and shortly after birth, and these may cause deafness together with other neurological abnormalities subsumed under the term of cerebral palsy.

Thus, I have accepted turbulent events in the neonatal period as a cause of deafness when there is evidence of profound jaundice, especially when this is supported by the presence of other types of neurological involvement, when there is evidence of the administration of streptomycin, and when there is evidence of birth injury such as cerebral palsy. In this way, however, only a minority of cases whose deafness is due to adverse events in the perinatal period will be accepted as such, since information of this type is difficult to document and, furthermore, such cases will not always show evidence of one or other of these specific types of events.

In the case of deafness acquired in the prenatal period the situation regarding diagnosis is again very complex. The most common such cause today is, of course, maternal rubella and, since this association became generally known, it has been eagerly accepted as a possible explanation of deafness, both by the parents of deaf children and by their medical attendants, where otherwise the cause would have been "unknown". Errors may again occur in the opposite direction also, in that deafness may be due to sub-clinical attacks of rubella of which the mother would not have been aware. Thus, particular attention has to be paid to the details of the mother's account of the attack of rubella in pregnancy and on close questioning it becomes clear in many cases that it is a spurious episode which has been adopted as an explanation post facto. More recently, antibody studies can be used as an aid to diagnosis of rubella embryopathy, but they are extremely fallible in a retrospective survey such as this. In fact, no attempt was made to use such evidence but much reliance was placed on the clinical evidence, discussed more fully in the next section.

Other much rarer causes of deafness acquired in the prenatal period include congenital syphilis (previously much more common), toxoplasmosis, possibly viruses other than rubella, and administration of drugs such as streptomycin, thalidomide and quinine to the mother. There are, of course, very great difficulties in accepting anamnestic evidence of such causation. This is particularly so in cases where the child is illegitimate or adopted, or where there is a suspicion or even a confession of attempted abortion; such problems are common in the study of all types of childhood handicaps.
Identification of cause on the basis of clinical evidence

The simplest type of evidence which is of assistance in identifying the cause of deafness is the audiogram. Unfortunately, however, it is rare for bone conduction findings to be recorded and it is not uncommon to discover a substantial conductive component of congenital hearing loss for the first time in an older child or even an adult. When such a conductive component was found in this survey, it was virtually never due to otosclerosis, which does not cause severe handicap in childhood, and only very rarely to otitis media, which is responsible today for only a few cases of

Fig. 1. A girl with an autosomal recessive syndrome of multiple malformations, which often includes deafness due to abnormalities in the development of the ossicles. This condition is often called the cryptophthalmos syndrome after the salient feature depicted here, a failure of formation of any cleft between the eyelids, the ocular globe itself being rudimentary. This is associated with widespread malformations of the face, skeleton, viscera and external genitalia. Although each component may be only partially present or even absent in a given case, the constellation of defects is rather specific. This variability of gene expression applies even to its ocular manifestations, giving rise to the paradox of the cryptophthalmos syndrome without cryptophthalmos. Renal hypoplasia is a constant feature of the syndrome and, when it is gross and bilateral, is incompatible with life. Thus, possibly only a minority of cases survive more than a few days and, in fact, the sister of this girl died for this reason soon after birth. (Reproduced by kind permission of the Editor of the Journal of Medical Genetics.)
hearing loss, some of which occur in persons who have malformations such as cleft palate predisposing them to recurrent attacks. More usually, a substantial conductive element in the hearing loss indicates a malformation of the middle and sometimes of the outer ear, and such malformations have been found in the present survey as components of the autosomal recessive syndrome of cryptophthalmos (Fig. 1), of a sex-linked condition described by Nance and co-workers (1970), and of at least two autosomal dominant conditions involving defective embryogenesis of the first and second branchial arches, mandibulo-facial dysostosis (Fig. 2) and the "deafness-earpits" syndrome (Fig. 3), described by Wildervanck (1962) among others. There are many other simply inherited syndromes which have conductive deafness as a component.

In some of these syndromes, the middle ear malformation is highly specific; for example, in the sex-linked syndrome mentioned above there

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Fig. 2. A case of the mandibulo-facial dysostosis in a female infant. As well as malformations of the auricle with atresia of the external meatus, anti-mongoloid slope of the palpebral fissures and macrostomia demonstrated here, affected persons often show malformations of the middle ear, colobomata of the lower eyelid, high palate and malformed teeth, blind fistulae between the angles of the mouth and the ears, and abnormal implantation of the facial hair. Abnormalities of the facial skeleton can often be demonstrated radiologically, involving principally hypoplasia of the malar bones, of the zygomatic processes of the temporal bones, and of the mandible. (Reproduced by kind permission of the Editor of the Journal of Medical Genetics.)
FIG. 3. A boy with the "deafness-earpits" syndrome. Apart from the marginal pit and the pre-auricular tubercle seen here, other deformities of the auricle including flapped ears, bat ears, low-set ears, and gross hypoplasia, or even aplasia, with atresia of the external meatus may occur. Fistulae may also occur in the neck and another facultative feature of the syndrome (which this boy shows) is cleft palate. Deafness is due to malformations of the middle ear and is often purely conductive. Sometimes, however, there is in addition a substantial perceptive component.

is a congenital fixation of the footplate of the stapes and an abnormal patency of the cochlear aqueduct which has resulted in a gush of perilymphatic fluid being encountered at surgery in several cases. Operation is frequently performed with a view to corrective surgery when there is a suspicion of middle ear malformation and operative findings are of substantial help in diagnosis; X-ray findings may also be helpful to a more limited extent.

In addition, conductive deafness due to malformations of the outer and/or middle ears may occur as part of the "first and second branchial arch syndrome" (Grabb, 1965) which is not associated with simple Mendelian inheritance. Such cases can often be distinguished from the autosomal dominant syndromes mentioned above on either clinical or genetical criteria, but confusion may occur in that they may represent fresh mutations for genes causing these syndromes or the expression of the gene in relatives may be so minimal that it may be missed.

In the vast majority of cases surveyed the deafness is entirely perceptive. Fisch (1955) showed that there was a correspondence between audiometric
patterns and the actiology of perceptive deafness and, although, of course, such correspondence is far from absolute and very many exceptions occur, the shape of the audiogram has been of some help in the identification of cause. In outline, a flat audiogram suggests rubella, a saucer-shaped audiogram kernicterus, a gently sloping audiogram with the high tones affected more than the low is often seen in dominant deafness, and a sharply sloping

![Diagram of family tree]

**Fig. 4.** This family, manifesting the association of perceptive deafness with sporadic goitre (Pendred's syndrome), shows the typical features of autosomal recessive inheritance (more than one sib affected, consanguinity of parents). The radio-iodine study shows in the affected individuals a discharge of inorganic iodide, administered one hour previously, with potassium perchlorate. In normal individuals, the perchlorate inhibits further uptake of radioactive iodide but there is no discharge since the iodide is almost instantaneously converted into organic form and therefore is no longer dischargeable. In this respect the two heterozygous daughters of the affected sisters show a normal reaction. The audiograms of the two cases show patterns typical of recessive deafness with some residual hearing in the low tones; the hearing of their heterozygous daughters is normal. (Reproduced by kind permission of the Editor of the *Quarterly Journal of Medicine.*)
audiogram with a residual island of hearing in the low tones suggests
autosomal recessive deafness. Failure to respond to maximal stimulation
over the whole range of frequencies of the audiometer is most often
associated with deafness acquired during a serious illness such as meningitis.

Tests of vestibular function are not very helpful since sophisticated
determinations are very difficult to perform and, in any case, not enough is
known about the range of vestibular defects associated with each type of
hearing loss. Radiological examinations could be of some use since visualization
of the inner ear is becoming increasingly practicable, and thus persons
in whom the bony structure of the labyrinth is abnormal may be differentiated
from the majority in whom the deafness is due to changes at the
microscopical level in the organ of Corti.

Otolological investigation, however, is not of as much use as the remainder
of the clinical examination. Thus, palpation of the neck may indicate cases
of the autosomal recessive syndrome of deafness with goitre (Pendred's
syndrome) and this diagnosis may be confirmed by appropriate tests using
radio-iodide (Fig. 4). Ophthalmoscopy may reveal cases of the autosomal
recessive syndrome of deafness with retinitis pigmentosa (Usher's syn-
drome). These persons frequently have an ataxic gait and there have been
suggestions that vestibular function is more often impaired in this condition
than in other forms of hereditary deafness. Finally, the electrocardiographic
tracings will uncover cases of the surdo-cardiac syndrome of Jervell and
Lange-Nielsen (1957), a third condition inherited in an autosomal recessive
manner, consisting of deafness in association with disturbances of cardiac
conduction (Fig. 5) leading to recurrent attacks of syncope which may
prove fatal.

Inspection of the head and neck region is also very helpful. Thus, a
whole group of auditory-pigmentary syndromes may be detected. The
classical form described by Waardenburg (1951) involves lateral dystopia
of the medial canthi of the eyelid (Fig. 6) as well as various pigmentary
anomalies such as partial albinism of eyelashes, hair and ocular fundi,
patches of hyper- as well as hypo-pigmentation of the skin, and hetero-
chromia or bilateral hypochromia of the irides. However, the eyelid
deformity is absent in many families with deafness in association with
pigmentary anomalies, and it seems probable that this combination repre-
sents a heterogeneous entity involving two or more distinct syndromes
inherited in an autosomal dominant manner. In a family of Moroccan
Jews from Israel this association was inherited in a sex-linked recessive
manner (Margolis, 1962; Ziprkowski et al., 1962). This family is apparently
unique, although there is a possibility that two American Indian brothers
Fig. 5. Electrocardiogram (lead II) of a case of the surdo-cardiac syndrome of Jervell and Lange-Nielsen.

(a) Shows the resting state with gross prolongation of the QT interval.
(b) One minute after unintentionally induced fright. The T waves are now inverted and biphasic.
(c) Three minutes after induced fright. The changes seen in (b) are accentuated.
(d) Ten minutes after induced fright. The T waves are now upright and monophasic but the tracing has still not completely reverted to its resting pattern (a).

(Reproduced by kind permission of the Editor of the Quarterly Journal of Medicine.)

from Arizona described by Woolf, Dolowitz and Aldous (1965) suffer from the same condition.

Inspection of the head and neck region can also reveal cases of Wildervanck's syndrome, or perceptive deafness with Klippel-Feil deformity of the spine (Fig. 7). This condition does not seem to be inherited in a simple Mendelian manner and shows a peculiar sex distribution in that ten or more females are affected for every male, even though the Klippel-Feil deformity itself occurs with equal frequency in the two sexes. Thus, Wildervanck's syndrome may be responsible for as much as 2 per cent of deafness among females. It seems that the deafness is due to gross deformity of the osseous labyrinth. Many other malformations, such as cleft palate and abducens palsy, to mention only the common ones, may be seen in association with this syndrome.

There are a large number of further malformation syndromes affecting particularly the head and neck region which may include deafness as a
This girl manifests several of the features of Waardenburg's syndrome. She has bilateral profound perceptive deafness, marked lateral displacement of the medial canthi of the eyelids and a white forelock.

Wildervanck's syndrome of profound perceptive deafness, associated with osseous malformations of the labyrinth, and Klippel-Feil deformity of the spine. The pre-auricular tubercle is a facultative component. (Reproduced by kind permission of the Editor of the Journal of Medical Genetics.)
Fig. 8. (a) The retinal appearance characteristic of rubella embryopathy. Even when present to such a pronounced degree, these retinal abnormalities do not interfere with sight and when visual loss occurs in these children it is always due to cataracts. More usually, the retinopathy is much milder and is manifested ophthalmoscopically only by stippling of the macular region (b).