"SYDROMES ASSOCIATED WITH HEARING LOSS"

- A Review.

Reg. No.1
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An indendent project work submitted on part part fullment for First Year M.Sc (Speech & Hearing to the University of Mysore, Mysore.

All India Institute of Speech & Hearing, Mysore

C E R T I F I C A T E

This is certify that the independent project entitled

Syndromes Associated with Hearing Loss"

- A Review

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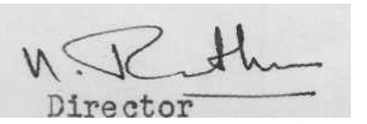

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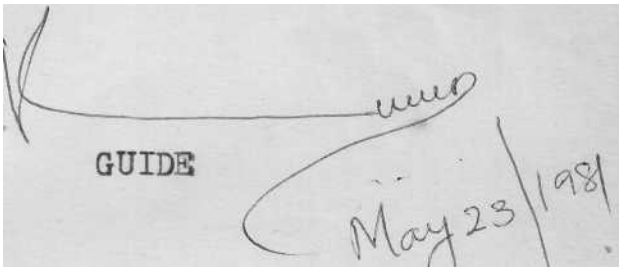
CERTIFICATE

This is to certify that the Independent project titled "SYNDROMES ASSOCIATED WITH HEARING LOSS - A REVIEW" has been prepared under my supervision and guidance.



D E C L A R A T I O N

This independent project entitled -

"Syndromes Associated with Hearing Loss"
- A Review

is the result of my work undertaken under the guidance of Mr. P.J. Kumar, Lecturer in Audiology All India Institute of Speech and Hearing, Mysore - 6 and has not been submitted at any University for any other Diploma and degree.

Mysore

Dated:29thMay1981 Register No. 1

A C K N O W L E D G E M E N T S

I express my gratitude to Mr. P.J. Kumar Lecturer in Audiology, All India Institute of Speech and Hearing, Mysore, for his invaluable guidance.

I thank Dr. Shailaja Nikam for providing me an opportunity to undertake this project.

My sincere thanks to Dr. N. Rathna, Director All India Institute of Speech and Hearing, who continues to be the source of inspiration.

Special thanks to V.U. Nandur and Veena for their valuable help and suggestions.

Finally, I acknowledge everyone who helped me to complete this work.

-Last but not the least, I thank Miss Padmavathi Bai for the efforts she has put in to neatly type this project in time.

DEDICATED

TO

MY PARENTS

AND ALL MY DEAR ONES

PREFACE

Hearing loss can be caused by multifarious factors. Usually hearing loss in an individual occurs as an isolated entity. But often we do come across individuals demonstrating hearing loss with various other abnormalities. In such cases, hearing loss can be an associative factor or a primary factor falling under the domain of a syndrome. In literature so far to date, about 300 different syndromes are reported where in the general outstanding characteristics of the associated hearing losses are described.

Inevitably, this literature has arisen from a wide variety of sources. Dedicated investigators in the allied disciplines of Psychology, Speech Pathology and Audiology and Medicine have contributed to the emergence of various syndromes thus giving us a finer insight into the definite nature and cause of hearing loss.

The purpose of this project is to collect within a single volume, the more important findings eminating from these diverse sources to enable the reader to get a comprehensive and varied knowledge about each syndrome that is associated with hearing loss. Since no attempt has been made in our country to integrate such an information. The information provided in the project will be of great help to researchers, teachers and future students in the field of Speech and Hearing.

This project contains Eleven Chapters broadly categorized into genetic and non-genetic types of hearing losses. The first ten of these chapters deal with various types of genetic hearing loss associated with abnormalities of various systems, namely, external ear, eye, renal, integumentary, musculo skeletal, nervous system, metabolic and chromosomal disorders. The last chapter deals with non-genetic type of hearing loss acquired during prenatal, perinatal period or in later life.

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INTRODUCTION

Any individual with a detectable impairment of hearing may be termed as being deaf. The deafness may be conveniently described as slight, moderate and severe.

Deafness is presumed to be present either at birth or acquired after birth. Therefore there is a natural distinction between 'Congenital Deafness' and 'Acquired Deafness'.

Congenital Deafness: may be defined as a more or less pronounced loss of hearing, present at birth, leading to mutism and transmitted by hereditary or acquired by chemical, physical or mechanical influences in the prenatal period (Van egmond 1954).

Congenital deafness is a common disease with an incidence of approximately one congenitally deaf child per thousand live births. The high incidence of congenital deafness presents a problem not only to the individual family, but to the entire community.

Analysis of the causes of congenital deafness in several communities in different countries have resulted in similar findings, i.e. there are two major causes (1) Genetic (2) Non-genetic or acquired causes. Approximately half of all congenital deafness is acquired as a result of Rh incompatibility,

infection with rubella during embryonic life, ototoxic drugs, prematurity, injury and various diseases. The other half of the congenitally deaf population is composed of children who are deaf because of specific genetically carried diseases.

Congenital deafness may be of two types. Conductive or sensorineural deafness. A child with congenital conductive deafness has either a major or a minor malformation or defect of the pinna, external auditory canal, middle ear ossicles and/or middle ear cavity.

The congenital sensorineural deafness are the most common. It may be produced by (l) failure of development (2) interruption of development (3) damage to tissues already developed. Those cases of congenital deafness which are due to failure in varying degree of internal ear to reach mature development have been grouped into four main types, named after the investigators who first gave a full description of the essential changes in the ear. The first type is Michel type where there is complete lack of the development of the internal ear as described by Michel. Second type is the Mondini-Alexander Type, in which there is the development of only a single curved tube representing the cochlea with similar immaturity of the vestibule and canals. The

third type is **Bing Scebenmann type** - where bony labyrinth is well developed, but membranous part is under developed. The fourth is the **Schiebes type** or cochleo-saccular type wherein the vestibular part of the ear is developed, and functional malformation is restricted to membranous cochlea and saccule.

Most cells of the inner ear are formed before the third month of gestation. If these cells die, no new ones are made The death of these cells result in permanent hearing loss.

In "dominant Transmission", in which only one of the parents need carry affected gene, the chances of the off-spring being affected is as high as 50 percent. On the other hand in recessive type in which both parents must be carriers of the particular gene and only 25% of the off-spring are affected. Consaguinity increases the probability of the children being affected. The sex linked inheritance, which is more complex, plays only a small role in deafness. The characteristic feature of sex linked inheritance is that only males are affected, and the males in the same family are related through carrier females.

Most cases of genetic hearing loss are recessive in nature and the hearing loss is usually sensorineural type. Several studies have shown that about 40% of profound child-hood deafness is autosomal recessive in origin, 10% is by dominant transmission and about 3% is caused by sex linked gene (Fraser 1964, Sank 1969). Genetic hearing loss may be congenital or be of late onset. It may be or may not be

progressive.

Congenital deafness may also result from factors other than genetic defects. One of the most commonly encountered diseases associated with acquired congenital deafness is German Measles (Rubella). The affected child is infected with German measles during the first three months of embryonic life. The child with congenital rubella can have several defects in addition to deafness like cardiac defect, mental retardation, cataracts, retinal degeneration etc. Another aignificant cause of acquired congenital deafness is Kernicterus. This syndrome usually consists of jaundice at birth, mental retardation, cerebral palsy and deafness. Prematurity is another common cause of acquired congenital deafness.after birth

Acquired Deafness: Deafness can also be acquired after birth. It may be acquired in post-natal period, or early childhood or adulthood or in later life. Deafness may be acquired as a result of infectious diseases, hereditory factors, vascular lesions, neurological deficits or unknown etiology. Meniere's Syndrome and Otosclerosis are the major examples of such acquisitions. The hearing loss which begins in later life may be a late manifestation of genetic hearing loss,as seen in Refrums and Alport's Syndrome. Acquired deafness may be temporary disappearing with adequate treatment or it may be permanent due to irreversible changes in the ear.

Hearing loss may occur as an isolated disorder or it may be associated with other symptoms. It has of course, been known for a very long time that many cases of congenital deafness have a strong tendency to occur in families and that congenital deafness may be associated with other congenital defects. Recent research has brought to light several conditions in which deafness forms but a part of a syndrome or a symptom complex hitherto unrecognized. Syndrome is a word derived from Greek, meaning "Syn"=together plus "Dramien" = to turn. Thus syndrome is an aggregate or set of concurrent symptoms indicating the presence and nature of a disease.

Uptodate in the literature, over 200 syndromes have been reported, which are associated with hearing loss. Each syndrome can be differentiated from the other by the type of hearing loss (Sensorineural or conductive), age of onset, severity of the hearing loss, mode of transmission (dominant, recessive or sex linked) and the abnormalities caused in other systems.

In 1951 Waardenburg first reported the association of deafness with pigmentary changes. The symptom complex described, included white forelock, broad nasal bridge, hetero chromia iridium and congenital sensorineural deafness.

There are several cardiac syndromes associated with deafness. The most startling of these is the cardio-auditory syndrome of Jarvell & Lange- Nielson. This Syndrome consists of sensorineural deafness, fainting spells and sudden death. A condition called Vander Hoeve's syndrome is characterized by fragile bones, blue sclera and hearing loss.

The triad of hearing loss, tinnitus and vertigo is popularly known as Meniere's syndrome.

It can be seen from the literature that every year many new syndromes are discovered and that more and more is being learnt about the already established syndromes.

Now, the question which has to be answered is "what is the need to study the syndromes associated with hearing loss?"

Audiology like medicine is an applied science, but there is an art of applying scientific knowledge and principles to ameliorate hearing disorders. An audiologist should understand the nature and causes of different hearing disorders before attempting to work with the hearing impaired at professional level. Unless the etiology and pathogenesis of hearing disorder is known or understood, there is little likelyhood that the disease will be prevented or treated effectively.

Deciding upon a specific diagnosis for deaf child is a common problem. If there is no evidence of acquired cause of deafness, hereditary etiology may be considered. When once the acquired causation is ruled out, the otologist and audiologist must recognize other diseases which are associated with deafness in their patients. Secondly the characteristics of hearing loss such as the age when it was first apparent, severity of loss, neural vs. conductive loss, progressive vs. non-progressive must be determined. Thirdly the family history may reveal other affected relatives who have or had similar hearing loss. With these three aspects of patients hearing loss in mind, reference books and lists of hearing loss symdromes can be consulted to determine whether the patient has a recognizable disorder. Sometimes follow up for a few years is necessary for important features of the disorder to become apparent. This is where a reference book consisting of discription of the characteristics and nature of hearing loss of all hearing loss syndromes would be very useful.

When once the patient's disorder is labelled, his/her problem can be communicated in a more meaningful way among different specialists of a team.

If the genetic aspect of the disorder is determined, then the patient can be given proper counselling as to

whether or not they may transmitt the disease to their children, and what is the probability of having other children similarly affected.

A thorough knowledge of the patient's disorder, will help to determine the future course of the disease, i.e. whether the patient has a good prognosis or is the prognosis poor.

If a patient's deafness is characterized and a proper syndrome identification is made, the research Otologist and Audiologist will be able to assemble groups of patients with similar disease. This in turn allows him to study these people in a meaningful way so that the underlying defects can be defined. Once these defects are defined, steps can be initiated either to prevent the defect from occuring in future cases or in those instances where there is progressive deafness, to prevent deafness from progressing further.

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CHAPTER I

GEMETIC HEARING LOSS

People can inherit various characteristics from their parents and grandparents. to Likewise hearing loss may also be transmitted from parents to offspring. Genes are the units of inheritance. There are thousands of genes in an organism and they are arranged on chromosome in a single row. like beads on a string. Each gene is a different substance, and is responsible for the expression of specific character. Genes operate in pairs. It is usual in genetics to say that each trait is determined by a single pair of genes. But this is incorrect, quite often many genes affect a single character or several pairs of characters are controlled by a single gene.

General Genetic Disorders:

Genetic disorders are of three types.

I. Chromosomal II. Single gene (Mendelian) and III. Polygenic (Multifactorial)

I. Chromosomal disorders:

Chromosomal disorders are by definition genetic, since they involve the major organizational elements of the genetic material namely chromosomes. In general when there are too few or too many chromosomes or segments thereof. Embryonic development of the fetus is disrupted. Multiple congenital

anomalies and with one or two exceptions, mental retardation are consistent features. The specific combination of findings reflect the chromosomal segment(s) involved. Deafness may be characteristic of some chromosome disorders eg. the Turner's syndrome, the condition due to loss of a segment of chromosome 18 (18iq- syndrome) and Trisomy 21 (Down's syndrome).

II. **Mendelian disorders**:

Mendelian disorders are due to specific mutations at certain gene sites on the chromosomes. The clinical behaviour of a mutation depends first on whether the gene site (locus) is on a sex chromosome (X or Y) or a non-sex-chromosome (autosome). Since genes operate in pairs (one on each member of a chromosome pair), expression of mutation depends on whether it is "dominant" (in which case, it is, expressed even in the presence of the normal gene) or "recessive" (in which case, it is masked by the presence of the normal gene).

There are three types of Mendelian inheritance.

a) Autosomal dominant
b) Autosomal recessive, and
c) X linked inheritance.

a) **Autosomal dominant disorder**:

In dominantly transmitted syndromes, a single gene is sufficient to produce the disease. This can be either in-

herited from a parent or derived anew as a fresh mutation. On the average an affected parent will transmit this gene to one-half of his children. Non affected children with a normal gene from each parent cannot transmit the disease, whereas affected children may propogate the gene to half of their offspring. Thus a typical pedigree of a dominantly transmitted disease will show transmission of the defect in each generation, to about half of each affected person's offspring. Dominant inheritance in man is characterized by variable expression of the disease inherited. This means that the disease may have many manifestations and a single individual may have any or all or none of these manifestations. Thus at risk family members including apparently normal parents must be checked for subtle manifestations. The Waardenburg and Alport syndromes exemplify these points.

b) **Autosomal recessive disorders**:

In a recessively transmitted disease, a pair of genes are abnormal. Heterozygous parents with a gene pair consisting of one normal and one abnormal gene are clinically normal. When both parents are heterozygous for the same abnormal gene, about one-quarter of their children are homozygotes receiving an abnormal gene from each parent and will have the syndrome. One-half of the heterozygotes children will be heterozygotes and able to transmit the syndrome, and

one-quarter will be homozygotes with a normal pair of genes. Recessive inheritance is seen more commonly in consaguinous marriages, because there is a greater chance that they will both have one of the recessive genes.

Recessive inheritance is characterized by homogeneity of the trait as opposed to dominant inheritance. All the affected people within a family with a recessively inherited genetic trait will be affected to approximately the same degree. eg. Ushers syndrome, Mohr syndrome.

c) **X Linked recessive disorders**:

This type of inheritance is more complex and plays only a small role in deafness. This disorder is characterized by expression of the mutation usually limited to males. While female with gene (carriers) are usually symptom free. A carrier female has a 50% chance that each son will be affected and 50% chance for each daughter to be a carrier. An affected male, if able to produce, cannot transmit the gene to his sons. All sons will be unaffected, while all his daughters must be carriers. As for dominant conditions, fresh mutations may also be a factor. X Linked dominant disorders are transmitted like X-linked recessives, but both males and females with the mutant gene manifest the disorder. Hunter's syndrome, Noorie syndrome are believed to have X-linked inheritance.

III. **Polygenic or Multifactorial traits:**

These traits entail a definite, though relatively low risk of recurrence, and environmental factors usually unidentified are presumed to play a role. All first degree relatives, parents, siblings and offsprings of the proband have a baseline two to five percent recurrence risk, though the actual number may change as a function of the traits severity, ethnic background of the family, the number of affected relatives and other factors. Disorders such as congenital heart disease, club foot, cleft palate and deafness associated with presumed allergic basis fall under this category. eg. Wildervanck syndrome.

Hearing loss due to genetic defects is termed as "genetic" or "Hereditary" hearing loss.

Genetic hearing loss may be congenital or of early onset or of late onset where the hearing loss does not manifest until long after birth (eg.deafness in Alport's syndrome). Each year between 2000 and 4000 profoundly deaf are born in the United States (Bergstrom et al 1971). Approximately 35 to 50% of the eases of profound childhood deafness may be classified as genetic and probably over ½ of these cases are syndromal. Most surveys have estimated that among the congenital or early onset hereditary deafness, autosomal recessive,genes are responsible for sixty to seventy percent dominant ... ... (contd)...

genes for 20 to 30 percent and X-linked genes for about 2% of hearing loss (Sank, 1963; Rosin , 1963; Fraser, 1964;1965; Lumio 1966; Brown, 1969; Chung et al, 1969).

Most cases of genetic hearing loss are sensorineural in nature and some may be conductive in nature as in OPD syndrome and Treacher Collins syndrome.

Some types of genetic hearing loss are progressive (deafness in Cockayne syndrome) and some are non-progressive (deafness in Waardenburg syndrome). Again most examples of hereditary hearing loss are recessive. Recessive deafness are characteristically associated with retention of hearing in low frequencies. Presumably this is due to the fact that most cases of recessive deafness are associated with the Scheibe type of inner ear abnormality. In dominantly inherited deafness, the audiogram is generally flat. However, in Waardenburg syndrome, the audiogram pattern and pathologic changes are the same as those seen in recessively inherited deafness (Ormerod, 1960; Fraser, 1964).

There are atleast 12 types of hereditary hearing loss with no associated abnormalities (Konigs Mark, 1976): They are:

1. Dominant Congenital Severe Deafness
2. Recessive Congenital Severe Deafness
3. Sex linked Congenital Deafness

4. Recessive Early Onset Deafness
5. Sex-linked Early Onset Deafness
6. Dominant Low Frequency Hearing Loss
7. Dominant Mid Frequency Hearing Loss
8. Dominant Progressive Hearing Loss
9. Dominant Unilateral Deafness
10. Otosclerosis
11. Recessive Congenital Moderate Hearing loss, and
12. Sex-linked Hearing Loss with Fixation of Stapedial Footplate.

Many of these can be separated from each other by mode of transmission, age of onset, severity of hearing loss and type of audiogram.

How to arrive at the clinical diagnosis of genetic hearing loss?

In studying a child with congenital severe deafness, one must first rule out meningitis, prenatal rubella, Kernicterus, birth injury, ototoxicity, viral infections and otitis media. A careful otological examination and hearing history should be taken to evaluate these various possible causes of the hearing loss.

When it is determined that the congenital severe deafness may be hereditary, a careful study of pedigree is necessary to determine whether the transmission is dominant, sex linked or recessive. In the dominantly transmitted deafness a good family history is important, identifying all members of the family with hearing loss as well as the age of onset and the severity of the hearing loss.

A thorough physical and neurological examination should be done to search for other possible associated anomalies which may help to define the disease. To Differentiate the congenital from early or late onset recessive deafness, a careful history of the development of the patient's speech will help in this differential diagnosis. When speech began to develop and when some evidence of facility with speech is present, the diagnosis of early onset recessive deafness can be considered. If the well developed speech started deteriorating later in life, late onset hearing loss should be suspected.

In all cases it is important to do vestibular testing to determine the intactness of the vestibular system. This test may help to separate out one of the types of dominant or recessive deafness.

There are more than 200 different genetic deafness syndromes reported in literature. In the following chapters genetic hearing loss associated with abnormalities of various systems like skin, renal, eye, skeletal, nervous are discussed.

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CHAPTER II

Genetic Hearing Loss with external ear abnormalities

The external ear changes make these hereditory deafness syndromes easier to diagnose. The external ear abnormalities range from large prominent auricles to normal auricles with preauricular pits or branchial fistulas, there may be microtia, or atresia of the external auditory canal.

Some of these syndromes are transmitted in autosomal dominant and some in autosomal recessive manner. In most of the cases the associated hearing loss is congenital and conductive in nature while in few, it is sensorineural. The degree of hearing loss varies from mild to severe form.

2.1 Otofacio Cervical Syndrome

Fara, Chlupackova and Hrivnakova (1967) described a syndrome with abnormalities of the external ear, face and neck in a father and four of his seven children.

2.1.1 Characteristics

1. Autosomal dominant inheritance
2. Prominant auricles with deep conchae
3. Preauricular pits and lateral neck fistulae
4. Hypoplasia and weakness of cervical muscles resulting in lowere shoulder girdle.
5. Hypoplasia of maxillozygomatic complex.

2.1.2 **Auditory system**

External ear :Atrophic and irregularly thickened Tympanic membranes were noticed.

Hearing: Moderate to severe conductive hearing loss. Audiometric tests done on four affected persons showed a 60-70 dB bilateral conductive hearing loss, most marked in the low and high frequencies with a 50 dB loss in mid frequencies.

Vestibular system: No studies were reported.

2.1.3 **Treatment and Prognosis**

Hearing loss may be minimized by hearing aid or tympanotomy with prosthesis insertion, excision of the fistulas and repair of deformed ears.

It was not clear whether deafness was congenital or progressed with age.

2.2 **Bar Malformations,, Cervical Fistulas or Nodules and Mixed Hearing Loss (Rowley's Syndrome)**

This syndrome has been described in several kindreds (Hall & Zimmel, 1958; Martins 1961; Wildervanck, 1962; Rowley, 1969; Shenoi, 1972; Hunter, 1974; Melnick et al, 1975; Fitch et al, 1975; Nakamura et al, 1977).

2.2.1 Characteristics

1. Autosomal dominant transmission with variable expressivity.
2. Unilateral or bilateral auricular deformaties in 75% of cases.
3. Preauricular pits in about 75%
4. Unilateral or bilateral cervical fistulas in 50%
5. Pre-auricular appendages in 5%
6. Atresia of external canal in 5%.

2.2.2 Auditory system

External ear: External ear deformaties may be unilateral or bilateral. In includes thickened and small auricles, preauricular pits, preauricular appendage, Atresia (Shenoi, 1972; Wildervanck, 1962).

Middle ear: Stapes fixation (Melnick et al, 1975)

Inner ear: Mandini type of cochlear defect (Memick et al 1975). Fitch et al (1975) found reduced No. of eochlear neurons and degeneration of stria vascularis.

Hearing: Conductive or mixed hearing loss in about 50 percent. Hearing loss was variable, ranging from 20-100 dB in severity. Sometimes

marked in lower frequencies. Usually hearing loss was more marked on the side with more severely malformed auricle or external auditory canal. Hearing loss may be unilateral or bilateral and speech discrimination varied from 34% to 100% (McClaurln et al,1966). Sensorineural hearing loss was reported by (McLaurin etal, 1966) (Bourget et al, 1968; Shenoi, 1972).

Vestibular system: No vestibular findings were described.

2.2.3 Treatment and Prognosis:

Middle ear exploration with prosthesis insertion should be considered in severe conductive hearing loss. Plastic surgery for correction of auricular deformities, preauricular appendages & Cervical fistulas/nodules (Hall & Zimmer, 1958) Hearing loss is congenital and non-progressive.

2.3. Preauricular pits, Branchial fistulae and sensorineural hearing loss

A syndrome characterized by branchial fistulae, preauricular pits and sensorineural hearing loss was studied in 21 members of a family by Brusis (1974) and Won et al (1977).

2.3.1. **Characteristics**:

1. Autosomal dominant transmission with variable expressivity.
2. Unilateral and bilateral preauricular pits in 85% .
3. Unilateral and bilateral brandhial fistulae in 20%.

2.3.2 **Auditory system**:

External ear: Affected persons had several types of ear anomalies including small pits at the anterior margin of the helix, discharging fistulas, cartilagenous nodule at the lower end of stesnocleido mastoid (Foulmann and fourmann), malformed auricles (Hall & Zimma, 1958; Mclaurln, 1966).

Inner ear: Histopathology of temporal bone revealed (No M.E. abnormalities were reported), 2 turns of the cochlea, degenerative changes, vascular congestion, thrombosis and free haemorrhage in the modi dus and spiral ganglion (Won et al, 1977).

Hearing: Mild to severe progressive hearing loss with onset in the first or second decade of life in about 90 per cent of affected persons. Hearing loss was the same in patients

higher frequencies. Hearing loss was the same in patients with or without earpits (Fourmann & Fourmann, 1955).

Vestibular system: Brusis (1974) reported vestibular disturbance in his kindred, while Fourmann & Fourmann (1955) reported no vestibular disorder.

2.3.3 **Treatment and Prognosis**: A hearing aid may be useful. Surgical incision is required for discharging branchial fistulae (Murray, 1973). Hearing loss is progressive.

2.4 Thickened earlobes and incudostapedial abnormalities

A syndrome of hereditory conductive deafness characterized by thickened earlobes, congenitally abnormal incudostapedial joints was described by Escher and Hirt (1968) Wilmot (1970) reported a mother and 2 sons with similar disorder.

2.4.1 Characteristics:

1. Autosomal dominant transmission with complete penentrance.
2. Hypertrophic ear lobes in most cases.

2.4.2 Auditory system

External ear: Hypertrophic and thickened ear is characteristic (Escher & Hirt 1968, and Wilmot, 1970).

Middle ear : Eschar and Hirt (1968) found that long clus of the incus was curved into long h&ok and the head of the stapes was absent.

In Wolmot's family (1970) Tympanotomy showed a shortened long process of the incus, stapes was mobile but headless and rotated with both cruva embedded in the promontary, in the son, the stapes footplate was fixed.

Inner ear : No. inner ear findings were described

Hearing: Congenital non-progressive conductive hearing loss due to malformation of the incudo-stapedial junction.

Vestibular System: Ho findings were reported.

2.4.3. **Treatment and prognosis:**

Patients can benefit from tympanotomy with correction of defect by prosthesis or by restoration of ossicular chain. Prognosis is reported to he excellent.

2.5. Lop ears, imperforate anus, triphalangeal thumbs and sensorineural deafness.

Towner and Brocks (1972) described a family in which the father and five of his seven children displayed this syndrome.

2.5.1. Characteristics.

1. Autosomal dominant inheritance with variable expressivity.
2. Satyr ears.

3. Imperforate anus with rectovaginal or recto perctoneal fistula.
4. the pahryngeal thumbs and Various other bony anomalies.

2.5.2. **Auditory system**

External ear : All affected persons had folding of superior helix (lop or satyr ears). No middle ear and inner ear findings were presented.

Hearing: Mild to moderate sensorineural deafness. The decibel loss was not specified. Vestibular system: No mention of vestibular testing was made.

2.5.3. **Treatment and Prognosis** : The lop ears and anorectal anomalies may be treated surgically. Prognosis is good. Hearing loss is congenital and non progressive skeletal anomalies are correctible orthopedically.

2.6 Cup shaped ears, mixed hearing loss and the Lacrimo auriculo dento digital syndrome:

Hollister, Klein, De Jerger, Lachman & Rimain (1973) reported a Mexican family in which the father and 8 of his children showed a new disorder which they designated as Lacrimoauriculo dento digital syndrome. Shiang and Holmer (1977) reported this syndrome in a mother and son.

2.6.1 **Characteristics**:

1. Autosomal dominant inheritance
2. Cup shaped ears
3. Nasolacrimal duct obstruction and hypoplasia of lacrimal puncta.
4. Various digital anomalies.
5. Maxillary lateral incisorns with conical crown form.
6. Mild amelogenesis imperfecta.

2.6.2. **Auditory System**:

External ear: Auricles were cup shaped in all affected persons.

Middle ear: Impedance audiometry revealed stiffness of conductive apparatus suggestive of otosclerosis or ossicular abnormalities.

Inner ear: The inner ear abnormalities were reported.

Hearing: In some of the affected persons there was severe conductive or sensorineural loss; others manifested mild higher low sensorineural or conduction deafness.

Vestibular system: No vestibular function studies were mentioned.

2.6.3. **Treatment and Prognosis**: A hearing aid may be employed. Cup shaped ears may be corrected for

improved appearance. Nasc-lacrimal duct atresia may be corrected surgically. Nasolacrimal duct atresia may result in dacryocystitis.

2.7. **Malformed Low set ears and Conduction Hearing Loss**

A syndrome characterized by unilateral or bilateral ( )malformed low set ears and mild to severe conductive hearing loss was found in 2 sibships in a single kindred of Mennonitis in Pennsylvania (Mengel, Konigsmark, Berlin & McKusick 1989).

2.7.1. **Characteristics**

1. Autosomal recessive inheritance.
2. Unilateral or bilateral low set ears
3. Unilateral or bilateral malformed pinnae
4. Mental retardation in about 30 percent of the cases.
5. Cardiac Murmur
6. Hypogonadism in males.

2.7.2. **Auditory system**:

External ear: Auricles in all six affected children manifested mild to severe abnormality. The pinnae were small, and frequently the helix folded forward. In one the auricle was represented by a small amount of cartilagenous tissue surrounding the external

auditory canal. In some one ear was located as much as 4 cm below the other ear. In each case, the opening of external auditory canal was displaced with the ectopic auricle.

Middle ear: In one patient, ossicular chain deformity was found. The malleus was slightly malformed and posteriorly positioned. Both the incus and stapes were absent. From the head of malleus a small fibrous band passed to the oval window area.

Inner ear: There was no mention of inner ear abnormalities.

Hearing: Congenital mild to severe conductive hearing loss. Hearing tests revealed marked variation in seventy, all children had 70-80dB in atleast one ear. In some hearing loss was more marked in one ear than the other. SISI tone decay tests were negative.

Vestibular system: Caloric vestibular tests were normal.

2.7.3. **Treatment and prognosis**: Hearing loss may be aided by hearing aid or by surgical therapy with prosthesis placement in the middle ear. Replacement of low set ears may be considered.

Hearing loss ia non-progressive.

2.8. **Microtia, Meatal Atresia and Conduction Hearing Loss**

The syndrome was described in two sibships by Ellwood, Winter and Dar (1968) and in Sibs by Konigsmark, Nager and Haskins (1972). An additional family was briefly described by Dar and Winter (1973).

2.8.1 **Characteristics :**

1. Autosoraal recessive inheritance
2. Unilateral or bilateral anotia or mucrotia
3. Unilateral or bilateral external meatal atresia.

2.8.2 **Auditory system**:

External ear: Konigsmark et al (1972) described male sibs with severe microtia, rudimentary pinnae, and absence of external meatal openings. Ellwood et al (1968) found that auricles were absent except for a slightly raised soft tissue mass beneath the skin at the usual sites. The external ear canal was represented by only a small dimple.

No middle and inner ear defects were mentioned.

Hearing: Moderate to severe congenital conductive deafness. One child showed 40-60 dB conductive

hearing loss with 100% bilateral speech discrimination, while the other showed normal hearing in one ear and severe sensorineural hearing loss in the other (Konigsmark et al 1972).

Sllwood et al (1968) found 70d3 hearing loss by air conduction and 30-50 d3 loss by bone conduction in one child, and normal hearing in another child.

Vestibular system: Vestibular testing was not described.

2.8.3. **Treatment and Prognosis**: External ear abnormalities can be partially rectified by plastic surgery (Edgerton 1969, Konigsmark et al, 1972). A prosthesis may be employed (Stallings et al 1971). Hearing aid may be of help.

Deafness is non progressive.

2.9 Microtia, Hypertelorism, Facial Clefting and Conduction Hearing Loss (MHC Syndrome).

Two sites with a syndrome of hypertelorism, clefting of lip and palate and microtia was described by 3oxler, Christian and Gorlin (1969).

2.9.1. Characteristics:

1. Autosomal recessive transmission
2. Microtia and meatal atresia

3. Cleft lip and palate
4. Microcephaly and mental retardation.
5. Ectopic kidneys.

2.9.2. **Auditory system**:

External ear: External ears were markedly abnormal with bilateral absence of tragus and the anterior superior helix. The external auditory canal was absent while other was atresic.

Middle Ear: Hypoplesia of left stapes and incus and of the right stapes and malleus was noted in one sister, while the other had fusion of ossicles on the left.

Inner ear: Inner ears were normal.

Hearing: Both had bilateral conductive hearing loss, but the degree was not specified.

Vestibular system:

Vestibular tests were not reported.

2.9.3. **Treatment and Prognosis**: The auricles and cleft palate and lip should be corrected surgically. A hearing aid may be employed.

Prognosis is good.

2.10 **Lop ears microsnathia and Conduction deafness**

Konigsmark & Gorlin (1976) described a syndrome characterized by prominent lop ears long thin hairs, micrognathia and hearing loss in a mother and her son and daughter.

2.10.1 **Auditory system**:

External, ear: Bars were prominent and lopoed, external auditory canals were remarkably narrow.

Middle ear : On tympanotomy both were found to have fixation of stapes footplate. The posterior clura were about 65% of their normal length and were not attached to the footplate. The stapedial muscle tendon was rudimentary.

Inner ear : Inner ear abnormalities were not described.

Hearing: Non-progressive, mixed, mostly conductive hearing loss of 30-60 dB was noticed in the affected members.

Vestibular system: No mention was made about vestibular testing.

2.10.3 **Treatment**: Surgical correction of lop ears for improved appearance and stapedectomy for improving hearing may be considered.

CHAPTER III

Genetic Hearing Loss Associated with Eye Disease.

Various syndromes characterized by eye disease and hearing loss have been reported in literature to date. The eye diseases may be in the form of retinitis pigmentosa, myopia, cotaract and optic atrophy. These eye diseases are characteristic and may be creppling to total loss of vision in some instances.

In addition to association with eye disease and hearing loss, some syndromes considered in this chapter include Obesity, diabetes melitus, mental retardation and also involvement of nervous and skeletal system. Although these syndromes might have been included in other chapters, they shall be considered here because the eye signs are constant and reasonably obvious.

In most of the cases the associated hearing loss is sensorineural rather than conductive. Hearing loss is congenital in some syndromes, while in others it appears later in life.

The most common disorder in this category is "Usher's Syndrome". The patients with Usher's syndrome are congenitally deaf and have a progressive visual loss due to retinitis pigmentosa. The prevalence of this syndrome among profoundly deaf children may be as great as ten percent.

3.1 **Retinitis Pigmentosa and Congenital Sensorineural Deafness (User Syndrome).**

The association of deafness and retinitis pigmentosa was described as early as 1858 by Von Graefe and was recognized as having an unusually high incidence among the Jewish deaf. The significance of increased consanguinity was pointed by Lie 3reich (1861) and Hammerschlag (1907). The disorder was extensively documented by Usher (1914.) who emphasized its genetic nature. Its prevalence among profoundly deaf children has been estimated by a number of investigators at 3-10 percent (Vernon 1959, Fraser 1964).

In 1977, Devenport and Omenn studied the heterogeneity of Usher's Syndrome and separated it into 4 distinctinct entities.

Type I: is characterized by profound congenital deafness with onset of retinitis pigmentosa by 10 years of age. It constitutes 90% of the syndrome.

Type II: is characterized by moderate to severe congenital deafness, retinitis pigmentosa seen in late teens or early twenties. This constitutes 10% of cases.

Type III: is characterized by progressive hearing loss and retinitis pigmentosa occuring at around puberty.

Type I, II and III exhibit autosomal recessive inheritance while type IV is compatable with X linked inheritance and exhibits a phenotype like Type IT.

3.1.1. **Characteristics**:

1. Autosomal recessive inheritance
2. Progressive Visual loss with retinitis pigmentosa.
3. Mental retardation and 1 or Psychosis (Occassionally)
4. Mild ataxia.

3.1.2. **Auditory system**:

Otological examination: No abnormal findings were reported.

Inner ear: Temporal bone changes involving the cochlea and its nerve and vascular supply have been reported by Nager (1927) Buch and Jorgenson (1963) These changes were typical of the Scheibe type.

Hearing: Congenital moderate to severe sensorineural hearing loss. About 90% of cases reported had severe bilateral congenital deafness, whereas 10 per cent had moderate sensorineural hearing loss, more marked in the higher frequencies (Hallgren, 1959) Lander and Feinmesser(1956) Kloepper et al 1966, Mcleod et al (1971). SISI scores were positive in the higher frequencies and

Bekesy tracings were type II, suggesting a cochlear origin for the deafness.

Vestibular system: Vestibular responses to caloric testing generally abnormal suggesting defective vestibular function (Hallgren, 1959; Verson, 1959, Mcleod (1971). Whether vestibular or cerebellar abnormalities are the cause of unsteadiness is not clear. But most investigators suggest labyrinthine anomalies.

3.1.3 **Treatment and Prognosis** :

In most cases the deafness is so severe that the use of hearing aid is not possible. There is no treatment for retinitis pigmentosa.

3.2 Retinal degeneration, diabetes meliitus_, obesity and Sensorineural hearing loss(Alstrpm Syndrome)

This syndrome was found in a Swedish kindred by Alstrom, Hallgren, Nilsson and Asander (1959). Other cases were described by Klein and Ammann(l989), Weinstein et al (1969), Lista et al (1972), Goldstein and Fialkow (1973) Edwards et al (1973).

3.2.1 Characteristics_:

Autosomal recessive inheritance.

Onset ia infancy of retinitis pigmentosa with loss of central vision.

Onset in childhood of diabetes mellitus.

Transient obesity

Onset in the second decade of posterior cortical cataract.

Onset of neuropathy in the third decade.

Acanthosis migricans.

3.2.2 **Auditory system**

No report of otologic examination and temporal bone histopathology was presented.

Hearing: Late childhood onset of progressive sensorineural hearing loss.

Sensorineural hearing loss has been first noted at about 7 years of age and has progressed be-cling moderately severe in the second and third decades. The Bekesy, tone decay and SISI tests suggest cochlear involvement (Goldstein and Fial-kow 1973).

Vestibular system: No vestibular findings have been mentioned.

3.2.3 **Treatment and prognosis**:

A Hearing aid may be used for progressive hearing loss. Cataracts may be improved by removal of the lens, obesity may be controlled by diet, the diabetes mellitus by appropriate medical therapy. Prognosis is poor, since vision and hearing dete-riorate progressively. Life span may be shorte-ned by renal dysfunction.

3.3 **Retinitis Pigmentosa, Nystagmus, Hemiplegic Migraine and Sensorineural deafness (Migraine Syndrome).**

Young, Leon Balth and Green (1970) reported a syndrome in 4 members of a family who were affected by hemiplegic migraine and nystagmus. Two of these individuals also had sensorineural deafness and retinitis Pigmentosa.

3.3.1 **Characteristics**:

1. Autosomal dominant inheritance with variable expressivity.
2. Retinitis pigmentosa
3. Hemiplegic migraine preceded or accompanied by sensory and motar phenomena.
4. Jerking nystagmus.

3.3.2 **Auditory system**:

No abnormalities of the conducting apparatus were reported. Histopathological studies of temporal bone were not mentioned.

Hearing: Bilateral sensorineural hearing loss of 70-80 dB in the frequency ranges of 750 to 4000Hz was demonstrated. There Was good speech discrimination bilaterally, no tone decay and type II Bekesy audiograms.

Vestibular system: Vestibular studies were not mentioned.

3.3.3 Treatment and Prognosis

Hemiplegic migraine can be treated with methysergide. Deafness can be lessened by using a

hearing aid. Retinitis pigmentosa and jerking nystagmus cannot be treated.

Life span is not apparently shortened. Blindness and deafness are progressive.

3.4 Retinitis Pigmentosa, Progressive quadriparesis Mental retardation and Sensorineural deafness

This syndrome was first described in 2 male sibs by Gorden, Capute and Konigsmark (1976).

3.4.1 Characteristics:

1. Probable autosomal recessive transmission.
2. Progressive retinitis pigmentosa.
3. Progressive quadriparesis.
4. Marked mental retardation.

3.4.2 Auditory system

Otologic examinations showed no abnormalities.

No histopathologic findings of the temporal bone were presented.

Hearing: Moderate sensorineural hearing loss. Audiometric testing was somewhat difficult in these mentally retarded brothers. EEG audiometry revealed moderately severe sensorineural hearing loss at least in the higher frequencies.

Vestibular system: Caloric vestibular tests showed no abnormalities.

3.4.3 Treatment and Prognosis

Since mental deficiency is rather severe, hearing aids are of limited usefulness. The disease appears to be very slowly progressive, resulting in complete debility.

3.5 Cockavne Syndrome

A disease characterized by cachectic dwarfism with senile appearance, mental retardation, retinal degeneration, and moderate sensorineural hearing loss was described in two sibs by Cockayne (1936). Since then, over 30 cases have been published.

3.5.1 Characteristics

1. Autosomal recessive transmission.
2. Visual lesions leading to blindness.
3. Onset in infancy of growth retardation with lack of subcutaneous fat and skeletal abnormalities including thickened skull and kyposis.
4. Joint contractures
5. Early arrest of mental development.
6. Light sensitive dermatitis involving the face and hands.

3.5.2 **Auditory system**

No external and middle ear abnormalities were reported. No histopathologic Studies were described.

Hearing: Moderate to severe sensorineural hearing loss. Most patients have normal hearing at birth, but usually develop a moderate to severe sensorineural hearing loss during childhood (Schon enberg & Frohn 1969). Hearing loss was somewhat variable in different patients, as reported by Mac Donald et al (1960) and Mossy (1967).

Vestibular system: Vestibular system testing has not been described.

3.5.3 **Treatment and Prognosis**:

Little can be done for the visual loss. Mental deficiency precludes the success of hearing aid. Since exposure aggravates the dermatitis, the patient should be protected from sun.

Prognosis is poor, with severe blindness and deafness usually developing and co-ordination deteriorating. During second or third decade patient may become bedridden. Death usually occurs prior to the 30th year of life.

3.6 **Refsum Syndrome**

(Heredopathia atactica, Polyneuritiformis)

A syndrome characterized by retinitis pigmentosa, hypertrophic peripheral neuropathy with both motar and sensory losses, ataxia and at times, sensorineural hearing loss was first roughly described by Refsum (1946) in 2 unrelated Norwegian families. Over 50 cases have been reported subsequently.

3.6.1 **Characteristics**:

1. Autosomal recessive inheritance.
2. Progressive retinitis pigmentosa with constricted visual fields and night blindness.
3. Hypertrophic peripheral neuropathy.
4. Mild cerebellar ataxia and nystagmus.
5. Increased plasma phytamic acid.
6. Ichthyosis of skin.

3.6.2 **Auditory system:**

No external and middle ear abnormalities were described.

Inner ear: Collapse of Reissner's membrane, degeneration of the stria vascularis, atrophy

of organ of corti and loss of spiral ganglion cells, were the temporal bone abnormalities described by Hallpike (1967) in a patient with Refsum syndrome.

Hearing: Progressive sensorineural hearing loss in about half of those affected(3ergstnark and Djupesland, 1968). Often the hearing loss is more severe on one side than on the other. There is mild variation in the degree of deafness in different affected individuals. Hearing loss most often begins in second or third decade of life and progresses slowly, involving the higher frequencies in particular. Tone decay and speech discrimination have been normal.

Vestibular system: Caloric vestibular tests have been normal (Fleming, 1957; Bergsmark and Djupesland, 1968).

3.6.3. **Treatment and prognosis**:

Hearing may be improved by hearing aid.

The course is variable. Usually there is progression of neurologic deficits resulting in complete incapacitation. Among reported cases, 20% died in the first decade, 30% in the 3rd decade,20% in the 4th decade and 10% in the 5th decade of life.

3.7 **Inverse retinitis Pigmeptosa, hvposonadium and Sensorvneural deafness**

Reinstein and Chalfin (1971) reported a syndrome of inverse retinitis pigmentosa, hypogenitalism and sensorineural deafness in two female and one male sib.

3.7.1 **Characteristics**:

1. Autosomal recessive inheritance
2. Inverse retinitis pigmentosa, early loss of central vision, preference for dim illumination.
3. Hypogonadism.

3.7.2 **Auditory system**:

No external ear and middle ear abnormalities or inner ear findings were described.

Hearing: Progressive sensorineural hearing loss with onset ranging from 11 years of age to 40 years. In most cases hearing loss slowly progressed to severe S.N. loss more marked in higher frequencies.

Vestibular system: Vestibular studies were not mentioned.

3.7.3. **Treatment and prognosis**:

Harmone treatment to initiate pubertal changes. Hearing aid may be useful.

Impaired vision, usually appearing in the third decade, progressively deteriorates to severe loss over the next decade.

3.8 **Retinal changes, muscular wasting, mental retardation and Deafness (small syndrome)**

A syndrome including deafness, retinal detachment, muscular dystrophy and mental retardation appearing in 4 of 7 sibs were described by small (1968).

3.8.1. **Characteristics**:

1. Autosomal recessive inheritance.
2. Retinal changes including tortuous vessels and exudative retinitis.
3. Moderate to severe mental retardation.
4. Muscle weakness and wasting involving the face, trunk and extremeties.
5. Mild but progressive ataxia.

3.8.2 **Auditory system**:

No external or middle ear abnormalities were described. Histopathological findings in temporal bone were not mentioned.

Hearing: Moderate to severe hearing loss was noticed in all of the affected children. One sib was deaf from birth, while in other hearing loss was not noticed until 9 years of age. No puretone or other audiometric tests were described.

Vestibular system: No vestibular findings were presented.

3.8.3 **Treatment and prognosis**

Patients should be referred for opthalmic treatment, use of hearing aid may be considered. Prognosis is poor due to progressive eye changes and mental retardation.

3.9 **Cryptopthalmia syndrome and mixed deafness**

First described by Zehender (1872). About 60 oases have been reported so far under a variety of names. (Chial, 1883; Elsching, 1914; Gupta and Saxena, 1962; Sugar, 1968; Schonerberg, 1973 and Shashikapoor, 1979).

3.9.1 **Characteristics**:

1. Autosomal recessive inheritance
2. Unilateral or more often bilateral extension of the forehead to complete cover the eye/ eyes.
3. Valuable soft tissue syndactyly of the fingers and/or toes.
4. Coloboma of the nasal alae.
5. Various urogenital anomalies.
6. Abnormal hair line.

3.9.2 **Auditory system**

External ear: The pinnae were small, poorly modeled or posteriorly rotated in 30% of cases.

The skin of the upper part of the helix was commonly continuous with that of scalp. The external auditory canals were often narrowed or completely stenotic in the outer third to outer half (Chari, 1883; Gupta & Saxena, 1962; Fraser, 1963; Ehlers, 1966; Francon, 1969; Schoaenberg, (1973). Narrowing or stenosis may occur bilaterally, even though the cryptothalmos is unilateral (Schonenberg, 1973).

Middle-ear: Ossicles have been noted to be malformed (ide and Wollschlaeger, 1969).

Inner ear: The same authors found the internal auditory canals to be normal. No inner ear pathology was described.

Hearing: Mixed, but mostly conductive deafness was noted.

Vestibular system: No studies have been reported.

3.9.3 **Treatment and Prognosis**:

Surgical correction of cryptopthalmos has been uniformly of no avail. The cutaneous syndactyly if severe may be corrected by plastic surgery, surgical correction of stenotic ear canal, and ossicular defects may be considered.

3.10 Myopia, Cataract, Saddle nose and Sensorineural hearing Loss (Marshall Syndrome),

Seven members in four generations of a family studied by Marshall (1958) had a syndrome that included saddle nose defect, congenital and juvenile cataracts, myopia and sensorineural hearing loss. Another kindred was reported by Ruppert et al (1970), and Zellweger et al (1974).

3.10.1 Characteristics:

1. Autosomal dominant transmission.
2. Severe myopia.
3. Congenital and Juvenile cataracts.
4. Saddle nose defect.
5. Various skeletal abnormalities.

3.10.2 Auditory system:

No external, middle or inner ear abnormalities were reported.

Hearing: Early onset progressive moderate sensorineural hearing loss.

Audiometric tests were reported as showing about 50 dB mixed or mostly sensorineural hearing loss in several members by Marshall (1958). Ruppert et al(1970) noted moderate hightone sensorineural loss, while Zellweger et al (1974) reported 30-60 dB sensorineural hearing loss in the affected members.

Vestibular system: Ruppert et al (1970) reported normal vestibular findings.

3.10.3 **Treatment and prognosis**:

Cataracts should be removed, and myopia corrected and hearing aids should be employed.Maxillofacial surgery can correct the midface hypoplasia for improved appearance.

Deafness is progressive.

3.11. **Myopia, Blue Sclerae, Marfanoid Habitus and sensorineural deafness**

Walker (1971) described this syndrome in three or four possibly four generations.

Characteristics:

1. Autosomal dominant inheritance.
2. Myopia blue sclerae and occassionally Keretoconus.
3. Arachnodactyly and loose jointedness.

3.11.2 **Auditory system**:

Otologieal examination indicated no abnormality. No histopathological studies of inner ear were described.

Hearing: Progressive sensorineural deafness that is more marked in the higher frequencies.

Vestibular system: Studies were not described.

3.11.3 **Treatment and prognosis:**

Hearing loss may be minimized by use of hearing aid.

This disorder is not crippling.

3.12 **Myopia, Peripheral neuropathy, skeletal abnormalities and Sensorineural deafness (Flynn Aird Syndrome)**

This syndrome was described in 15 members of a family by Flynn and Aird in 1965. Bilateral S.N. hearing loss and myopia developed in the first decade of life with Ataxia, Peripheral shooting pains, joint symptoms and cerebral changes following in the second and third decades.

3.12.1 **Characteristics:**

1. Dominant transmission with variable expressivity.
2. Eye defects including myopia, cataracts and retinitis pigmentosa.
3. Peripheral neuropathy with shooting pains, sensory loss and weakness.
4. Skeletal abnormalities including Kyphoscoliosis
5. Central nervous system involvement including peculiar seizures and abnormal EEG findings.

3.12.2 **Auditory system**:

External, middle and inner ear abnormalities were not mentioned.

Hearing: Bilateral sensorineural hearing loss was variable in different affected persons, beginning in the first decade and progressing either slowly or moderately rapidly to severe deafness by the second to sixth decades.

Vestibular system: No vestibular findings were described.

3.12.3 **Treatment and Prognosis**:

The myopia can be corrected by glasses, and the hearing loss can be minimized by a hearing aid. Hearing add visual loss caused severe disability early in life. The slowly progressive neuropathy may have been a factor in some of the patients developing pneumonia, thereby shortening the life span.

3.13 Myopia and Congenital Sensorineural Hearing loss

A combination of congenital sensorineural hearing loss, myopia and low intelligence was described in a sibship by Eldridge, Berlin, Money and McKusick(l968), who studied an Amish family in which four of seven sibs had this syndrome.

3.13.1 Characteristics

1. Autosomal recessive transmission
2. Congenital severe myopia
3. mild intellectual impairment in some affected persons.

3.13.2 **Auditory system**:

Otologic examination revealed normal external auditory canals and tympanic membranes.
No inner ear abnormalities were mentioned.
Hearing: Congenital moderate to severe non-progressive sensorineural hearing loss.
Puretone audiometric tests showed a 30 to 100DB sensorineural hearing loss, which was more marked in the higher frequencies. SISI test in one child was positive suggesting a cochlear locus for the hearing loss.
Vestibular systems Calorie vestibular tests showed normal vestibular function.

3.13.3 **Treatment and prognosis**:

Affected persons can be aided by glasses for extreme myopia and by a hearing aid for the sefere hearing loss.
Myopia and hearing loss are non-progressive.
So prognosis is fairly good,

3.14 **Myopia, Secondary telecanthus (Hypertelorism) and congenital sensorineural deafness:**

Holmes and Schepens (1972) reported a sister and brother with severe eye abnormalities, telecanthus and

congenital sensorineural deafness. The same children were reported by Murdoch and Mengel (1971) and by Ozer (1974).

3.14.1 **Characteristics**:

1. Autosomal recessive inheritance
2. Secondary telecanthus and prominent brow
3. Myopia, choroidal atrophy, cataract, iris hypoplasia and possibly retinal detachment.

3.14.2 **Auditory system**

No data regarding external and middle and inner ear abnormalities were presented.

Hearing: Both sibs had severe congenital sne sensorineural deafness. No other data were presented.

Vestibular system: No vestibular tests were described.

3.14.3 **Treatment and Prognosis**:

Hearing aid may be used if necessary, eye abnormalities require opthalmologic consultation. Prognosis is variable.

3.15 **Optic Atrophy, Polyneuropathy and Sensorineural Deafness (Rosen berg - Chutorian syndrome**

A syndrome characterized by polyneuropathy, optic atrophy and sensorineural hearing lossvas described

by Rosenberg and Chutorian (1967). Similar cases were reported by Iwashita et al (1970), Taylor (1912) and Jequier and Deonna (1973).

3.15.1 **Characteristics**:

1.X linked autosomal recessive transmission

2. Progressive visual loss with optic atrophy beginning at about 20 years of age.

3. Progressive peripheral polyneuropathy beginning in e!arly childhood.

3.15.2 **Auditory system**

No external, middle or inner ear abnormalities were mentioned.

Hearing: Progressive sensorineural hearing loss leading to severe deafness by 6 years of age. (Rosenberg and Chutorian, 1967).

Iwashita et al (1970) noted S.N. hearing loss in that patient at around 15 years of age.

Vestibular system: No vestibular tests were described.

3.15.3 **Treatment and Prognosis**:

A hearing aid may be useful during the first few years of life.

Prognosis is poor because of progressive nature of hearing loss and visual problems.

3.16 Optic atrophy, Juvenile diabetes and sensorineural hearing loss:

Several families have been described in which sibs had a syndrome comprising optic atrophy, progressive sensorineural hearing loss and diabetes mellitus (Barjon et al 1964, Rose et al 1966, Herrera Pombo et al 1971, Moore 1971, Stevens and Macfayden, 1972).

3.16.1 Characteristics:

1. Autosomal recessive transmission.
2. Onset in childhood of progressive visual loss due to optic atrophy.
3. Diabetes mellitus with onset in the first or second decade.

3.16.2 Auditory system:

Otologic examination revealed no abnormality.

Hearing: Hearing difficulty has been noted as early as in the first few years of life. (Shaw and Duncan 1958, Herrera Pombo et al 1971). Deafness becomes progressively worse, resulting in bilateral symmetrical moderate to severe sensorineural hearing loss in the second decade (Ikkos et al 1970, Cordier et al 1970, Moore 1971, Stevens and Macfayden 1972; Saucer et al 1972).

There may be some variation in age of onset and severity of hearing lass, it is more marked at higher frequencies,other audiometric tests were not described.

Vestibular system: Vestibular tests on 10 and 13 year old brothers showed diminished vestibular reaction (Barjon et al 1964).

3.16.3 Treatment and prognosis

Medical therapy for diabetes mellitus has been quite effective. Obesety was treated by diet or insulin. Little can be done for optic atrophy although the sensorineural hearing loss can be minimized by a hearing aid.

Although patients develop a severe visual and hearing loss by middle age, their span was probably normal.

3.17 Progressive optic atrophy and congenital sensorineural deafness

Konigsmark, Khox, Hussels and Moses (1974) reported a syndrome of congenital severe sensorineural deafness and progressive midlife visual failure due to optic atrophy. Similar cases were described by Gernet (1964), Michal et al (1968).

3.17.1 **Characteristics**

1. Autosomal dominant transmission
2. Progressive optic atrophy

3.17.2 **Auditory System**:

No external and middle ear abnormalities were described.

Inner ear: Temporal bone tomograms were nornal.

Hearing: Severe congenital bilateral sensori-neural hearing loss most marked in the mid-frequencies was noted.

In the son, the defect was greater than 90dB in all frequencies. In other affected relatives, there was some mild residual low frequency hearing (Konigsmark et al 1974).

In the kindred documented by Michal et al(1968) all affected persons were deaf mutes.

Vestibular system: Vestibular testing indicated no spontaneous or positional nystagmus. The optokinetic responses were normal, and caloric vestibular tests were bilaterally active and normal in both kindreds.

3.17.3 **Treatment and prognosis**:

Hearing aid is generally useless because of the severity of congenital deafness. No treatment for optic atrophy.

Prognosis is not good, as the vision decreases progressively from midlife.

3.18 **Optic atrophy, ataxia and progressive sensorineural hearing loss**

A syndrome characterized by progressive optic atrophy, progressive sensorineural hearing loss and ataxia occuring in a father and in six of his nine children was described by Sylvester in 1958.

3.18.1 **Characteristics**:

1. Autosomal dominant transmission with variable age of onset.
2. Progressive visual loss due to optic atrophy beginning in childhood.
3. A Variable degree of ataxia, particularly involving the legs.
4. Weakness and muscle wasting, particularly involving the shoulder girdle and hands.

3.18.2 **Auditory system**:

External, middle and inner ear abnormalities were not mentioned.

Hearing: Moderate to severe progressive sensorineural hearing loss beginning in childhood. No further audiometric findings were described.

Vestibular system: No vestibular findings were noted.

3.18.3 **Treatment and prognosis:**

Little therapy other than a hearing aid for the auditory loss can be given.

The onset of symptoms are was variable. In father, the slow progression of the disorder resulted in severe hearing loss and poor vision in middle age. In children the age of onset ranged from 2½ to 9 years, with death occuring between 8 months and 4 years after onset.

3.19 **Optico Cochleo dentate Degeneration.**

A syndrome characterized by progressive visual and sensorineural hearing loss and progressive spastic quadriplegia was reported in two male sibs by Muller and Zeman (1965). Similar cases were described earlier by Meyer (1949), Levy (1951) and Hasaerts (1957).

3.19.1 **Characteristics:**

1. Autosomal recessive transmission
2. Onset in infancy of progressive visual loss due to optic atrophy.
3. Onset in infancy of progressive spastic quadriplegia.
4. Progressive mental deterioration.

3.19.2 **Auditory system:**

No external and middle ear abnormalities were reported. Histopathological studies revealed

cochlear and dentate degeneration and neural loss have been found in the medial lemniscal system.

Hearing: Hearing was considered normal during the first year of life. Because of mental deterioration it was Impossible to determine whether they could hear. The age at which hearing loss became evident varied, but in nearly all patients deafness occured during the first decade of life. Hearing deteriorated resulting in severe deafness.

Vestibular system: Evaluation could not be carried out.

3.19.3 **Treatment and prognosis**: No treatment is known, Of the nine possible cases, five have died, four before the twelth year of life. The blindness, mental retardation and neurologic deficits do not permit any normal function.

3.20 Iris dysplasia, Ocular Hypertelorism. Psychomotor retardation and Sensorineural deafness.

De.Hanwere, Leroy, Adriaenssens and Henle (1973) described this syndrome in two generations. A similar disorder was reported by Van Noorden and Bailer (1963).

3.20.1 **Characteristics:**

1. Autosomal dominant inheritance.
2. Rieger's mesodermal retardation.

3. Hypertelorism

4. Psychomotor retardation

5. Hypotomia with joint hypermobility.

3.20.2 **Auditory system**:

No external/middle/inner ear abnormalities were reported. Mild sensorineural deafness was noted in each patient. No other data is available.

Vestibular system: Vestibular studies were not mentioned.

3.20.3 **Treatment and prognosis**:

Esotropia and glaucoma, if present should be corrected.

Prognosis depends largely on the degree of psychomotor retardation.

3.21 **Congenital corneal dystrophy and progressive Sensory Neural hearing loss (Harboyan syndrome)**

The combination of congenital corneal dystrophy and progressive sensorineural hearing loss was described in two of ten sibs from a first cousin mating and in one of ten sibs from another first cousin mating by the same father. (Harboyan et al 1371).

3.21.1 **Characteristics**:

1. Autosomal recessive transmission

2. Congenital dystrophy with slow progression.

3.21.2 **Auditory system**:

No external or middle ear abnormalities were described.

Hearing: Sensorineural hearing loss was first noticed in patients at the age of 10 to 25 years, the loss slowly progressed. Speech discrimination was 90 percent to 100 percent and SISI and tone decay tests were negative.

Vestibular system: Caloric vestibular tests were normal in all three patients.

3.21.3 **Treatment and prognosis**:

Corneal transplants and treatment for the glaucoma was clearly indicated. A hearing aid should be employed.

The loss of vision and hearing is slowly progressive.

3.22 **Familial Corneal degeneration. Abnormal calcium Metabolism and hearing loss (Hallerman syndrome)**

A syndrome comprising ribbon like degeneration of the cornea, hearing loss and abnormal calcium metabolism occuring in three of five brothers was described by Hallerman and Doering (1964).

3.22.1 **Characteristics**:

1. Possible autosomal dominant transmission with variable expressivity.
2. Ribbonlike degeneration of cornea with onset in the later decades.
3. Abnormal calcium metabolism characterized by prolonged transit time of calcium in the metabolically active pool.

3.22.2 **Auditory system**:

No external or middle ear abnormalities were described.

Hearing: Hearing loss was noted in each of 3 brothers. Age of onset, severity of hearing loss or passible progression of hearing loss was not mentioned.

Vestibular system: No vestibular tests were mentioned.

3.22.3 **Treatment and prognosis**:

Patient should be referred for opthalmic treatment. Hearing aid may be employed, if hearing loss is severe.

Apparently, this disease appears in the later decades of life and is slowly progressive.

3.23 **Noorie syndrome(Occuloacoustico cerebral degeneration)**

A syndrome characterized by lens opacities, atrophic irises, and proliferating retiolental mass was

probably first described by Fernandez - Santos (1905), although clarke (1898) may have noted it earlier* Noorie (1927) reported two affected families. Subsequently many families were described by Warburg (1966) and Brini et al (1972).

3.23.1 **Characteristics**:

1. X Linked recessive transmission
2. Eye changes, including retinal glial proliferation, cataract and microphthalmia
3. Mild to severe mental deficiency in about two thirds of the cases.

2.23.2 **Auditory system**:

No external and middle ear abnormalities were reported.

Hearing: Mild to severe sensorineural hearing loss is seen in about one third of the patients. Audiograms showed a 20 to 100 dB, usually symmetric Sensorineural hearing loss. Hearing loss developed in the 2nd or 3rd decade and progressed slowly (Sarburg 1966).

Electrocochleography and 3rain stem evoked responses revealed the hearing loss to be of cochlear origin with no involvement of brain stem (Parving et al 1978).

Vestibular system: Vestibular tests were not performed by Warburg (1966) because several patients had nystagmus and some had enucletation.

3.23.3 **Treatment and prognosis**:

The occasionally occuring eye pain is relieved by enucleation. Hearing aid may be effective for hearing loss, if severe mental retardation does not preclude its use.

Prognosis is poor. All affected persons became blind. The oligophrenia is progressive, with affected children appearing mentally normal for only the first one or two years of life. Several patients with acute psychosis have died in mental institutions.

3.24 **Keratoconus, blue sclerae, Loose ligaments and conduction deafness**:

A syndrome including Keratoconus, blue sclerae, middle ear conduction defects and spondylolisthesis was reported in sibs by Greenfield, Romano, Stein and Goodman (1973). Only these authors and Behr (1913) noted hearing loss. Lamba et al (1971) documented another example.

3.24.1 **Characteristics**:

1. Autosomal recessive inheritance
2. Keratoconus or keratoglobus with thin fragile cornea.
3. Blue Solera
4. Loose ligaments.

3.24.2 **Auditory system**:

No external ear or inner ear abnormalities were described.

Middle ear: Bilateral otosclerosis was established by Greenfield et al (1973). No other defects were reported.

Hearing: Bilateral conduction deafness beginning between 10 years and 15 years of age was described by Greenfield et al (1973), 3ehr (1913) and Lambe et al(1971).

Audiometry disclosed air/bone thresholds of 45/ to 60/ 15 to 20 dB in one sib and 60/30DB loss bilaterally in another sib (Greenfield 1973).

3.24.3 **Treatment and prognosis**:

Stapedectomy will improve hearing, contact lens can be effectively employed for keratoconus.

The outlook for these patients is generally good.

3.25 Progressive external opthalmoplegia, retinal pigmentary degeneration, Cardiac conduction defects and mixed hearing loss (Kearns syndrome)

Kearns and Sayre (1958) first described a syndrome of retinitis pigmentosa, external opthalmoplegia, and complete heart block in two unrelated patients. Subsequently, Kearns (1965, 1966) added an additional nine patients six

with "complete" syndrome and three with "incomplete" syndrome. Additional cases were reported by Jager et al (1960), Drachman (1968), Danta et al (1975) and Gadoth (1976).

3.25.1 **Characteristics**:

1. Hereditory is not established, because all cases described have been isolated examples.
2. Progressive external opthalmoplegia.
3. Retinal pigmentary degeneration.
4. Ptosis of eyelids
5. Optic atrophy
6. Proptosis in some individuals
7. Bulbar weakness(dysphonia, dysphagia & Hoarseness
8. Cerebellar ataxia and corticospinal tract signs occasionally.
9. Cardiac conduction defects.
10. Delayed sexual development.

3.25.2 **Auditory system**:

No external and middle ear defects were described.

Hearing: Hearing loss has been of a mixed type in most patients, although only sensorineural deafness was documented in a few. Loss was most pronounced, in the higher frequencies. Bekesy and SISI tests revealed recruitment phenomena at high frequencies but not at lower one, suggesting a cochlear or brain stem lesion.

Vestibular system: Caloric testing revealed markedly diminished or absent responses to vestibular stimulation.

3.25.3 **Treatment and prognosis**:

Patient should be referred to a cardiologist for management of heart conduction defect.

Plastic surgery may be required for correction of ptosis.

The various facets of the syndrome are progressive, in most cases the condition has not resulted in markedly shortened life span.

3.26 **Miscellaneous eye .disorders in which deafness is inconsistently associated**:

3.26.1 **Laurence Moon Biedel(Syndrome and Bardel Biedel Syndrome**

Laurence Moon Biedl Syndrome is characterized by retinitis pigmentosa, mental retardation, hypogeintalism and spastic paraplegia. Those with the Bardet Biedl Syndrome show obesity, retinitis pigmentosa in association.

Hearing: Deafness is rarely associated with Laurence Moon or Bardet Biedl Syndrome (Burn 1950, Garstecki et al 1972).

3.26.2 Fehr's recessive corneal atrophy

Fehr described a syndrome of corneal dystrophy inherited as an autosomal recessive trait occuring at around 5-10 years of age.

Hearing: some children with this condition develop a progressive severe sensorineural deafness. The only example of association of Fehr's corneal dystrophy with congenital deafness was reported by Moro and Amerdi (1957)

3.26.3 Abducens Palsy with retracted bulb (Duane's Syndrome)

Duane's syndrome is characterized by limited abduction with retraction of the eyeball and narrowing of the palpebral tissue on adduction. Inheritance is associated autosomal dominant, unilateral in 50% of cases, with female preponderance of 3 to 2 (Livingstone & Delahunty 1968)

Hearing: Sometimes it is associated with deafness, either sensorineural or conductive due to auricular malformations.

Mein (1968) in analysis of 77 cases of Duane Syndrome found two with deafness, while Kirkham (1969) found 12 persons among 112 patients to be deaf. The type and degree of hearing loss was not specified.

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CHAPTER IV

Genetic hearing loss with Renal Disease

Renal malformations are also commonly associated with deafness and are inherited. Renal diseases may be in the form of nephritis, renal failure, heimaturia and uremia. The early diagnosis of these renal diseases are most important, because in some eases, it may be so severe as to threaten the life of the affected individual. The diagnosis of renal problems are made based on radiographic studies, fenal biopsies and various other laboratory tests.

In addition to hearing loss, the renal diseases may be associated with other abnormalities like hypertension, mental retardation and genital abnormalities. In most of the cases, the associated deafness is sensorineural and slowly progressive.

The most important syndrome which is associated with renal disease is "Alport syndrome". This syndrome is characterized by progressive renal in-sufficiency which may be fatal and progressive sensorineural deafness beginning in early teens. This is common in males.

Many of the syndromes described in this chapter, have been reported in one or very few families. More documentation is necessary for definite establishment of these entities. However, a basic knowledge of the features of these entities will bring to light many other similar disorders, and help in early diagnosis and treatment of these serious diseases to reduce the ensuing complications.

Nephritis and Sensorineural Deafness(Alport Syndrome)

Alport (1927) described a syndrome of chronic nephritis with intermittent or gross hematuria and progressive renal insufficiency, progressive sensorineural deafness and a prediction for males (20%). Since then several hundred publications have appeared on Alport syndrome, which accounts for 1 percent of genetic deafness.

4.1.1 Characteristics:

1. Autosomal dominant inheritance, with males being more severely affected.
2. Progressive nephritis with uremia.
3. Dcular lens abnormalities including spherophakia, lenticonus or cataracts in about 10% of cases.

4.1.2 Auditory system

No external or middle ear abnormalities were noted.

Inner ear: There are several reports concerning temporal bone pathology in Alport's syndrome. Winter et al (1968) found §0% loss of spiral ganglion cells in the basal turn of cochlea. Gregg and Becker (1963), Babai and 3ettez (1968) described degeneration of striavascularis and hair cells of organ of corti particularly in the basal turn of cochlea. Fujita and Hayden (1969) Westergaard et al (1972), Meyers and Tyler (1972) and Bergstorm et al (1972) were unable to find temporal bone changes characteristic of Alport syndrome.

Hearing:

There is marked variation in the degree of deafness. Symmetric progressive sensorineural hearing loss, more often in the middle of high frequencies, usually appears during the second decade, but is relatively mild and rarely requires a patients admission to deaf school. (Klotz, 1959; Johnson and Hagan, 1965, Gekle et al, 1969). Hearing loss occurs more frequently in affected males than in females (Cassidy et al, 1965; Chricosta et al 1970; Ferguson and Rance 1972 and Hanser, 1974). Speech Discrimination was

usually normal. SISI test was in more number of cases, while tone decay was positive in one or two cases, suggesting that the hearing loss is cochlear in origin (Spear et al 1970, Muller et al 1970).

4.1.3 **Treatment and Prognosis:**

The deafness is usually ameliorated by use of a hearing aid. Renal transplantation should be considered.

Prognosis is variable. In some patients the disease may be mild and show practically no effect, whereas in other patients renal failure is severe, resulting in early death.

4.2 Severe hypertension, renal failure, abnormal steroidogenesis, hypogenitalism and sensorineural deafness

Hamet et al (1973) reported 3 sibs with severe hypertension, hypogenitalism, renal failure and sensorineural deafness.

4.2.1 Characteristics

1. Autosomal recessive Inheritance.
2. Progressive renal failure
3. Severe nypertension appearing during adolescence
4. Hypogenitalism manifested by cryptorchidism or primary amenorrhea.

4.2.2 **Auditory system**

No external/middle/inner ear abnormalities were mentioned.

Hearing: Bilateral sensorineural deafness appear in childhood, and progresses to total loss of hearing within next few years. No other information was available.

Vestibular system: No data were published.

4.2.3 **Treatment and prognosis**

Hypertension should be treated medically, and use of hearing aid may be considered.

Prognosis is poor. The male and female sib described by Hamet et al (1973) died of cerebral haemorrhage at the age of 30 and 35 years respectively.

Chalot- Marie - tooth syndrome, nephritis and and sensorineural deafness (Lemieun-Neemeh syndrome)

Lemieum and Neemeh (1967) described a syndrome appearing in two families and characterized by childhood onset of progressive distal muscle atrophy, neuropathy with proteinuria and hematuria and progressive sensorineural hearing loss. A sporadic case was reported by Hanson et al (1970).

4.3.1 **Characteristics**

1. Probable autosomal dominant inheritance
2. Nephropathy
3. Charat-Marie-tooth syndrome.

4*3.2 **Auditory system**

No external or middle or inner ear abnormalities were reported.

Hearing: Hearing loss began in childhood and was slowly progressive. Hearing loss is moderate (about 50 dB) and more marked in high frequencies (Lemieun and Neemeh 1967, Hanson et al (1970). No other audiometric tests were reported.

Vestibular system: Caloric responses were absent bilaterally in the boy described by Hansan etal (1970).

4.3.3 **Treatment and prognosis**:

A hearing aid is beneficial. It is difficult to establish prognosis, because all cases affected with nephropathy were relatively young.

4.4. Macrothrombocytopathia,Nephritis and Sensorineural Deafness

Epstein et al (1972) reported a syndrome consisting of giant platelets associated with thrombocytopemia, nephritis and sensorineural deafness in two unrelated kindreds.

Ekstein etal (1975) documented a syndrome affecting another kindred in a similar manner, but there was normal platelet function and different ultrastructural morphology.

4.4.1 **Characteristics**:

1. Dominant inheritance, probably autosomal.
2. Neuropathy resembling that seen in Alport syndrome.
3. Giant platelet with thrombocytopenia.

4.4.2 **Auditory system**

No external or middle or inner ear abnormalities were described.

Hearing: Audiograms revealed bilateral moderate to severe sensorineural hearing loss, more marked in the higher frequencies. The time of onset occurs between 5 and 10 years of age.

Vestibular system: No vestibular function tests were reported.

4.4.3 **Treatment and prognosis**:

Splenectomy failed to improve the thrombocyto-pemia, renal transplantation was carried out in the patient.

Prognosis was poor, death form uremia occured in some patients.

4.5 Infantile renal tubular acidosis and congenital Sensorineural deafness

Cohen et al (1973) reported four children, all products of consanguineous matings in two separate subships stemming from

a large inbred kindred, who had congenital sensorineural deafness and infutile renal tubular acidosis. Other cases were documented by Nance and Sweeney (1971) and by Donckelwolcke et al (1978).

4.5.1 **Characteristics**:

1. Autosomal recessive inheritance.
2. Infantile renal tubular acidosis manifested by hyperchloremia and an inability to acidify the urine normally.
3. Growth retardation.

4.5.2 **Auditory system**:

No external, middle or inner ear structural abnormalities were reported.

Hearing: A marked sensorineural deafness, more pronounced at higher frequencies, was demonstrated in infancy. No other audiometric tests were reports

Vestibular system: No studies have been published.

4.5.3 Treatment and prognosis:

A hearing aid was beneficial. Life expectancy does not seem to be reduced if the disorder is recognized and treated early. Growth retardation is persistent.

4.6 Adolescent or young adult renal tubular acidosis and slowly progressive sensorineural deafness

Konigsmark (1966) described a 17 year old girl and her 20 year old brother with renal tubular acidosis and slowly progressive sensorineural deafness that first became manifest

during adolescence. Walker (1971, 1974) reported those sane sibs several years later.

4.6.1 **Characteristics**:

1. Autosomal recessive inheritance
2. Mild renal tubular acidosis with onset in adolescence or early adulthood.

4.6.2 **Auditory system**:

No external, middle or inner ear abnormalities were described.

Hearing: The Sensorineural deafness was slowly progressive and moderate in degree, being more marked in the higher frequencies. Walker (1971) noted hearing loss at 5 years. Speech discrimination was normal and the result of the SISI test was 100 percent, suggesting a cochlear locus for the deafness.

Vestibular system: No studies have been reported.

4.6.3 **Treatment and prognosis**:

Hearing aid should be employed if necessary. Prognosis is reasonably good. Renal tubular acidosis may be treated effectively.

4.7 **Hyperprolinemia, Renal Anomalies and Hearing Loss (Hyperprolinemia type I)**.

The syndrome is characterized by hyperprolinemia, photo-

sensitive convulsions, mental retardation, renal disease and deafness. Mode of transmission is autosomal, recessive.

4.7.2 **Auditory system:**

No external or middle ear abnormalities were described.

Inner ear : Histological examination of organ of corti, showed patchy loss of ganglion cells. Perkoff (1968) reported loss of the inferior olive and also diffuse loss neurons in the cortex, delayed central myelination of white matter, suggesting the possibility of a central nervous system defect which manifests itself as a sensorineural loss audiometrically.

4.7.3 **Treatment and prognosis**:

A hearing aid may be useful, treatment for renal disease is not indicated except in case of uremia. Life span is not decreased, hearing loss is slowly progressive.

*4.8 **Nephritis, Utricaria, amyloidosis and sensorineural deafness (Muckle-wells syndrome).**

A syndrome characterized by recurrent episodes of fever, urticaria, progressive sensorineural hearing loss, amyloidosis and terminal uremia was described by Muckle

and Wells (1962), Kennedy et al (1986) Mamon et al (1984, 1974), Anderson et al (1967), Van Allen et al (1968), Black (1969), Largue et al (1972), Perrotlet et al (1974), Champion (1975).

4.8.1 **Characteristics**:

1. Autosomal dominant transmission with variable expressivity.
2. Adolescent onset of recurrent episodes of urticaria, fever and limb and joint pain.
3. Amyloidosis resulting in neuropathy and uremia.

4.8.2 **Auditory system**:

No external and middle ear abnormalities were described.

Inner ear: Histopathologic examination of inner ear showed absence of the organ of corti and vestibular sensory epithelium, atrophy of the ccchlear nerve and ossification of the basilar membrane (Muckle and Wells 1982), Legent et al (1976) found no characteristics pathological findings.

Hearing: Hearing loss usually appears in childhood or adolescence, progressing slowly to severe loss in the 3rd or 4th decades of life. Progressive sensorineural hearing loss of moderate to severe

degree has been reported by Muckle & Wells(1962) Kennedy et al (1966), Anderson et al (1987), Black (1969), Perrotlet et al (1974). Conduction may be impaired in certain cases, either in isolation or associated with perception impairment. (Legent et al 1976).

Vestibular systems :

No vestibular findings have been reported.

4.8.3 **Treatment and prognosis**:

Deafness may be helped by hearing aids. Anerson et al (1967) reported relief from limb pains with 40-60mg of prednisone daily.

Prognosis is poor. Hearing loss slowly progresses resulting in severe deafness in all patients.

4.9 Renal, Genital and Middle ear anomalies

A syndrome characterized by renal hypoplasia, internal genital malformations, and malformations of the middle ear appearing in 4 female sibs was described by Winter et al (1968). A second family with the same syndrome was reported by Turner (1970).

4.9.1 Characteristics

1. Autosomal recessive transmission.
2. Unilateral or bilateral renal hypoplasia or agenesis.

3. Variable involvement of the genital system with occasional hypoplastic ovaries, tubes or vagina.

4.9.2 **Auditory system**

External ear: External auditory canals were narrowed, ow set ears was reported by Winter et al 1968.

Middle ear : Unilateral endaural surgery revealed a malformed incus with fixation of the malleus and incus in the artic. In another case tympa-notomy revealed an absent incus.

Inner ears : No inner ear abnormalities were described.

Hearing: Moderate to severe conductive hearing loss due to the malformation of the ossicles was reported by Winter et al (1968) and Turner(1970).

Vestibular system: Vestibular ey function tests were not reported.

4.9.3 **Treatment and prognosis**:

Hearing loss can be improved by middle ear surgery for the osslcular abnormalities. The vaginal aplasia should be corrected by plastic surgery. There is moderate variation in the degree of severity of the lesions in affected persons. If a single kidney is involved, a patient can live an essentially normal life.

4.10 Renal Disease, Digital anomalies and Conduction Hearing Loss :

A syndrome characterized by renal anomalies, nephrosis, digital anomalies, cleft uvula and conductive hearing loss was described by 3raun and Bayer (1962) in five male sibs.

4.10.1 Characteristics:

1. X linked or autosomal transmission.
2. Shortened bulbous thumbs and halluces with bifurcation of the distal end of the terminal phalam.
3. Renal anomalies including ureteral constrictions and duplication of the renal pelvis.
4. Bifurcation of the uvula.

4.10.2 Auditory system:

No external/middle/inner ear abnormalities were described.

Hearing: Congenital moderate to severe conductive hearing loss was noticed in affected members, Other audiometric tests were not reported.

Vestibular systems : No vestibular findings were described.

4.10.3 Treatment and prognosis

Extensive medical care for the nephrosis is important. Hearing aid may help the patient with Hearing loss.

Prognosis rather poor because of the renal disease.

CHAPTER V

Genetic hearing loss with integumentary system disease.

There are many types of integumentary system diseases associated with deafness which are inherited. These usually manifest themselves as pigmentary changes of the eye and various types of albanism. They can be diagnosed rather easily because of skin, nail or hair changes that occur along with the generally severe hearing loss.

Waardenburg syndrome is by far most outstanding of these, and is seen quite commonly in schools for the deaf. This accounts for 2 percent of the congenitally deaf.

Many of the other disorders discussed in this chapter have been described in only one or perhaps a few families. However a knowledge of the basic features of these syndromes should bring the light many other cases of these rarer disorders.

5.1 Waardenburg Syndrome:

The characteristic features of this syndrome have been well documented in the literature.

Although certain aspects of this disorder were described by Vander Hoeve (1916) and by Mende (1926), the syndrome was

first well defined by Waardenburg (1948, 1961).

Incidence :

Waardenburg (1951) estimated that 1.4 percent of all deaf mutes in the Netherlands had this syndrome. Digeorge et al (1960) suggested that about 2.3 percent of the congenitally deaf have this disorder.

5.1.1 **Characteristics**:

1. Autosomal dominant transmission with variable expressivity.
2. Lateral displacement of medial canthi and lacrimal points in nearly all affected.
3. Broad nasal root in about 75 percent.
4. Hyperplasia of medial eyebrows in about 50 percent.
5. Heterochromia irides and loss of pigment epithelium of optic fundus in about 25 percent.
6. Skin pigmentary changes including vitiligo and spotty hyper-pigmentation.
7. White forelock in about 20 percent.
8. Cleft lip and/or cleft palate in less than 5 percent.

5.1.2 **Auditory system**:

Otoloaical examination: reported normal external auditory canal and tympanic membranes. No middle ear anomalies were described.

Inner ear: inner ear pathology has been described in a 3 year old girl (Fisch, 1959). The organ of corti was found to be absent in all coils. The basal membrane was slightly thickened and smooth except for a small area covered by hydropic limbus type cells. Only a few neurons remained in the spiral ganglion.

Tomograms on two patients described by Marcus (1968) showed hypoplasia of the cochlea and of the superior and horizontal semicircular canal walls as well as completed absence of the posterior semicircular canal.

Hearing: Over 20 percent of those affected have some hearing loss. The extent of loss is quite variable ranging from no measurable clinical deafness to severe congenital unilateral or bilateral sensorineural deafness.

Fisch (1959) divided the audiogram patterns of those affected with hearing loss into two types;

Type I - almost total deafness with some residual hearing only at lower frequencies.

Type II- moderate deafness with uniform hearing loss in the lower and middle frequencies but with improvement in higher tones.

Vestibular system: Vestibular hypofunction has been reported in about 75 percent of the cases (Zelig, 1961; DeHaas and Tan, 1966;). The most complete survey of vestibular function was presented by Marcus (1968). He found variable responses to caloric stimulation. Although most sonographic studies of the inner ear have shown normal findings (Marcus and Valvassori, 1970; Nemansky and Hageman, 1975) a few investigators (Jensen, 1967; Kanzaki et al, 1971) have found abnormal labyrinthine development.

5.1.3 **Treatment and Prognosis**:

Hearing aids may be used for those patients with moderate to severe hearing loss. This disease is not life threatening. Prognosis is good. Hearing loss is progressive.

5.2 Oculocutaneous Albinism and Congenital Sensorineural Deafness

A syndrome characterized by total oculocutaneous albinism and congenital severe deafness was found in four children in two sib ships in a kindred and described by Ziprkowski and Adam (1964).

5.2.1 Characteristics

1. Autosomal recessive inheritance.
2. Albinism of the entire body including the optic fundi and irides.
3. Deficient medial eyebrows.

5.2.2 **Auditory system**

No external or middle or inner ear abnormalities were noted.

Hearing: Congenital severe sensorineural hearing loss was noted in the affected cousins. Audiometric tests on the two sibs showed a response only at 500Hz at 90d3 in one ear.

Vestibular system: No vestibular function tests were described.

5.2.3 **Treatment and prognosis:**

In some cases, a hearing aid might be of help. There is no apparent change in the albinism or hearing loss throughout the life span of affected persons.

5.3 Multiple Lentigines(leopard) syndrome

The term LEOPARD syndrome is an acronym derived from the following elements: Lentigines, Electrocardiographic defects, Ocular hypertelorism, Pulmonary Stenosis, Abnormalities of genitalia, Retardation of growth and sensorineural Deafness. (Gorlin, Anderson and Blaw, 1969). Earlier case reports were thoroughly reviewed by Gorlin, Anderson and Holler (1971) and Voron et al (1976).

5.3.1 **Characteristics**:

1. Autosomal dominant transmission with variable expressivity.
2. Lentigines developing after birth.
3. Electrocardiographic defects exhibiting some combination of block in the bundle branch system.
4. Pulmonary stenosis and/or hypertrophic cardiomyopathy.
5. Ocular hypertelorism.
6. Abnormalities of genitalia
7. Somatic and mental retardation.
8. Winged scapulae and various minor skeletal abnormalities.

5.3.2 **Auditory system**:

No external/middle/inner ear abnormalities were reported.

Hearing: Sensorineural hearing loss has been observed in about 25 percent (Pickering et al 1971). There is marked variation in the degree of hearing loss in different affected persons, but in most, it is mild. But in contrast, Capute et al (1969) described 2 cases with congenital severe S.N. hearing loss with very poor Speech development. Lassonde et al (1970) noted deaf mutism in their patient.

Vestlbular system: Caloric tests showed no abnormalities (Capute et al 1969).

5.3.3 **Treatment and Prognosis**:

Severe pulmonary stenosis requires cardiac surgery (Gorlin et al 1969). The Lentigines have been treated by dermabrasion (Selmanowitz et al 1971). Patients with hearing loss may require hearing aids. Genital abnormalities should be corrected.

Lentigines is the only feature progressing in number throughout the first two decades of life. Some patients with severe obstructure cardlomyopathy have met early death (Somerville and Bonham Carter 1972), but most have experienced a normal life span.

5.4 **Recessive Piebaldness and Congenital Sensorineural Deafness**

A syndrome consisting of piebaldness and congenital sensorineural deafness was reported in two of three Hopi Indian brothers by Woolf,Dolowitz and Aldous (1965).

5.4.1 **Characteristics**

1. Probable recessive transmission
2. Pigmentary changes including depigmentation of head and portions of the arms, and hyper pigmented spots in depigmented areas.

5.4.2 **Auditory system**

No external/middle/inner ear abnormalities were described.

Hearing: The brothers were congenitally deaf. Audlograms showed a bilateral 60 to 100 dB sensorineural hearing loss. No other audiometric tests were described.

Vestibular system: Caloric vestibular tests were normal.

5.4.3 **Treatment and prognosis**:

No treatment other than the use of hearing aid appears to be necessary.

Neither the pigmentary loss nor the deafness was progressive.

5.5 **X Linked pigmentary abnormalities and congenital Sensorineural deafness**

A Moroccan Jewish family having 14 congenitally profoundly deaf males appearing in three generations was described by Ziprkowski and coworkers (1962) and by Margolis (1962). Four of the affected persons were studied in detail and all showed similar clinical features. An Isolated example was reported by Campbell et al (1962).

5.5.1 **Characteristics**:

1. X Linked transmission.
2. Pigmentary changes of the skin beginning in infancy characterized by large irregular spots of hypopigmentation and hyper pigmentation.

5.5.2 **Auditory system**:

Otoloaic examination: showed normal auricles, auditory canals and ear drums.

No inner ear histopathological studies were described.

Hearing: All affected persons were profoundly congenitally deaf. Puretone testing showed no response to frequencies above 500Hz. No other audiometric tests were described(Fried etal 1969)

Vestibular system: Caloric vestibular tests showed no vestibular responses in three patients tested. A fourth showed moderate depression of vestibular response, more marked on left side.

5.5.3 **Treatment and prognosis**:

Hearing aid may be used, if practical. There is no known treatment for the pigmentary abnormalities other than use of covering creams. Hearing loss is nonprogressive. Pigmentary changes with increasing spotty pigmentation continue from infancy through second decade of life, but change little thereafter.

5.6 Dominant Pie bald tract, ataxia and sensorineural Bearing Loss (Telfer Syndromel)

Although possibly described earlier by Hammerschag (1908), this syndrome was well defined by Teyler, Sugar,

Jerger and Mulchay (1971) in studies of two Pennsylvania kindreds. In the first family 11 persons in 4 generations were affected. In the second kindred a father and daughter manifested the disorder.

5.6.1 **Characteristics**:

1. Autosomal dominant transmission.
2. Congenital piebaldness
3. Ataxia or coordination difficulties in about 80 percent.
4. Mental retardation in about 80 percent.

5.6.2 **Auditory system**:

No external/middle inner ear abnormalities were described.

Hearing: Variable, sometimes asymmetric sensorineural hearing loss in about 60 percent. In some hearing was normal in one ear, and the other ear showing moderate deafness. Others exhibited mild loss in one ear and profound deafness in the other. The hearing loss appeared to be progressive.

Vestibular system: Vestibular testing was not described.

5.6.3 **Treatment and prognosis**: A hearing aid should be used by patients when indicated.

The hearing loss is progressive, whereas the pigment loss is not.

5.7 **Vitiliso, muscle wasting, Achalasia. and Congenital sensorineural deafness**

A brother and sister with congenital severe sensorineural deafness, congenital depigmented areas on the neck and Torso, marked muscle wasting in hands, feet and legs and achalasia were described by Rozycki, Ruben, Rapin and Spiro (1971).

5.7.1 **Characteristics**:

1. Autosomal recessive transmission
2. Mild vitiligo
3. Short stature
4. Distal neuropathic muscle wasting, more marked in the legs.
5. Abnormal esophageal motility.

5.7.2 **Auditory system**:

No external/middle/inner ear abnormalities were reported.

Hearing: Congenital severe sensorineural deafness was noted in both sibs. No other audiometric tests were reported.

Vestibular system: Caloric vestibular tests were normal.

5.7.3 **Treatment and Prognosis**:

The males achalasia was relieved by esophageal dilatation.

The syndrome is not life threatening. The deafness was nonprogressive.

5.8 Atypical erythrokeratoderma, Somatic retardation, Peripheral Neuropathy and Congenital Sensorineural deafness

Beare, Nevin, Froggat, Kerndran and Allen (1972) reported an 8 year old female with an atypical form of erythrokeratoderma, Somatic Retardation, neurologic disturbances and sensorineural deafness. Patients having similar features were reported by Haxthausen (1955), Pindborg and Gorlin (1962), Schnyder, Wissler and Wendt (1968) and By croft et al (1976).

5.8.1 Characteristics

1. Uncertain inheritance
2. Atypical erythrokeratoderma
3. Peripheral neuropathy.

5.8.2 Auditory system:

No external/middle/inner ear abnormalities were described.

Hearing: Profound bilateral congenital generalized sensorineural hearing loss with minimal residual low tone retention in both ears and slight middle tone retention in one ear were demonstrated by Beare et al (1972). The patients of Haxthausen (1955) and pindborg and Gorlin (1962) were congenitally deaf.

Vestibular system: No vestibular tests were described.

5.8.3 **Treatment and prognosis**:

There is no therapy for the skin lesions. A hearing aid may be employed as needed.

There is no evidence that the deafness or skin lesions are progressive.

5.9 Generalized spiny hyperkeratosis, universal Alopecia and Congenital sensorineural deafness

Morris, Ackerman and Koblenzer (1969) reported a syndrome of generalized hyperkeratosis, universal alopecia and sensorineural deafness. Meyers etal (1971) reviewed the same patient and described another infant with the same disorder. Wilson et al (1973) and Solomon et al (1974) described other examples.

5.9.1. Characteristics

1. Whether this syndrome represents a genetic entity requires documentation of additional cases.
2. Generalized spiny hyperkeratosis
3. Universal alopecia
4. Hypohidrosis
5. Obstruction of lacrimal punctae and vascularlzatlon of cornea.

5.9.2 **Auditory system**

Otological examination: The external auditory canals were filled with hard thick debris. When this was removed, the tympanic membranes were noted to be thickened.

Inner ear: The temporal bones in one infant showed scheibe's cochleosaccular abnormality (Myers et al 1971).

Hearing: Congenital bilateral moderately severe sensorineural loss, more marked in the high tones was noted.

Vestibular system: Vestibular testing was not mentioned.

5.9.3 **Treatment and prognosis**:

The skin can be treated with topical lubricants. A hearing aid can be employed. One child died in infancy from aspiration. Whether this death resulted from the child's having the syndrome cannot be ascertained from the limited number of examples.

5.10 **Keratopachydermia, Digital constructions and Sensorineural deafness**

5.10.1.

Congenital sensorineural deafness, hyperkeratosis involving the palms, soles and knees and elbows and ringlike furrows developing on the fingers and toes were the major

features of a syndrome affecting 4 members of a kindred described by Nockmann (1961). A similarly involved individual was reported by Drummond (1939). An affected father and daughter were documented by Gibbs & Frank (1966).

5.10.2 **Auditory system**:

No external/middle/inner ear abnormalities were mentioned.

Hearing: All individuals reported by Nockemann (1961) and Drummond manifested congenital profound deafness.

The female patient documented by Gibbs and Frank (1966) had bilateral mild high frequency sensorineural hearing loss. No other audiometric information was presented.

Vestibular system: No mention was made of vestibular tests.

5.10.3 **Treatment and prognosis**:

Rearing aid may be helpful. Surgical amputation for the constricted fingers.

Hearing loss remains unchanged with age.

Prognosis for involved digits is poor, since there is usually continuing constriction of the phalanges and eventual loss of some digits.

5.11 Anhidrosis and Progressive sensorineural Hearing loss

Congenital anhidrosis is one of many ectodermal dysplasias. In 1946, Helweg-Larsen and Ludvigsen described a syndrome characterized by congenital anhidrosis and progressive sensorineural hearing loss.

5.11.1 Characteristics

1. Autosomal dominant transmission
2. Congenital anhidrosis.

5.11.2 Auditory system

No external/middle/inner ear abnormalities were mentioned.

Hearing: Progressive sensorineural deafness was first noticed at 35 to 45 years of age. Audiograms obtained on two affected members showed severe hightone sensorineural hearing loss. No further description of the deafness was made.

Vestibular system: Vestibular tests were not mentioned.

5.11.3 Treatment and prognosis:

Hearing loss may be lessened by hearing aid.

Treatment for anhidrosis is synptomatic.

Patients should refrain from heavy exertion or exposure to hot temperatures, since they are subject to hyperthermia.

Hearing loss is slowly progressive.

5.12 Generalized alopecia, hypogonadism and Sensorineural deafness

Crandall, Samec, Sparkes and Wright(1973) reported three affected brothers with short stature. Two had secondary hypogonadism, sensorineural deafness and alopecia. A third brother was similarly involved exhibited only minimal hypogandism.

5.12.1 Characteristics:

1. Recessive inheritance, probably autosomal.
2. Generalized alopecia with Pilitorte.
3. Growth retardation.
4. Hypogonadism.

5.12.2 Auditory system:

No external/middle/inner ear abnormalities were mentioned.

Hearing: A sensorineural hearing loss was detected at the time of schooling. The deafhess was described as being slowly progressive and ranged from 65 to 85 dB at the time of testing at 18 to 21 years.

Vestibular system: No studies were reported.

5.12.3 Treatment and prognosis:

Growth harmone therapy is indicated. A wig may be worn for cosmetic purposes. A hearing aid may be of some benefit.

Prognosis is fairly good.

5.13 **Knuckle pads, Leukonychia and mixed hearing Loss**

A syndrome consisting of Leukonychia, Knuckle pads and mixed hearing loss was described by Schwann (1963) and by Bart and Pumphrey (1967).

5.13.1 **Characteristics**:

1. Autosomal dominant inheritance.
2. Knuckle pads over the fingers and toes.
3. Leukonychia.
4. Hyperkeratosis of the palms and soles.

5.13.2 **Auditory system**:

External ear: No abnormalities were noted.

Middle ear: Exploration of middle ear of one patient showed such disorganization of the middle ear structures that the ossicles and facial nerve could not be identified.

Inner ear: Roentgenograms of the temporal bones showed normal cochlear and labyrinthine structures.

Hearing: Audiometric findings in five patients were variable (Bart and pumphrey 1967). A 10 to 100 dB hearing loss, most marked in the higher frequencies, was found. In two cases a pure sensorineural hearing loss was present. In the three remaining cases mixed hearing

loss was present atleast one ear. Schwann (1963) noted congenital severe hearing loss, otherwise unspecified.

Vestibular system: Vestibular system of the 3 persons tested, one showed normal response to caloric testing, whereas the other showed no response, indicating vestibular paresis. A third patient had a hypoactive response on the left side and normal response on the other side (Bart and Pumphrey 1967).

5.13.3 **Treatment and prognosis**

A hearing aid should be employed as indicated. Knuckle pads are not sufficiently displeasing to merit surgical removal.

The deafness was not progressive.

5.14 Dominant onychodystrophy, coniform teeth and Sensorineural hearing loss

A syndrome consisting of small fissured nails, malformed teeth and sensorineural deafness was described by Robinson, Miller and Bensimon in 1962.

5.14.1 **Characteristics** :

1. Autosomal dominant transmission.
2. Onychodystrophy
3. Teeth with coniform crowns and oligodontia.
4. Elevated sweat electrolyte concentrations.

5. 14.2 **Auditory system**:

No external/middle/inner abnormalities were mentioned.

Hearing: A generally symmetric sensorineural hearing loss of 10 to 100d3 was found in all affeeted persons. Higher frequencies Mere more strikingly involved. Apparently, the hearing loss was congenital, since no progression was noted to develop in later years. Other audiometric tests were not described.

Vestibular system: No vestibular tests were reported.

5.14.3 **Treatment and prognosis**:

There is no specific therapy for the onychodystrophy. The teeth may be crowned, the partial dentures may be constructed. Hearing aid may be employed, if necessary. The nail, tooth anomalies and hearing loss do not change with time.

5.15 **Dominant onychodystrophy, triphalangeal thumbs and congenital sensorineural deafness**:

A syndrome characterised by Rudimentary finger nails and toenails and congenital severe snesorineural

hearing loss was described by Goodman, Lockareff and Gwinup (1969) and by Moghadam and Staten (1972).

5.15.1 **Characteristics**:

1. Autosomal dominant transmission.
2. Onychodystrophy of fingernails and toenails.
3. The pharangeal thumbs.

5.15.2 **Auditory system**:

Otolaaic Examination: showed no abnormalities of ear canal or drums. No middle/inner ear abnormalities were mentioned.

Hearing: Both mother and son in the study of Goodman et al (1969) had congenital severe sensorineural hearing loss.

In the family studied by Moghadam and Statten (1972), the son had severe congenital sensorineural deafness, where the mother exhibited a bilateral low tone moderate (30 to 40dB) SN deafness.

Vestibular system: Vestibular findings were not reported.

5.15.3 **Treatment and prognosis**:

There is no known treatment for onychodystrophy Hearing aid may be employed, if indicated. The disease is non progressive.

S.16 **Recessive onychodystrophy, triphalangeal thumbs and Halluces mental retardation, Seizures and congenital sensorineural deafness:**

A syndrome characterized by congenital severe sensorineural deafness, rudimentary fingernails and toe-nails and dysplastic terminal phalanges was reported by Walbaum, Fontaine, Lienhardt and Piquest (1970) in male and female sibs. Similar cases were described by Qazi and Smithwick (1970) and by Cantwell (1975).

5.16.1 **Characteristics:**

1. Autosomal recessive transmission
2. Rudimentary fingernails and toenails
3. Digital abnormalities, including tri-phalangeal thumbs and halluces and hypoplastic terminal phalanges of the remaining digits.
4. Mental retardation.
5. Grand mal seizures.

5.16.2 **Auditory system:**

No external/middle/inner ear abnormalities were reported.

Hearing: Severe congenital sensorineural hearing loss was evident in all affected.

Vestibular system: No tests of vestibular function have been reported.

Treatment and prognosis:

Use of hearing aid, if deemed possible.

The deafness is profound.

5.17 Recessive onychodystrophy and congenital sensorineural deafness

A syndrome characterized by congenital deafness and onychodystrophy occuring in two of five sibs was descfibed by Feinmesser and Zelig (1961).

5.17.1 Characteristics

1. Autosomal recessive inheritance
2. Congenital onychod?ystrophy with small short, fingernails and toenails.

5.17.2 Auditory system:

Otoscopic examination: showed normal right ear and evidence of old otitis media on other side in one sister. No inner ear abnormalities were noted.

Hearing: Congenital severe sensorineural hearing loss was noticed in all affected members. Audiograms showed a 60 to 100 d3 sensorineural hearing loss, most marked in the higher hypoactivity of the labyrinth in the older girl and normal vestibular reaction in the younger sib.

5.17.3 Treatment and prognosis:

Artificial nail coverage for nail dystrophy. Deafness may be lessened by using a hearing aid.

5.18 **pili torti and sensorineural hearing loss**

A syndrome characterized by pilitorti (flat,twisted hair) and sensorineural hearing loss has been described by Bjornstad (1965) Reed et al (1967), Robinson and Johnston (1967) and Cremers and Geerti (1979).

5.18.1 **Characteristics**:

1. Probable autosomal recessive inheritance
2. Congenital pilitorti.

5.18.2 **Auditory system**:

No external/middle/inner ear abnormalities were mentioned.

Hearing: Congenital moderate to severe sensorineural hearing loss. 6 of the 7 reported patients had a 20 to 60 d3 hearing loss (Bjornstad, 1965). The patient described by Robinson and Johnston (1967) had severe bilateral sensorineural hearing loss.

Vestibular system: Vestibular tests were not reported.

5.18.3 **Treatment and prognosis**:

A wig is useful for cosmetic purposes. A hearing aid should be employed.

There is no evidence that the deafness is progressive.

5.19 **Scanty hair, camptodactyly and sensorineural hearing loss**

A syndrome characterized by Congenital alopecia with later scanty, brittle hair, flexion contractures of the little fingers, and moderately severe sensorineural hearing loss was described in a brother and sister by Mikaelian et al (1970).

5.19.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Sparse hair.
3. Camptodactyly.

5.19.2 **Auditory system**:

No external/middle/inner ear abnormalities were mentioned.

Hearing: Hearing loss, probably congenital, was first noticed in early childhood. Although it was slowly progressive, this point was not documented.

Hearing tests showed a 45 to 80 dB sensorineural hearing loss more marked at higher frequencies with speech reception thresholds of about 60 dB bilaterally. A threshold tone decay test showed no fatigue, and the SISI test was positive bilaterally, suggesting a cochlear locus for the hearing loss.

Vestibular system: Vestibular tests were normal.

5.19.3 **Treatment and prognosis**

A hearing aid and wig may be used.

There is poorly documented evidence that deafness is slowly progressive.

5.20 Atopic dermatitis and sensorineural hearing loss

Two brothers and a sister from a sibship of four manifested nonprogressive sensorineural hearing loss and atypical atopic dermatitis (Konigsmark, Hollander and Berlin 1968).

5.20.1 **Characteristics**:

1. Autosomal recessive inheritance.
2. Atypical atopic dermatitis with onset at about 10 years of age and involvement of the trunk and arms.

5.20.2 Auditory system:

Otologic examination: showed no external or middle ear abnormality. No histopathological studies of the inner ear were described.

Hearing: Hearing loss was first noted at 3 to 5 years of age. Hearing tests at 5 or 6 years of age showed a bilateral symmetric sensorineural hearing loss of 15 to 55 d3 for both air and bone conduction. Speech reception thresholds corresponded to the expected hearing loss. Speech discrimination was over 90% in

all the three sibs. SISI test was 100 percent at 2000 and 4000 Hz, and tone decay tests were negative. Hearing tests repeated over a 10 year period showed no progression of the deafness.

Vestibular system: Calorie vestibular tests showed no abnormalities.

5.20.3 **Treatment and Prognosis**:

Treatment consists of local therapy for the atopic dermatitis and a hearing aid, when necessary for the hearing loss.

The hearing loss was apparently non-progressive.

5.21 **Von Winkel's syndrome.**

Von Winkel's syndrome is a rare familial skin disorder, also known as multilating keratoderma. Although this syndrome was first described by Hyde and Montgomery in 1905, the syndrome is usually associated with the name of Von Winkel. It usually affects white European females and invariably begins during childhood (Gibbs & Feinty, 1960).

5.21.1 **Characteristics**:

1. Autosomal dominant inheritance.
2. Diffuse hyper keratosis of palms and soles.
3. Constricted digits
4. Linear keratosis of elbows and knees.

5.21.2 **Auditrory system**:

Otoloaical examination: showed no structural abnormalities. No inner ear deformaties were Described.

Hearing: Congenital sensorineural hearing loss. One patient studied by Deummond (1939) was a deaf mute. Gibbs and Frank (1966) reported a mild high frequency hearing loss. Llamas et al (1974) found 2 affected members in a family to be deaf.

Audiotaetric test revealed a cochlear type of sensorineural loss varying from moderate to severe degree, tone decay being absent and the loudness discomfort level was normal (gibbon and Watson 1978).

Vestibular system: Vestibular tests were normal.

5.21.3 **Treatment and prognosis**:

Hearing aid may be used, if necessary.

No evidence that hearing loss is progressive.

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CHAPTER VI

Genetic hearing loss associated with Musculoskeletal disease

There are numerous genetic diseases that exhibit hearing loss and musculoskeletal abnormalities. The skeletal diseases range from bone abnormalities that are limited to only a few bones such as mandibulofacial dystosis and oro-facial digital II syndrome to generalized skeletal disorders such as paget disease, craniometaphyseal dysplasia and scle-rosteosis. Several syndromes are very rare, with only a single kindred recorded as being affected, as in deafness and tibial dysgenesis. In some syndromes the hearing deficit is conductive while in others it is sensorineural or mixed type.

The syndromes involving genetic hearing loss and musculoskeletal disorders can be broadly grouped under 3 categories.

1. Otocranial facial syndromes, involving ear-skull-face. eg. Treacher collins syndrome, Goldenhar syndrome etc.
2. Otocervical syndromes, involving ear-neck-shoulder eg. Klippel pel syndrome, Wildervanck's syndrome.
3. Otoskeletal syndrome involving ear,face,limbs. eg. Page_s disease, Mohrs syndrome.

6.1 **Craniofacial dysostosis (Cruzon syndrome)**

Cruzon syndrome involving ear, skull and face is a well documented disorder named after Cruzon.

6.1.1 **Characteristics**:

1. Autosomal dominant inheritance.
2. Premature variable craniosynostosis
3. Occular hypertelorism, shallow orbits and exopthalmos.
4. Beaked nose.
5. Maxillary hypoplasis with relative mandibular prognathism.

6.1.2 **Auditory system**:

External ear: Stenosis or atresia of the external auditory canal was reported by Aubrey (1935), Nager and de Reymer (1948), Wiegand (1954) and Baldwin (1968). Absence of tympanic membrane was noted by Naga and Reymer (1948) and Baldwin (1968).

Middle ear: Surgical exploration and temporal bone studies have shown deformity of the ossicles, ossicular fixation with intratympanic bony masses, distortion and nallowing of the middle ear and mastoid air spaces. Closure of the oval window, or nallowlng of of oval and/or round window. (Boedts 1967, Terrahe 1968, Nager & deReymer (1948, Baldwin 1968).

No inner ear abnormalities were mentioned.

Hearing: One third of patients with Crouzon syndrome have hearing loss, mostly conductive or sometimes mixed.

Recruitment was absent. BC was reduced. (Schurmans & Mariga 1963). No other audiometric tests were reported.

Vestibular system:

Aubrey (1935) described normal vestibular function.

6.1.3 **Treatment and prognosis**:

Cosmetic and functional correction of prematurely fused sutures and facial deformaties - stapedectomy and/or correction of ossicular abnormalities, if the hearing loss is severe. With increasing age, divergent, alternating and concomitant strabismus, frequently optic atropb and the hypoplastic midface become more accentuated with age.

6.2 Apert Syndrome (Acrocephalosyndactyly - Type I)

Apert (1906) was credited with the discovery of this disorder, although the condition has been reported earlier.

Over 200 cases have been reported upto date B1ank (1960) divided acrocephalosyndactyly into typical and atypical forms. Typical (Apert type) acrocephalosyndactyly included only those patients who had a mid digital hand mass consisting of osseous and soft tissue syndactyly of digits 2 through 4.

Although the frequency of the syndrome is about 1 in 160,000 births, because of the high neonatal mortality rate, the disorder is seen in about 1 in 2,000, 000 in the general population.

6.2.1 **Characteristics**

1. Autosomal dominant inheritance. Nearly all cases reported are sporadic.
2. Craniostenosis eventuating in turribrachycephaly.
3. Soft tissue syndactyly and progressive synostoses of hands and feet.
4. Mental retardation

6.2.2 Auditory system

External ear: No external ear abnormalities were described.

Middle ear: Lindsay et al (1975) reported cartilaginous fixation of the stapes footplate, an incompletely developed annular ligament, and an enlarged subarcuate fossa. Congenital stapes fixation is believed to be the frequent finding (Bergs trom et al 1972).

Inner ear: Petrous pyramid polytomography performed on one patient showed no internal auditory meatus. In another case, when the stapes was removed a perilymphatic gusher ensued - possibly as a result of a widened eochlear aqueduct.

Hearing: Perhaps because of the frequent mental retardation, the relatively mild congenital conductive deafness associated with the syndrome has been largely ignored. Data concerning the frequency of hearing loss in the syndrome are non existent, the only information available is case reports. Cooper (1953) reported bilateral conduction deafness in his patient and Grebe (1944) noted that one of eight patients was"completely deaf". Bergstorm et al (1972) described conduction deafness in four patients.

Vestibular system: No studies have been reported.

6.2.3 Treatment and, prognosis:

The hands should be corrected by plastic surgery.

Stapedectomy with prosthesis placement should be considered if the hearing loss is severe.

The disorder is congenital and in general does not progress with age.

6.3 **Hereditary arthro-opthalmopathy (Stickler, Syndrome)**

This condition was first defined by Stickler and coworkers (1965, 1967). An earlier example was described by David(19

6.3.1 **Characteristics**:

1. Autosomal dominant inheritance
2. Numerous but often subtle ossification disturbances, including epiphyscal abnormalities, diaphyscal narrowing and platyspondylia
3. Joint hypermobility
4. Hypoplasia of the midface
5. Severe myopia and often retinal detachment
6. Occasionally cleft palate, submucous cleft palate or bifid uvula.

6.3.2 **Auditory system**:

No external/middle/inner abnormalities were described.

Hearing: About 15 percent of the affected members experience sensorineural or mixed deafness (Hermann 1974, Popkin and Polomeno Konigsmark and Gorlin 1976).

Stickler and Pugh (1967) described sensorineural hearing loss of about 25 to 30d3. Spranger(l968) reported conductive hearing loss.

Vestibular system: No studies have been reported.

6.3.3 **Treatment and prognosis**:

Early referral to an opthalmologist is mandatory. The arthropathy becomes progressively worse. The retinal detachment usually recurs in spite of surgery.

6.4 **Branchial arch syndromes**

The growth and development of face and ear have been shown to be closely interrelated with the formation of the first and second branchial arches. The embryogenesis of the branchial arches may be disturbed due to genetic defects or otherwise, causing various anomalies of the first and second branchial arch derivatives.

Various malformative syndromes have been reported in which embryogenesis of the first and second branchal arches is disturbed, resulting in deafness associated with malformations of the outer, middle and occassionally inner ear. Such deafness is therefore usually conductive in nature, though there may be an additional perceptive component. It may be sometimes sufficiently severe to cause serious difficulties in childhood.

The most important branchial syndromes reported in literature include:

1. Mandibulafacial dysostosis (Treacher collins syndrome)
2. Oculoauriculo vertebral syndrome (Goldenhar syndrome and hemifacial microsomia).
3. Pierre Robin Syndrome

Each of these syndromes will be described in turn.

6.4.1 **Mandibulofacial dysostosis** (Treacher Collins Syndrome, Franceschetti - Klein Syndrome).

Although the syndrome was probably first described

by Thomson (1846-1847), credit for its discovery is usually given to Berry (1889) or especially, to Treacher Collins (1900) who described the essential components of the syndrome. Franceschetti and Klein (1949) published extensive reviews of the syndrome and gave it the name mandibulofacial dysostosis. More than 250 examples have been published since then.

6.4.1.1 **Characteristics**:

1. Autosomal dominant transmission with variable expressivity.
2. Hypoplastic zygomas with resultant antimongoloid palpebral fissures.
3. Coloboma of the lower eyelids and lack of cilia medial to the colobomas.
4. Handibular hypoplasia.

6.4.1.2 **Auditory system**:

External ear: The pinnae are often deformed (in 85%), crumpled forward or misplaced. The external auditory canal is absent, in of cases, when present, the auditory canal is often narrow and sloping (Harrison 1957, Stovin et al (1960). Extra ear tags and blind fistulas may also occur.

Middle ear: Radiographic studies have shown sclerosis of the middle ear, the auditory ossicles may be absent or severely malformed. (McKenzie and Craig 1955, Pavsek 1958, Herberts 1961).

Surgical investigation has revealed such abnormalities as fixed malleus, fusion of malformed malleus and incus, absence of stapes and oval window, absent stapedius tendon, deformed incus and stapes, absent incus, ankylosis of footplate of stapes, ear and epitympanic space. The middle ear cavity may be filled with connective tissue (Altmann 1955, Plester 1961, Holborow 1961, Keerl 1962). Monopodal stapes and a thinned long process of the incus was noted by Plesta 1961, Keerl 1962, Edwards 1964.

Inner ear: The cochlear and vestibular apparatus may be absent or severely malformed (McKenzie & Craig 1955, Pavsek 1958, Herberts 1961, Stovin et al 1960).

Hearing: Most of the affected members have conductive deafness. A sensorineural component has also been noted (Kittel and Fleischer - Peters, 1963, Partsch and Hiilse 1975).

Vestibular system: No vestibular studies have been reported.

6.4.1.3 **Treatment and prognosis**:

A team approach should be employed for

correction of the microtia, mandibular hypoplasia, mabcclusion, and hypoplasia of the malar bones. Tympanotomy with insertion of a prosthesis will usually improve hearing. There is no progression of the deafness.

6.4.2. **Oculoauriculovertebral syndrome**

(Hemifacial microsomia, Goldenhar Syndrome) Hemifacial microsomia was the term introduced by Gorlin and Pindborg (1976) to encompass anomalies of the first and second branchial arch derivatives which manifest clinically as unilateral ear and face abnormalities. Goldenhar syndrome, a possible variant form is distinguished by associated eye abnormalities. A triad of congenital abnormalities consisting of epibulbar dermoids, preauricular appendages and pretragal fistulas was first described by Goldenhar in 1952. Gorlin (1963) noted the frequent association of congenital anomalies of the vertebral column and introduced the term "Oculoauriculo vertebral dysplasia". Since then very few cases of the syndrome are reported by Miyamoto etal 1976, Singh and Gandhi 1978, Parving 1978.

6.4.2.1 **Characteristics**:

1. Probably multifacial inheritance.
2. Epibulbar dermoids.
3. Facial asymmetry.
4. Unilateral hypoplasia of the mandible in 70% of patients.
5. Unilateral facial palsy.
6. Vertebral anomalies.
7. Macrostomia.

6.4.2.2. **Auditory system**:

External ear: External ear malformations include low set, tilted and cupshaped auricles with or without Pre-auricular tags. Unilateral microtia in 50% of cases, atresia or stenosis of the external auditory meatus in 40% of cases.

Middle ear: Ossicular malformations consist of incudo mallelar fusion with osseous fixation to the epitympanic walls, alterations in size of the stapedial crura, stapes foot plate fixation, lack of oval window differentiation. Fallopian tube may be absent. Facial nerve may course abnormally in the middle ear.

Inner ear: Chandrashekar et al (1978) in temporal bone study of patient with hemifacial microsomia found total superior

dehisence of internal acoustic meatus. The otic capsule was deformed with an under developed cochlear modiolus grossly deficient in spiral ganglion population. Cochlear duct was shorter than normal. The vestibular system did not show any structural abnormality except for the degeneration and reduction of the scarpas ganglion cells and nerve fibers.

Hearing: Bearing loss is mostly unilateral and predominantly conductive in nature. Sometimes perceptive component is present. Dijkstra (1977),of the five cases evaluated, found complete deafness in one case, while the other 4 had bilateral asymetrical mixed hearing loss. No other audiometric tests were described.

Vestibular system: No vestibular tests were described.

6.4.2.3 **Treatment and prognosis**:

Surgical correction of microtia, atresia, Mandibular hypoplasia. Tympanotomy with insertion of prosthesis or hearing aid may be employed to improve hearing.

The disease appears to be non progressive and it is not crippling.

6.4.3 **Pierre Robin Syndrome:**

Pierre Robin syndrome is a first arch syndrome.

6.4.3.1 **Characteristics:**

1. Autosomal dominant inheritance with variable expressivity.
2. Mlcrognathia.
3. Glossoptosis.
4. Cleft palate.
5. Sometimes eye abnormalities including strabismus, infantile glancoma, cataract, micropthalmos, retinal detachment.
6. Malformations of the facial bones.

6.4.3.2 **Auditory system:**

External ear: Pinnae may be malformed. microtia, atresia or stenosis of the external auditory canal have been reported.

Middle ear: Various ossicular malformations have been described. In some otitis media was reported.

Inner ear: No inner ear abnormalities were described.

Hearing: Associated hearing loss is usually conductive in nature. Secondary to middle ear anomalies or otitis media. Black et al noted conductive deafness, but sensorineural hearing loss may also occur. No other audiometric tests were described.

6.4.3.3 **Treatment and prognosis**:

Tracheostomy is advised if there is respiratory strider tube feeding or gastrostomy. Glosoptosis should be surgically corrected. Mortality rate is high (40 - 60%).

6.5 **Klippel - Feil Syndrome**

Within the classification of otocervical syndromes, the greatest incidence of otopathology occurs in the Klippel Feil Syndrome.

6.5.1 **Characteristics**:

1. Autosomal dominant inheritance with poor penentrance and variable expressivity.
2. Short neck.
3. Decreased mobility of head.
4. Low occipital hair line.
5. It may be associated with other abnormalities as cleft palate, mental retardation, eye abnormalities.

6.5.2 **Auditory system**:

External ear: Microtia, stenosis and atresia of the external auditory canal have been reported.

Middle ears Everberg (1968) noted absence of oval window. Fixation of stapes footplate was

reported by Jarvis and Selvars (1974).

Other abnormalities include absence of stapes supra structure, afibrous incudostapedial articulation, and hypoplasty of tympanic cavity.

Inner ear: Inner ear malformation consisting of marked stenosis or a bony septum in internal auditory meatus, labyrinthine dysplasia, defective cochlear development with a number of turns missing.

Hearing: There are no consistent audiologic patterns. Hearing loss may be conductive, sensorineural or mixed in nature (Stalk and Borton 1973). No other audiometric tests were reported.

6.5.3 **Treatment and prognosis**:

Use of hearing aid and stapedectomy may lessen the hearing impairment.

The disorder is congenital and non progressive.

6.6. Klippel-Feil anomalad and abducens paralysis with retracted bulb and sensorineural or Conduction Deafness(Wildervanck syndrome, Cervico-oculoacoustic dysplasia):

Wildervanck and colleagues (1952, 1960, 1966) brought attention to the syndrome of Klippel-Feil anomalad,

abducens palsy with retracted bulb and severe sensorineural deafness. Since then many cases have been reported, extensively by Mein (1968), Kirkham (1970).

6.6.1 **Characteristics**:

1. Multifactorial inheritance
2. Fusion of cervical vertebrae
3. Abducens palsy with retracted bulb (Duane syndrome)
4. Occasional cleft palate and/or torticollis.

6.6.2 **Auditory system**:

External ear: Various ear anomalies have been described. Pre auricular tags, malformation atresia or absence of external auditory canal (Everberg et al 1962), Fraser and Mac Gillivray 1968).

Middle ear: abnormal ossicles and absence of oval window were the abnormalities reported Everberg et al 1962).

Inner ear: Stenosis or bony Septum within the internal auditory meatus, abnormal semicircular canals and underdevelopment of the labyrinth has been reported by cross and Pfaffenbach (1972), Baumeister and Terrahe (1974).

Hearing: Severe congenital sensorineural or conductive hearing loss has been described by several authors. (Mac Gillivray (1968), Kirkham (1970) Stark and Borton 1973). No other audiometric tests have been described.

Vestibular system: Vestibular response has usually been abnormal (Sverberg et al 1963, Wildervanck et al 1966).

6.6.3 **Treatment and prognosis**:

The restriction of the abduction of the eye can be partly or completely corrected by temporal transplantation of the superior and inferior recti combined with resection of the internal rectus (Gobin 1971). Hearing aid may be employed, if the hearing loss is severe. The disorder is congenital and non progressive.

6.7 Cranio Metaphyscal Dysplasia (CMD or Pyles Disease)

This condition was originally described by Pyle in 1931. There are 2 heriditable forms, dominant and recessive type. Clinically and pathologically the recessive type is more severe than dominant type. Gorlin et al (1970) suggest that it is erroneous to equate CMD with pyles disease because the latter is different in that the changes

are more severe and generalized, and the facial and cranial bones are unaffected.

6.7.1 **Characteristics**

1. Autosomal dominant and recessive inheritance.
2. Hyperostosis of the cranial and facial bones.
3. Metaphyscal dysplasia affecting long bones.
4. Cranial nerve paralysis.
5. Characteristic Leonine facies with hyper-telorism and broad nasal bridge.

6.7.2 **Auditory system**

External ear: No external ear abnormalities were reported.

Middle ear: Ankylosis of stapedial footplate or bony overgrowth of ossicles with resultant immobilization was reported by Gray (1965), Kietzer and Paparella (1969).

Inner ear: Narrowing of internal auditory meatus with enroachment on auditory nerve has been identified in radiographs (Rimoin et al 1969, Miller et al 1969). Polytomographs showed deposit of bone in the region of the cochlea (Gladney and Monteleone, 1970).

Hearing: Various degrees of hearing loss have been found in nearly all cases. Not uncommonly, it is the presenting symptom (Saunders).

Although the loss is largely conductive in many cases it has a sensorineural component (Saunders, 1957, Grat 1965 and Kietzer and Paparella 1969, Gladney and Monteleone (1970). The hearing loss begins in childhood and is slowly progressive until there is moderate to severe (30 to 90 dB) deafness in the third or fourth decade. In 2 of 3 cases SISI tests that were initially negative became positive at about 12 years of age (Gladney and Monte-lene 1970).

6.7.3 **Treatment and prognosis**:

The bone dysplasia may be treated by surgical contouring (Millard et al 1967). A hearing aid may lessen the deafness. Stapedectomy should be considered for persons with predominantly conductive hearing loss.
The hearing aid visual impairment and facial palsy are slowly progressive.

6.8 Craniodiaphyscal Dysplasia

Gorlin, Spranger and Kozzalka (1969) employed the term "craniodiaphyscal dysplasia" to designate a very severe bone disorder characterized by massive generalized hyper ostosis and sclerosis, involving especially the skull and facial bones.

6.8.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Massive enlargement and sclerosis of cranial and facial bones, ribs and clavicles.
3. Cylindrization of long bones and diphyscal endostosis.
4. Elevated levels of alkaline phosphatase.
5. Bony overgrowth of cranial foramina resulting in blindness and deafness.

6.8.2 **Auditory system**

No external/middle/inner ear abnormalities were mentioned.

Hearing: Deafness has been noted in all cases. In some, the deafness was congenital (Stransky etal 1962). The deafness was described as mixed by Gemmell (1935) and as sensorineural by Halliday (1949). No other audiometric tests were described.

Vestibular system: Wo studies have been reported.

6.8.3 **Treatment and prognosis**:

Therapy is of no avail. The prognosis is poor. The disorder progresses and results in severe mental and somatic retardation, blindness, deafness and often early death.

6.9 **Frontometaphyscal dysplasia (Gorlin-Hart Syndrome).**

This is a rare but distinguishable variant of the craniotubular osseous dysplasias with clinical features that may overlap with cranio metaphyscal dysplasia. Such cases were reported by Gorlin and Cohen (1969), Walker (1969), Holt et al (1972), Danks et al (1972), Jarvis and Jenkins (1975) and Weiss and Reynolds (1976).

6.9.1 **Characteristics**:

1. Autosomal dominant or X linked recessive inheritance.
2. Characteristic facies marked by pronounced supra-orbital ridge and pointed chin.
3. Wasting of arm and leg muscles with flexion de-formity of joints.
4. Characteristic skeletal changes,

6.9.2 **Auditory system**

External ear: Usually external auditory canal and tympanic membrane are normal.

Middle ear: Tympanic cavity may be narrowed by osseous infiltrations, ossicular chain fixation occurs in multiple locations. On tympanotomy Arenberg et al (1974) found fixed malleus and incus.

Inner ears : Radiographic studies have shown osseous infiltration of the cochlea in some cases.

Hearing: Hearing loss is mostly conductive (Gorlin and Cohen 1969, Walker 1969). But Holt et al (1972) and Arenberg et al (1974) noted symmetric progressive mixed hearing loss that appeared prior to puberty.

Vestibular system: No vestibular tests were reported

6.9.3 **Treatment and prognosis**

A hearing aid may be employed. This disorder does not limit the life span.

6.10 Recessive Osteopetrosis (Albers-Schonberg Disease)

Osteopetrosis sometimes known as"marble bone disease" is a rare skeletal disorder characterized by a generalized increase in bone density occuring in early childhood. Deafness has been Reported only in the recessive form. So far only about 300 cases of osteopetrosis have been reported.

6.10.1 Characteristics

1. Autosomal recessive transmission
2. Osteosclerosis with involvement of all bones of the skeleton.
3. Facial palsy and visual loss in over half the cases.
4. Anemia, hepatosplenomegaly, thrombocytopenia are the other associated abnormalities.

6.10.2 **Auditory system**:

External ear: The deformaties of the external ear consist of large soft auricles lacking in cartilagenous support (McKusick 1960,1966).

Middle ear: Temporal bone changes described by Myers and Stool (1969) revealed a smaller than normal middle ear cavity with marked hypertrophy of mucosa. A portion of facial nerve was herniated into the middle ear. There was a small incomplete fallopian canal. Abnormal otosclerotic ossicles lacked medullary cavities, The stapes was thickened, preserving its fetal shape through lack of remodeling. There was no pneumatization of mastoid cells, these areas being filled with chondrocytes and osteoblasts. In about half the cases there was history of otitis media.

Inner ear: The organ or corti, vestibular labyrinth and the spiral ganglion were normal. Hearing: About 25 and 50 percent of the patients have mild to moderate mixed sensorineural and conductive hearing loss beginning in childhood (Johnston et al 1968), Myers and Stool, 1969).

In general investigators have not reported detailed audiometric findings. Enell and Pehrson (1958) however have described the audiogram of their 9 year old patient as resembling that found in otosclerosis.

Vestibular systems:No vestibular findings have been described.

6.10.3 **Treatment and prognosis**:

Surgical enlargement of the optic foramina has been carried out. Splenectomy and prednisone have been employed to treat anemia (Moe and Skjaeveland 1969). Hearing aids will help those with deafness.

The clinical course is variable. In some cases, Facial palsy, Visual or hearing loss may appear rapidly and then may improve slightly. But death usually results within the first few years of life from anemia or secondary infection.

6.11 Pagets Disease of Bone (Osteitis Deformans)

Paget (1876) described a form of "chronic osteitis" that begins in middle age and is characterized by changes in the shape, size and direction of involved bones.

6.11.1 Characteristics

1. Autosomal dominant transmission with incomplete penentrance and variable expressivity.
2. Onset in middle age.
3. Involvement of the sacrum, pelvis, vertebrae, long bones of the legs and skull.
4. Neurologic deficits and spinal cord compression in a small percentage of patients.

6.11.2 Auditory system

Marked involvement of the auditory system more often accompanies advanced skull changes.

External ear: Patients may have narrowing and/or tortuosity of the external auditory meatus (Sparrow and Duvall 1967, Davies 1968).

Middle ear: Temporal bone X rays revealed stapes foot plate thickening (25%), Stapes foot plate fixation, and less frequently incudomalleal fixation within the epitympanum (petasmick 1969).

Inner ear: There have been several reports on the histopathologic changes in the temporal bones.

The earliest changes include increased remodeling of the hone surrounding vascular

channels near the labytinthine capsule and finally enroaching upon the endosteum of of the membranous labyrinth (Glussen 1970). There is a variable degree of degeneration of sensory cells of the Saccular and Utricular maculae and cristae of the semicircular canals (Lindsay and Lehman 1969).

In the organ of corti there is degeneration of the stria vascularis and hair cells, ederma of the tectorial membrane and dilatation of the coehlear duct (Davies 1968, Nager 1975), Kornfeld (1967) showed that when the innermost portion of the capsule was affected, there was thickening of the stria vascularis, atrophy of portions of the stria adjacent to the thickenings, and formation of intravascular concrements.

Applebaum (1977) found pagetic bone invading the internal auditory canal and compressing the cochlear division of the 8th cranial nerve resulting in severe neural degeneration.

Hearing: Goldstein et al (1926) noted hearing impairment in only 5% of the cases, Rosenkrantz et al (1952) found in 12% and Davies found

hearing loss in 40%. The type of hearing loss varies from conductive to sensorineural and may be unilateral or bilateral (Wyllie 1923).

Clemis et al (1967), Sparrow and Duvail (1967) and Calvet et al (1967) found mixed deafness most frequently.

Petasnick (1969) however found sensorineural deafness more common, while Davies (1968) noted most patients to have conductive deafness in low frequencies.

SISI scores were negative (Konigsmark and Gorlin 1976), But o1ems et al (1967) found low SISI scores at low frequencies, but high scores at high frequencies.

Vestibular system: Caloric reaction was variable. Among 28 patients complaining of Vertigo, Davies (1968) found a diminished response in only two individuals. Out of 3 cases studies (Konigsmark and Gorlin 1976) only one had no response to caloric stimulation, whereas the other two were normal.

6.11.3 **Treatment and prognosis**:

Hearing aid is the best treatment for hearing loss. Attempts to mobilize the stapes have met with generally poor results (Davis 1968). Therapy for generalized disease includes high protein diet with adequate vitamin C, a high intake of calcium and anabolic steroids for increasing bone repair.

The disease is slowly progressive but does not appear to shorten life. Fractures are frequent, but there is minimal trauma only a small/portion of patients develop /prosevere neurologic or renal complications or sarcomatous degeneration of bone. Increased vascularity may induce high output cardiac failure.

6.12 Hyperostosis Corticalis Generalisata (van Buchem's Disease)

A syndrome characterized by a generalized otosclerotic overgrowth of skeletal bones was described in seven cases by Van Buchem et al in 1962. An isolated case was described by Fosmoe et al (1968). Van Buchem (1971) documented another eight patients.

6.12.1 **Characteristics**

1. Autosomal recessive transmission
2. Generalized osteosclerotic overgrowth of skeleton including mandible, skull, ribs, long and short bones.
3. Narrowing of skull foramina causing cranial nerve paralysis with visual loss.
4. Markedly increased levels of serum alkaline phosphatase in mose patients.

6.12.2 **Auditory system**

No information is available regarding the conditions of external, middle or inner ear.

Hearing: Hearing loss is sensorineural or mixed type. Gradual impairment of hearing begins at about 15 years of age (Van Buchem et al 1962). All the 7 patients described by Wonden (1968) had bilateral symmetric hearing loss. Some cases showed sensorineural hearing loss, whereas others manifested mixed deafness. There was loss of speech discrimination. Tone decay and S I S I tests were positive in some cases.

Vestibular system: No vestibular findings were described.

6.12.3 **Treatment and prognosis**

A hearing aid may be useful. Decompression of the optic and facial nerves should be considered when there is sign of involvement.

The disorder begins at 10 years of age and progresses slowly thereafter. It does not result in early death.

6.13 **Sclerosteosis**

Hirsch (1929) probably described the first cases of this disorder. Additional examples are those of Kretzmar and Roberts (1936), Falconer and Ryrie (1937), Higinbotham and Alexander (1941), Kelly and Lawlah (1946), Pietruschka (1958), Truswell (1958), Klintworth (1963) and Sugiura (1975), Beighton et al (1976).

6.13.1 **Characteristics**:

1. Autosomal recessive inheritance.
2. Square appearance of mandible.
3. Generalized osteosclerosis and hyperostosis of calvaria, mandible, clavicles and pelvis.
4. frequent asymmetric cutaneous syndactyly of index and middle fingers.
5. Bony impingement on cranial foramina producing facial palsy or optic atrophy.

6.13.2 **Auditory system**:

No external or inner ear abnormalities were described.

Middle ear: Beighton et al (1976) described fixed ossicles.

Hearing: Bilateral sensorineural, conductive or mixed deafness is a constant feature of

the disorder. It may appear early in infancy, during childhood or late in adolescence. No other audiometric tests were described.

Vestibular system: Pietruschka (1958) found negative reaction to caloric stimulation.

6.13.3 **Treatment and prognosis**

Surgical intervention for relief of cranial nerve compression and raised intracranial pressure. Orbital decompression may be indicated for the proptosis. The syndactyly and mandibular prognathism can be surgically corrected. A hearing aid my be useful.

The facial palsy at first transient and unilateral usually becomes bilateral. The deafness is progressive. In sibs described by Beighton et al (1976) death from compression of the medulla.

6.14 Electrodactyly, Ectodermal dysplasia, Clefting and Mixed hearing loss.(EEC Syndrome).

The syndrome of Lobster-claw deformity of the hands and feet, nasolacrimal duct obstruction and cleft lip-palate was possibly first described by Eckoldt and Martens

(1804), Cockayne (1936) originally described a pedigree of two generations with lobster claw hands and feet, cleft lip, palate and dacrocytosis. Rudiger (1970) stressed the association of ectodermal dysplasia and suggested the name EEC syndrome.

6.14.1 **Characteristics**

1. Autosomal dominant inheritance with incomplete penentrance and variable expressivity.
2. Hand and foot deformaties including absent phalanges and metapodial bones and syndactyly of some remaining digits.
3. Absence of lacrimal puncta.
4. Occasional cleft-lip-palate.
5. Occasional albinoid changes in the skin and hair.

6.14.2 **Auditory system**:

External ear: Berndorfer (1970), noted absence of pinna, while Robinson et al (1973) described abnormal modeling of the pinna.

Middle ear: After tympanotomy Robinson et al (1973) found absence of the stapes and part of the incus in one patient. Bystrom et al (1974) noted absence of the incus.

Inner ear: Berndorfer (1970) noted lack of inner ear. No other abnormalities were reported.

Hearing: Hearing loss has been a relatively uncommon component of this syndrome. Hearing loss is mostly conductive.

Conductive deafness of unspecified degree was noted by Patterson and Stevenson (1964), Robinson et al (1973), Beckerman (1973), and Pashayan et al (1974). Mild to moderate degree of conductive deafness was described by ernest and Pullon (1974) and Bystrom et al (1974).

Wilder vanck (1963) described 40 to 100 dB sensorineural hearing loss in the affected members. Meller (1893) and Birch Jensen (1949) described patients who were deaf mutes without otherwise categorizing the deafness.

Vestibular system: Caloric vestibular test on one patient showed marked depression of the vestibular response and minimal nystagmus produced by cold water (Wildervanck,1963).

6.14.3 **Treatment and prognosis**

Hearing aid may be of help to those with residual hearing. The cleft lip and/or palate should be corrected surgically. In cases of obstruction of the inferior lacrimal puncta, a plastic tube should be inserted to carry away the tears (Beckerman 1973). In cases correction of ectrodactyly is indicated for cosmetic improvement.

Hearing loss is progressive. Patients adapt well to the deformity of their extremeties.

6.15 **Otopalatodigital (OPD) Syndrome**

As the name indicates OPD syndrome is a musculoskeletal disorder affecting the ear, face and limbs. Several groups from the University of Minnesota (Dudding, Gorlin and Langer 1967, Langer 1967, Buran and Duvall 1967) extensive radiologic study of a large kindred was carried out by Pozhanski et al (1973).

6.15.1 **Characteristics**:

1. X Linked recessive inheritance.
2. Pugilistic facies, including broad nasal root, hypertelorism, frontal and occipital bossing and small mandible.
3. Cleft palate.
4. Growth retardation
5. Abnormalities of hands and feet

including widely spaced first and second digits and shortened halluces.

6. A wide variety of skeletal abnormalities
7. Mild mental retardation.

6.15.2 **Auditory system**:

External ear: No external ear abnormalities were described.

Middle ear: On tympanotomy (Buran and Duvall 1967) found thickened ossicles, in one case, the long process of the incus was thickened forming an unstable incudostapedial joint. The stapedial head was widened, and the anterior crus did not reach the footplate. In another case, neither crus of the stapes reached the footplate. Histological sections of the stapes removed revealed normal but poorly modeLed hone.

Inner ear: No inner ear abnormalities were reported.

Hearing: Audiometric tests on 3 sibs showed a 30 to 90 dB bilateral conductive deafness (Buran and Duvall 1967).

Vestibular system: Vestibular rests were not described.

6.15.3 **Treatment and prognosis**

The cleft palate may be repaired surgically. Hearing loss can be treated by a hearing aid and by tympanotomy with a prosthesis replacing the abnormal ossicles.

This disorder is not crippling.

6.16 Orofacial Digital II Syndrome (Mohr Syndrome).

This syndrome was described by Mohr (1941) and Claussen (1946) in four of the seven sibs and by Rimoin and Edgerton (1967) separated the orofaciodigital syndrome into two distinct genetic entities - one inherited in an X-linked dominant manner (OFDI) and the other inherited in an autosomal recessive mode (OFD II).

6.16.1 **Characteristics**:

1. Autosomal recessive inheritance.
2. Facial deformities with hypoplastic mandibular body, flat nasal ridge and widely spaced medial canthi.
3. Digital abnormalities including polydactyly, syndactyly and brachydactyly.
4. Lobulated tongue.

6.16.2 **Auditory system**:

No external and inner ear abnormalities were described.

Middle, ear: Various types of ossicular malformations have been reported. Tympanotomy revealed congenital malformation of the incus with failure of articulation with the stapes. The long process of the incus had the appearance of a bluntal sausage and the lenticular process was absent (Rimoin and Sgerton 1967). Stapes fixation, absence of incudostapedial joint.

Hearing: Moderate conductive hearing loss has been noted in the affected members (Rimoin and Sdgerton 1967, Goldstein and Medina 1974).

Vestibular system: Vestibular tests were not described.

6.16.3 6.16.3 **Treatment and prognosis**:

The cleft lip, palate and tongue may be surgically repaired. The polydactylous digits may be removed. The hearing loss may be treated surgically with insertion of a prosthesis to replace the abnormal ossicles. A hearing aid may also be employed.

The deafness is congenital and nonprogressive. Although most affected persons have

a normal life span, several infants have died of respiratory infection (Gorlin et al 1976).

6.17 **Osteogenesis Imperfecta (Vander Hoeve's Syndrome).**

Credit is usually given to Ekman (1788) for performing the first comprehensive study of this syndrome and for discussing the inheritance. Vander Hoeve and de-Kleijn (1918) first mentioned deafness as part of the syndrome. The incidence varies from about 2 to 5 per 100,000 births in different populations (Seedorff 1949, Schroder 1964, McKusick 1972).

The disease can be classified into two types according to its manifestation: (1) Osteogenesis Imperfects Congenita (2) Osteogenisis Imperfecta tarda.

Ostepgenesis Imperfecta Congenita (Lobstein-Vander Hoeve Syndrome)

This congenital form was first described by Lobstein in 1835. Hereditary plays a questionable role. Fetus may have multiple fractures and be dead at birth, and survive only a short time and die even before their hearing can be evaluated.

Osteosenesis Imperfecta tarda: (Vander Hoeve-deKleyn syndrome).

This delayed form was first described by Malebranche in 1964. Autosomal dominant inheritance has been established. Patients become hard of hearing at about 30 years of age which corresponds to the circumstances in otosclerosis.

About 90 percent of the reported cases represent the "tarda form" of osteogenesis imperfecta.

6.17.1 **Characteristics**:

1. Autosomal dominant transmission.
2. 31ue sclerae in 56% of cases.
3. Fragile bones in 66%.
4. Loose ligaments.
5. Frequently changes in the teeth resembling those seen in dentinogenesis imperfecta.

6.17.2 **Auditory system**:

External ear: In some patients the tympanic membrane is found to be thinned and bluish in colour.

Middle ear: The relationship between otosclerosis and osteogenesis Imperfecta is still unsettled.

Earlier authors (Bronson and Fraser 1917, Ruther 1922) consider the hearing impairment

in osteogenesis imperfecta due to otosclerosis. Wullstein and colleagues (1960) believe that otosclerosis is a localized form of osteogenesis imperfecta differing only in degree extent and localization. But Altman and Kornfield (1967) found no histological evidence for a common etiology. Kosoy and Maddox (1971) found that the stapes footplate had a heavy growth of white, chalky, soft mounded bone, but the footplate margins were discrete and showed only slight fixation in contrast to firm fixation found in otosclerosis. Hall and RØhrt (1968) found a normal stapes footplate, Opheim (1968), Hall and RØhrt (1968), Bretlan et al (1971) and Muller (1974) noted degeneration of the stapes crura with replacement by fibrous threads. The stapes footplate and adjacent oval window showed no evidence of otosclerosis. Brosan et al (1977) believe that there is greater degree of structural organization and greater area is occupied by resorption spaces than in otosclerosis.

Inner ear: The otosclerotic change may involve the labyrinthine capsule also in some cases (Bretlan and Jorgensen 1969, Bretlan et al 1970, Miller 1974).

Hearing: The deafness is usually conductive and symmetric, can be mixed or purely sensorineural (Robertson and Gregory 1962, Kosoy and Maddox 1971). Deafness usually begins in the third decade and increases progressively with time, becoming profound in some individuals (Robertson and Gregory 1962). Severely impaired hearing is found in 30 to 60 percent of patients with the tarda type (Dessoff 1934, Seedorff 1949). Complete deafness is rarely observed, hearing appears to be more severely impaired in patients with marked bone involvement (Caniggia et al 1958).

Vestibular system: No vestibular tests were reported.

6.17.3 **Treatment and prognosis**

Stapedectomy is the treatment of choice. Care should be taken to avoid fractures.

6.18 **Joint fusions, mitral insufficiency and Conduction hearing loss (Forney's syndrome)**

A mother and two daughters having this syndrome was described by Forney, Robinson and Pascoe (1966).

6.18.1 **Characteristics**:

1. Autosomal dominant transmission with variable expressivity.
2. Skeletal abnormalities including fusion of the cervical vertebrae and carpal and tarsal bones.
3. Mild to moderate mitral insufficiency.

6.18.2 **Auditory system**:

No external and inner ear abnormalities were noted.

Middle ear: Surgical exploration of one ear in each subject showed fixation of the footplate of the stapes.

Hearing: Moderate, probably congenital, conductive hearing loss was noted in the affected members. Puretone audiograms on each patient showed a 30 to 70 dB conductive hearing loss.

Vestibular system: No vestibular findings were described.

8.18.3 **Treatment and prognosis**:

The mitral insufficiency is of only moderate degree and does not warrant surgical correction.

The hearing loss may be minimized by use of a hearing aid and by insertion of a prosthesis. The disorder is non progressive. Mitral insufficiency may result in cardiac failure later in life.

6.19 **Kniest syndrome**

Kniest (1952) described a rare form of disproportionate dwarfism, characterized by depressed nasal bridge, cleft palate, and prominent knees.

6.19.1 **Characteristics**

1. Autosomal dominant inheritance.
2. Short extremities, club feet and large knees, all noted at birth.
3. Late development of walking.
4. Stiff joints and waddling gait.
5. Severe myopia and often retinal detachment.
6. Cleft palate.
7. Characteristic radiographic alterations.

6.19.2 **Auditory system**:

No external, middle or inner ear abnormalities were reported.

Hearing: Conductive deafness has been described by a number of authors (Roaf et al 1967, Maroteaux and Spranger 1973, & Siggers etal 1974).

Vestibular system: No studies have been reported.

6.19.3 **Treatment and prognosis**

Referral for periodic opthalmologic examination is mandatory. Cleft palate should be repaired.

The patient becomes progressively deformed. Gait is difficult. Retinal detachment is a distinct hazard.

6.20 Multiple Synostoses and conduction deafness (Symphalangism-Brachydaotyly Syndrome).

Maroteaux et al (1972) and Hermann (1974) reported kindreds with multiple synostoses and conduction deafness.

6.20.1 **Characteristics**

1. Autosomal dominant inheritance.
2. Lack of nasal alar flare.
3. Progressive proximal symphalangism of all the fingers and distal symphalangism of the last finger.
4. Carpal and Tarsal coalition.
5. Subluxation of the radial heads.
6. Short first metapodial bone.
7. Hypoplasia or aplasia of various distal phalanges and corresponding finger and toe nails.

6.20.2 **Auditory system**

No external or inner ear abnormalities were reported.

Middle ear: Total ankylosis of the stapes, malformed stapes and incus were described by Maroteaux et al 1972.

Hearing: Progressive conductive hearing loss appearing during early childhood or adolescence was noted in 4 of 6 patients, reported by Hermann (1974) and 4 of 7 patients examined by Maroteaux et al (1972). No other audiometric data is available.

Vestibular system: No data have been reported on vestibular function.

6.20.3 **Treatment and prognosis**

Stapedectomy and insertion of a prosthesis may improve hearing. Orthopedic surgical help should be sought for relief of the skeletal problems.

The disorder is progressive.

6.21 **Hereditary hyperphosphatasia(Juvenile pagets disease, Hyperostosis corticalis Juvenilis deformans)**

Hereditary hyperphosphatasia is characterized by progressive skeletal deformities that becomes apparent

during the second or third deoade of life. It was possibly first described by Sorrell and Legrand-Lambling (1938).

6.21.1 Characteristics

1. Autosomal recessive inheritance.
2. Progressive enlargement of the head and bending and thickening of long bones of the extremities.
3. Elevated alkaline and acid phosphatase levels.

6.21.2 Auditory system

External ear: The ear canals were narrowed. No middle and inner ear abnormalities were mentioned.

Hearing: Progressive mixed 60 to 80 dB hearing loss has been evident from the fourth to fourteenth year of life (Thompson etal 1969). gyring and Eisenberg (1968) described high frequency sensorineural hearing loss. Mitsudo (1971) noted diminished hearing bilaterally.

Vestibular system: Studies have not been reported.

6.21.3 Treatment and prognosis

Sodium fluoride, at a dose of /mg/bg/day was given by Eyring and Eisenberg (1968) with mildly encouraging results.

The disease is progressive and sometimes result in sporadic cranial nerve involvement.

6.22 Spondyloepiphyscal dysplasia congenita and Sensorineural deafness

Spondyloepiphyscal dysplasia congenita, first defined by Spranger and Wiedemann (1966) is a skeletal dysplasia recognizable at birth. Earlier probable cases were reported by Uhlig (1954) and Braun and Meythaler (1962). The disorder constituted as much 10 percent of cases of dwarfism (Bailey 1973).

6.22.1 Characteristics

1. Autosomal dominant inheritance
2. Short trunk and proximal extremities
3. Distinctive skeletal changes.
4. Severe myopia and at times retinal detachment.
5. Cleft palate in about 40%.
6. Mental retardation in 10%

6.22.2 Auditory system:

No external/middle/inner ear abnormalities were described.

Hearing: Deafness is not a constant feature. It occurs in about 30 percent of cases (Kbnigsmark and Gorlin 1976). Moderately severe (30 to 60 dB) sensorineural deafness,especially masked in the hightones was described by a number of

authors (Fraser et al 1969, Michaelis etal 1973).

Vestibular system: No studies have been reported.

6.22.3 **Treatment and prognosis**

Early correction of cleft palate. Referral to an opthalmologist for evaluation and/or correction of the myopia and retinal detachment is extremely Important.

While life expectancy is not shortened, gait becomes progressively more difficult and scoliosis becomes more severe with age.

6.23 Calcification of cartilages. Brachytelephalangy, Multiple peripheral pulmonary stenosis and mixed deafness

This syndrome was described by Kentel, Jargenson and Gabriel (1971, 1972) in two sibs.

6.23.1 **Characteristics**:

1. Autosomal recessive inheritance
2. Brachytelephalangy
3. Calcification and/or ossification of cartilages of nose auricles, trachea and ribs.
4. Multiple peripheral pulmonary stenoses and bronchitis.

6.23.2 Auditory system

External ear: Pinnae were somewhat too large and prominent. They were pale, stiff and hard in consistency. The ear-drums were perforated bilaterally.

Middle ear: Recurrent middle ear infections was observed in both sibs.

Inner ear: No inner ear abnormalities were reported.

Hearing: Mixed hearing loss of 40 to 75 dB being greater at higher frequencies was found in both Sibs prior to admission to School.

Vestibular system: Normal caloric response was noted.

6.23.3 **Treatment and prognosis**

No treatment is required for the pulmonary stenosis. The deafness may be ameliorated with a hearing aid. Prognosis for an essentially normal life is good.

6.24 Metaphyscal dysostosis. mental retardation and conduction deafness

Rimoin and McAlister (1971) reported three male sibs with this syndrome.

6.24.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Short stature due to metaphyscal dysostosis
3. Mild mental retardation.
4. Eye abnormalities including hyperopia, strabismus, cataract.

6.24.2 **Auditory system**:

No external ear abnormalities were noted.

Middle and Inner ear: Polytomography of the mastoid areas revealed bilateral low placement of the ossicles as well as striking upward angulation of the internal auditory canals. Recurrent middle ear infection was observed in all sibs.

Hearing: Bilateral moderate conduction deafness appearing around adolescence was noted in all three sibs.

Vestibular system: No vestibular tests were described.

6.24.3 **Treatment and prognosis**:

A hearing aid may be useful. Orthopedic therapy may be used to correct skeletal abnormalities.

The deafness and mental retardation is non-progressive.

6.25 Unnamed Bone dysplasia(s) and Sensorineural Deafness

Insley and Astley (1974) described this syndrome in two sisters. Nance and Sweeney (1970) reported the same disorder in an adult male, his deceased sibs and female cousins.

6.25.1 Characteristics

1. Autosomal recessive inheritance.
2. Severely depressed nasal bridge.
3. Skeletal alterations, including platyspondylia and carpal fusion.

6.25.2 Auditory system

No external/middle/inner ear abnormalities were described.

Hearing: Both sibs described by Insley and Astley (1974) exhibited sensorinenral deafness, one had a conductive component thought to be due to otitis media. The patient studied by Nance and Sweeney (1970) had slowly progressive mixed hearing loss that was more severe at high frequencies.

Vestibular system: No vestibular studies were reported.

6.25.3 Treatment and prognosis

The depressed nasal bridge may be corrected

surgically. A hearing aid may be employed if the hearing loss is severe.

Information is insufficient to determine prognosis.

6.26 Dominant Symphalangism and Conduction Deafness

Conduction deafness due to fixation of the footplate of the stapes to the round window in combination with hereditary absence of the proximal interphalangeal joints and carpal and tarsal bone coalition has been described in several kindreds (Vessell 1960, Strasburger et al 1965, Gorlin et al 1970, Maroteaux et al 1972, Gloede and Stenger 1974, Spoendlin 1974, Murakami 1975).

6.26.1 Characteristics

1. Autosomal dominant transmission with variable expressivity.
2. Symphalangism involving proximal interphalangeal joints most marked in the ulnar digits.
3. Carpal and tarsal coalitions.

6.26.2 Auditory system:

No external or inner ear abnormalities were noted.

Middle ear:Tympanotomy revealed bony fusion between the stapes and the petrous portion

of the temporal bone (Strasburger et al 1965). Gorlin et al (1970) also described ankylosis of the stapes.

Hearing: Mild to severe conductive hearing loss in infancy or early childhood was reported by Vessell (1960), Strausberger (1965), Gorlin et al (1970), Vase and Pedersen (1975).

Vestibular system: Vestibular studies have not been reported.

6.26.3 **Treatment and prognosis**

No treatment is required for symphalangism. The hearing loss can be effectively treated by stapedectomy.

Prognosis is good.

6.27 Dysplasia of the capital femoral epiphyses, Severe myopia and Sensorineural deafness

Pfeiffer, Junemann, Polster and Bauer (1973) described this syndrome in three brothers.

6.27.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Epiphyscal dysplasia, especially of the femoral capital epiphyses.
3. Severe myopia.

6.27.2 **Auditory system**:

No external/middle/inner ear abnormalities were described.

Hearing: A symmetrical, sensorineural deafness with abrupt high tone loss above 3000 to 4000 Hz was noted in all brothers. Speech reception threshold was at 30 to 35 dB. Speech discrimination showed a 20 percent loss.

Vestibular system: No vestibular testing was described.

6.27.3 **Treatment and prognosis**

No therapy other than glasses was necessary. There was progressive improvement of the epiphyscal dysplasia. The hearing loss was not progressive.

6.28 Absence of tibia and congenital deafness

In 1931, Carraro described a syndrome characterized by absence of tibias and severe congenital hearing loss in four of 6 sibs.

6.28.1 **Characteristics**:

1. Autosomal recessive transmission
2. Congenital absence of one or both tibias and shortened malformed fibulas.

6.23.2 **Auditory system**

No abnormalities of the ear were reported.

Bearing: Each of the sibs exhibited congenital severe hearing loss. No further audiometric testing was mentioned.

Vestibular system: No vestibular findings were described.

6.28.3 **Treatment and prognosis**

Referral to orthopedic surgeon is indicated. The hearing loss is congenital and severe.

6.29 Broad terminal phalanges, abnormal facies and sensorineural deafness

Keipert, Fitzgerald, and Danks (1973) described two brothers with thef syndrome.

6.29.1 **Characteristics**

1. Recessive inheritance wither autosomal or X linked.
2. Broad terminal phalanges of fingers and toes.
3. Unusual facies
4. Mental retardation.

6.29.2 **Auditory system**:

No external/middle/inner ear abnormalities were mentioned.

Hearing:In one brother there was severe sensorineural hearing loss in one ear, but normal hearing in the other ear. The other sib exhibited moderately severe bilateral high tone sensorineural deafness.

Vestibular system: No studies were reported.

6.29.3 **Treatment and prognosis**

A hearing aid may be employed, if found useful.

Prognosis depends on degree of mental retardation.

6.30 Arthrogrypotic hand anomaly and Sensorineural deafness

Stewart and Bergstrom (1971) reported a combination of arthrogrypotio hand anomaly and sensorineural deafness in 12 individuals in 5 generations.

6.30.1 **Characteristics**

1. Autosomal dominant inheritance with variable expressivity.
2. Growth retardation.
3. Atthrogrypotic alterations of the hands.
4. Some limitation of joint mobility.

6.30.2 **Auditory system**:

No external/middle/inner ear abnormalities were reported.

Hearing: 7 of the 12 affected persons manifested congenital sensorineural deafness of moderate to profound degree. In some it was unilateral in others bilateral. No other audiometric data was available.

Vestibular system: No studies were reported.

6.30.3 **Treatment and prognosis**

In most cases hearing aid benefitted the patients. The deafness and hand anomalies were non progressive.

6.31 **Hypoplasia of upper extremities, cardiac arythmia, malformed pinnae and unilateral conduction deafness**

Stoll et al (1974) reported this apparently unique syndrome in a father and son.

6.31.1 **Characteristics**

1. Autosomal dominant inheritance.
2. Hypoplasia of the upper extremities
3. Sinus arrhythmia.

6.31.2 **Auditory system**:

External ear: The pinnae were malformed. The external auditory meatus was reduced in size.

Middle ear: The stapes and oval window were absent in the son.

Inner ear: No abnormalities were noticed.

Hearing: Profound unilateral conduction deafness was noticed. No other information is available.

Vestibular system: Vestibular studies apparently were not carried out.

6.31.3 **Treatment and prognosis**

Plastic surgery may be indicated for hypoplasia of upper extremities and external ear abnormalities.

This disorder is not life threatening.

6.32 Carpal and tarsal abnormalities, cleft palate Oligodontia and Stapes-fixation

Gorlin, Schloff and Paparella (1971) described the above syndrome in two sisters.

6.32.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Cleft palate
3. Oligodontia
4. Carpal and especially tarsal anomalies.

6.32.2 **Auditory system**

The external ears were normal. No inner ear pathology was reported.

Middle ear: Exploratory surgery revealed bilateral congenital fixation of the footplate of the stapes.

Hearing: Reduced hearing was noted prior to puberty. Audiometric testing demonstrated bilateral conductive deafness. The degree of hearing loss was not specified.

Vestibular system: vestibular studies were not carried out.

6.32.3 **Treatment and prognosis**

Hearing loss in each patient was satisfactory corrected by Stapedectomy. Dentures can be constructed.

Prognosis is excellent. Carpal or tarsal abnormalities are not problematic.

6*33 Exomphalos, Macroglossia, Gigantism (EMG) Syndrome (Beckwith - Wiedemann Syndrome)

This syndrome was first described by Beckwith (1963) in 3 siblings. Wiedemann in 1964 described 3 more siblings with the same disorder. Subsequently more than 60 cases have been reported.

6.33.1 Characteristics

1. Autosomal recessive transmission.
2. Macroglossia.
3. Omphalocele
4. Hyperplasia of several organs.
5. Hypoglycemia.
6. Mild to moderate retardation in some cases.

6.33.2 **Auditory system**

External ear: Pinna showed characteristic oblique retractions, behind the antitragus and very fleshy lobules.

Middle ear: Exploration of middle ear revealed fixation of stapes.

Inner ear: No abnormalities were reported.

Hearing: Paulsen (1973) reported a case who at the age of 10, an almost bilaterally equally progressive conductive deafness. No other audiometric tests were reported.

Vestibular system: No studies were mentioned.

6.33.3 **Treatment and prognosis**

Normal hearing was established by stapedectomy. The disease is non progressive.

6.34 Skeletal dysplasia, Mental retardation, Skin Granulomata and profound Congenital Sensorineural deafness

Fountain (1974) reported four mentally retarded sibs with severe congenital deafness. Two developed granulomata.

6.34.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Mental retardation.
3. Reduced height.

4. Skin granulomata

5. Thickened calvaria and poor modeling of bones.

6.34.2 **Auditory system**

No external/middle/inner ear abnormalities were reported.

Hearing: All the sibs were described as congenitally deaf. The deafness was not otherwise characterized.

Vestibular system: No vestibular studies were reported.

6.34.3 **Treatment and prognosis**

Therapy is unknown, Deafness is profound. Although the disorder is not life threatening, general outlook is poor.

6.35 Miscellaenous Skeletal Disorders in which Deafness is inconsistently associated

There are several skeletal disorders in which deafness is an inconsistent feature, and it is poorly documented. Perhaps in some cases the association is aleatory. Nevertheless there should be some documentation of the co-occurrence.

6.35.1 Progressive diaphyscal Dysplasis (Camurate - Engelmann Disease)

Engleman's disease appears to be a familian and probably autosomal dominantly inherited systemic condition

of which most of the manifestations can be attributed to a disorder of osseous and muscular systems. From early infancy there is leg pain associated with waddling gait, poor muscle mass (especially in lower extremeties) and easy fatigability. Puberty may be delayed.

Auditory system:

Graham noted (1972) slit like internal auditory canals.

Hearing: Deafness has been rarely mentioned and when noted poorly documented.

Paul (1953) reported a gradual impairment of hearing.

Lennon et al (1961) described mixed deafness.

Trunk et al (1969) noted progressive sensorineural hearing loss. Nelson and Scott (1969) noted conductive hearing. Graham (1972) noted severe deafness.

Vestibular system: Decreased vestibular function was reported by Lennon et al (1961).

6.35.2 Marfan syndrome

This is a dominantly inherited disorder of connective tissue by arachnodactyly, scoliosis, joint hypermobility, dislocated lens and cardiac anomalies.

Auditory system:

Ganther (1972) described numerous middle ear infection in his patient.

Keleman (1965) in the temporal bone study of a 11 month old infant found that a bony lip protruded from the external aperture of an abnormally narrowed vestibular aqueduct. In the cochlea, the round window bulged toward the scala. The utriculo-ampullary space and endolymphatic duct were dialated

Hearing: Deafness has been rarely associated. Ganther (1972) found deafness but attributed it to numerous middle ear infection. The deaf patients reported by Lloyd (1951) were poorly documented examples of the Marfan syndrome.

Vestibular system: No vestibular findings were reported.

6.35.3 Fibrodysplasia Ossificans Progressive (Myositis Ossificans Progressive)

This is a disorder of connective tissue transmitted by an autosomal dominant gene with reduced penentrance. (Mc Kussick 1972). Usually, there is microdactyly of the great toes and thumbs and progressive ankylosis of the cervical. Spine followed by ossification of the paraspinal and limb girdle.

Auditory system:

No ear abnormalities were mentioned.

Hearing: Hearing loss apparently is not a common feature of the disorder. Deafness is sansorineural in some cases and conductive in others (Lutwak 1964, Ludman et al 1968, Letts 1968,1969).

Vestibular system: No vestibular studies were described.

6.35.4 Cleidocranial Dysplasia/Dysostosis

The syndrome of absence or hypoplasia of the clavicles and various other skeletal anomalies is inherited in an autosomal dominant manner.

Auditory system:

External ear: Concentric narrowing of the external auditory canals were reported by many authors,

Middle ear: Tomography has demonstrated deformed ossicles (FØns 1969).Mastoid cells are absent.

Inner ear: No inner ear abnormalities were reported.

Hearing: Rarely there has been associated progressive conductive or mixed deafness (Nager and DeReymer 1948, Davis 1954, Gay 1958, Jaffee 1968, FØns 1969).

Vestibular system: Vestibular study by Gay (1958) showed somewhat reduced response to caloric stimula-

tion, but those studies of FØns (1989) were normal.

6.35.5 Dyschondrosteosis (Madelung's deformity, Leri-Weill disease)

Dyschondrosteosis is characterized by deformity of the distal radius and ulna and proximal carpal bones and by mesomelic dwarfism (Heldman et al 1966).

Auditory system:

External ear: External ear canals were narrow.

Middle ear: The malleus was absent and the incus was vestigial with no connection with the deformed stapes. In one ear chorda tympani could not be identified.

Inner ear: No abnormalities were mentioned.

Hearing: Bilateral non progressive conductive hearing loss has been described sporadically. Nassif and Harboyan (1970) described brothers with 40-50 dB bilateral conductive hearing loss.

Vestibular system: No vestibular studies were reported.

6.35.6 Achondroplasia

Achondroplasia is a hereditary dominant skeletal anomaly characterized by retarded cartilagenous growth, reduction in endochondral ossification and near normal periosteal bone formation. As a result the affected individual appear dwarfed with very short extremities and a relatively large head and trunk.

Auditory system:

External ear: No external ear abnormalities were mentioned.

Middle ear: Exploration of middle ear revealed fusion of the ossicular chain to multiple sites within the tympanic cavity.

Inner ear: Generalized malformation of the entire cochlear capsule and a thickened intracochlear partition are the known abnormalities.

Hearing: Conductive or mixed hearing loss occurs occasionally.

Vestibular system: No studies were described.

6.35.7 Oculodento Osseous Dysplasia and Conduction Deafness

Occulodento-Osseous dysplasia is a syndrome consisting of a narrow nose with hypoplastic alae, microcornea with iris anomalies, soft tissue syndactyly of the fourth and fifth fingers, poor modeling of long bones, and enamel hypoplasia. The disorder has autosomal dominant inheritance (Reisner et al 1969).

Auditory system:

No external/middle/inner ear abnormalities were reported.

Hearina: Among 45 cases, there have been three individuals who have manifested conduction deafness of vadable degree (Gorlin et al 1963, Gillespie 1964, Reisner et al 1969).

Vestibular system: No vestibular studies were reported.

6.35.3 Pfeiffer Syndrome and Conduction Deafness

Pfeiffer syndrome consists of craniosynostosis which results in turribrachy cephaly and broad thumbs and halluces. There may be partial soft tissue syndactyly of the first and second and second and third toes, less often the third and fourth fingers are involved. Inheritance is autosomal dominant (Saldino et al 1972).

Auditory system:

No external/middle/inner abnormalities were reported.

Hearing: Hearing loss has been described in a few cases. It has not been severe. In three patients the deficit was conductive (Konigsmark and Gorlin 1976).

Vestibular system: No studies were reported.

6.35.9 Saethre-Chotzen Syndrome and Conduction Deafness

This syndrome is characterized by craniosynostosis, lowset frontal hair line, facial asymmetry, ptosis of one or both eyelids, deviated nasal septum and variable cutaneous syndactyly.

Auditory system

No information regarding the condition of the ear is available.

Hearing: Pantke (1975) reported that 15 percent of the patients have mild conduction deafness - in some cases unilaterally. In most of these cases type and/or degree of hearing loss was not specified. However Chotzen (1932) and Hammar and Rogenkamp (1967) noted conduction deafness of moderate degree. Grebe (1940) found deaf mutism otherwise undefined. Dolvio and Gillierson (1955) reported mixed hearing loss.

Vestibular system: No vestibular studies were reported.

6.35.10 Focal dermal hypoplasia syndrome and mixed deafness

This syndrome is characterized by atrophy and inner hyperpigmentation of the skin, localized cutaneous

deposits of superficial fat multiple papillomas of mucous membranes or periorificial skin, atrophy of nails and a host of skeletal abnormalities. These have been reviewed by Goltz et al (1970) and by Ginsburg et al (1970). Inheritance is probably X-linked dominant.

Auditory system:

External ear: Daly (1968), Ginsburg etal (1970) and Ferrara (1972) described a narrowed external auditory meatus.

No middle and inner gar abnormalities were mentioned.

Hearing: Perhaps 5 to 10 percent of patients with this syndrome have hearing deficit.

Holdern and Akers (1967) and Goltz et al (1970) reported mixed hearing loss noted at 3 years of age in their patient. Stollman (1967) made brief note of sensorineural deafness in their patients.

Vestibular system: No studies were reported.

6.35.11 Oculopharyngeal muscular dystrophy and Sensorineural deafness

This is one of several disorders exhibiting a myopathic facies. Onset is late, usually in middle life. Facial musculature is weakened to the point of

flaccid paralysis involvement of the masticatory muscles is reflected in hollowing of the temporal areas and sagging of the mandible. The brow is usually furrowed. There is increasing difficulty encountered in eating and drinking.

Inheritance is autosomal dominant.

Auditory system:

No mention was made regarding the conditions of external, middle and inner ears.

Hearing: Hearing loss is variable. A slowly progressive sensorineural deafness has been reported in a kindred (Graf 1971). Conversely, Roberts and Bamforth (1968) noted no hearing loss among 26 patients with this disorder. Kuhn and Ey (1966) noted that 80 of 23 patients with myotonie dystrophy exhibited hearing loss, of these four were the result of chronic middle ear infections.

Vestibular system: No studies were reported.

6.35.12 **Mobius syndrome**

Symptoms presently referred to as Mobius syndrome were described by several investigators in late 19th

century named after Mobius who reported extensively on the problem. It is characterized by congenital usually bilateral facial paralysis, unilateral or bilateral loss of abductors of the eye, anomalies of the extremities, aplasia of brachlal and thoracic muscles, frequently there is involvement of other cranial nerves especially hypoglossal and occulomotor, trigeminal. Mode of inheritance is not agreed upon.

Auditory system:

External ear: Sometimes abnormalities of pinna were reported.

Middle ear: Tympanometry revealed Eustachian tube malfunctioning and middle ear fluid.

Hearing:Deafness is present in 5% of cases. A conductive deafness of about 30-40 dB was reported in a 8 year old boy by Kahane (1979). Speech discrimination scores were in 90%. No other information regarding hearing is available.

Vestibular system: No studies were reported.

6.35.13 **Compomelic Syndrome**

The compomelic syndrome was first described by Maroteaun et al (1971) who derived the term from Greek

words for Curvature (Champa) and extremity (Melos). The underlying pathologic feature appears to be disturbance in cartilage growth involving the affected bones and respiratory tract cartilage. Characteristics include various craniofacio anamolies like macrocephaly, prominent occipit, flat facies, prominent forehead, flat nasal bridge, occular hypertelorism, cleft palate, mandibular hypoplasia and congenital bowing of tibia. Inheritance is autosomal recessive. It usually results in respiratory distress and early death.

Auditory system:

External ear: Low set ears with poor cartilage development was observed.

No middle ear abnormalities were reported.

Inner ear: Histopathologic studies showed that the endochondrial layer of otic capsule contained no cartilage cells. The cochlea was short and flattened presenting a scala communis. The vestibule and semicircular canals were deformed by bone Invasion (Tokita et al 1979).

Hearing: There may be associated deafness. No audiometric data is available regarding the type and/or degree of hearing loss.

Vestibular system: No studies were reported.

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C H A P I E R VII

Genetic Hearing loss with nervous system disease

Hearing loss sometimes occur in conjunction with various nervous system diseases. These diseases manifests themselves in the form of ataxia, epilepsy, mental retardation, mental deterioration and various psychological disturbances.

The associated hearing loss is invariably sensorineural,external or middle ear abnormalities have not been reported. In majority of cases hearing loss is progressive, The well known syndromes under the category are Richards-Reindle syndrome, Hermann syndrome, Von Reckling hausen's disease. Many of the other syndromes have been described in a single family. The prognosis is usually poor because of the progression of the disorders.

7.1 Richards-Rundle syndrome

This syndrome was first described in two sibs by Koennecke (1919) and in five sibs by Richards and Rundle (1959).

7.1.1 Characteristics

1. Autosomal recessive transmission
2. Progressive severe mental deterioration

3. Early onset of progressive mild ataxia and horizontal nystagmus

4. Muscle wasting, particularly involving the distal extremities

5. Absent development of secondary sexual characteristics.

6. Reduced urinary estrogen, pregnanedool and total neutral 17 ketosteroids.

7.1.2 **Auditory system**

Inner ear: No temporal bone studies were reported.

Hearing: Early onset of severe progressive sensorineural hearing loss was noted in all the affected members. Hearing loss was first noted at 2 years of age (Richards and Rundle 1959) and at 7 years (Koennecke 1919). Affected persons learned to say a few words in their first few years of life and then their speech deteriorated. No other audio-metric tests were reported.

Vestibular system: No vestibular tests were described.

7.1.3. **Treatment and prognosis**

At present only supportive therapy can be offered.

The disease progresses from the first year through childhood and becomes fairly static during early adult life. It does not appear to shorten the life span.

7.2 Ataxia, Oligophrenia, Myocardial sclerosis and Sensorineural Deafness

In 1963, Jeune, Tommasi, Freycon and Nivelson described the syndrome in two Gypsy sibs.

7.2.1 Characteristics

1. Autosomal recessive transmission.
2. Childhood onset of progressive oligophrenia.
3. Progressive cerebellar ataxia.
4. Skin myocardial dystrophy.

7.2.2 Auditory system

Inner ear: No inner ear findings were reported.

Hearing: Hearing loss was first noted when the children were about six years old. Hearing tests on one child at 6 years and an other at 11 years showed bilateral sensorineural deafness. There was history of progression of hearing loss.

Vestibular system: No vestibular tests were described.

7.2.3 Treatment and prognosis

The deafness may be ameliorated by a hearing aid.

7.3 **Ataxia, Mental Retardation and Sensorineural Hearing loss**

Belman, Konigsmark, Capute and Migeon (1973) reported this syndrome in three male sibs.

7.3.1 Characteristics

1. Autosomal recessive or X linked transmission, infantile onset.
2. Progressive ataxia.
3. Mental retardation.
4. Upper and lower motar neurone disease.

7.3.2 **Auditory system**

Inner ear: No inner ear findings were reported

Hearing: Audiometric testing during the first few years of life showed a hearing deficit. Within the next few years, there was progressive hearing loss, terminating in severe sensorineural deafness.

Vestibular system: Normal caloric responses were elicited.

7.3.3 **Treatment and prognosis**

A hearing aid is useful during the early stages of the disorder. Lengthening of Achilles tendon is necessary for correction of the heel contraction. Prognosis is poor. All components of the syndrome were progressive in severity.

7.4 Ataxia, Pes Cavus and Sensorineural Deafness

Schimke (1974) reported an eventually "Pureform" of progressive adult onset cerebellar ataxia and sensorineural deafness in four sibs.

7.4.1 Characteristics

1. Autosomal recessive transmission
2. Progressive adult onset of ataxia and dysarthria.
3. Per Cavus which precedes the ataxia.

7.4.2 Auditory system

Inner ear: No inner ear abnormalities were describe

Hearing: Progressive sensorineural deafness appeared during adolescence. This preceded the onset of ataxia. The deafness slowly progressed and became profound in middle life.

Vestibular system: Notests were described.

7.4.3 Treatment and prognosis

At present only symptomatic therapy,such as surgica correction of the Pes Cavus can be offered.

. Both the ataxia and the deafness are progressive.

7+5 Ataxia, Hyperuricemia, Renal insufficiency and Sensorineural Deafness

This syndrome was described in five members of three generations of a kindred (Rosenberg, Bergstorm, Troose and Barthol mew 1970).

7.5.1 **Characteristics**

1. Autosomal dominant transmission with variable expressivity.
2. Hyperuremia.
3. Ataxia, beginning in the second decade and progressing very slowly.
4. Renal insufficiency.

7.5.2 **Auditory system**

No inner ear abnormalities were described.

Hearing: Hearing loss was first noticed in the 2nd or 3rd decade. Younger affected persons had only hightone sensorineural hearing loss, whereas the oldest affected patient had a severe sansorineural deafness with apparent progression. Speech discrimination varied markedly. Detailed audiometric testing on one patient suggested a cochlear locus for the hearing loss.

Vestibular system: All members with ataxia had electronystagmography examination. Two showed abnormal pendular thickening one had abnormal optokinetics, the other had severe nausea and vomiting on caloric stimulation.

7.5.3 **Treatment and prognosis**

Symptomatic treatment of varying defects is necessary. Little can be done for the ataxia and weakness.

Ataxla and hearing loss are slowly progressive and become severe. The hyperuricemia may lead to gout.

7.6 Ataxia, Hypotomia, Depressed deep tendon reflexes and progressive sensorineural deafness.

This combination of progressive severe hearing loss and ataxia described in two sibships may represent a syndrome distinct from Friedreichs ataxia (Lichtenstein and Knorr 1930, Pires and de Carvalho 1935),

In Friedreichs ataxia, which is inherited as an autosomal recessive disorder, there is involvement principally of spino cerebellar and pyramidal tracts and dorsal columns with resultant limb incordination, dysarthria nystagmus, diminished or absent tendon reflexes, scohosis, Babinskis Sigh, and impairment of vibratory and position senses and per cavus. The disorder has preadolexcent onset. Although hearing loss has been reported in Friedreichs ataxia, it is mild in degree and infrequent in occurrence.

7.6.1 Characteristics

1. Autosomal recessive transmission.
.2. Adolescent onset of slow, progressive ataxia
3. Depression of reflexes.
4. Dysarthric speech.
5. Hypotomia
6. Per cavus.

7.6.2 Auditory system

No inner ear abnormalities were described.

Bearing: Childhood onset of mild/severe sensorineural hearing loss which progresses into moderate/profound hearing loss by 20 years of age was reported by Lichtenstein and Knorr (1930), Pires and de Carvalho (1935). No other audiometric tests were reported.

Vestibular system: Vestibular function was normal.

7.6.3 **Treatment and prognosis**

Hearing aid may be useful in early years.

The hearing loss becomes severe, and ataxia worsens with age.

7.7 Ataxia, Cataract, Psychosis and/or dementia and Sensorineural deafness,

Stromgren, Dalby, Dalby and Ranheim (1970) reported the syndrome as occuring in nine members of five generations of a family.

7.7.1 Characteristics

1. Autosomal dominant inheritance.
2. Cerebellar ataxia that appears after the age of 40.
3. Intention tremor of trunk and extremities.
4. Slurred speech.
5. Central type nystagmus.
6. Paranoid psychosis and dementia.
7. Posterior polar cataract appearing during the third decade.
8. Intrabulbar hemorrhage.

7.7.2 **Auditory system**

No inner ear abnormalities were reported.

Hearing: Impaired hearing appeared some years after the occular symptoms started. After the age of 45 years, the occular symptoms started. After the age of 45 years audiometry indicated severe or profound deafness in all patients.

Vestibular system:

Vestibular reflexes were diminished or lost.

7.7.3 **Treatment and prognosis**

Treatment is apparently of no avail.

5 affected members died between 57 to 60 years from bronchopneumonia, intractable diarrhea and cerebro vascular disease.

7.8 **Photomyoclonus, Diabetes mellitus, neuropathy and Sensorineural deafness (Hermann's syndrome).**

Hermann, aguilar and Sacks (1964) described this syndrome in three generations of a family in which 13 members were affected.

7.8.1 **Characteristics**

1. Autosomal dominant inheritance with variable expressivity.
2. Photomyoclonic epilepsy beginning in early adult life.
3. Adult onset mild diabetes mellitus.
4. Nephropathy with accumulation of PAS-positive material in renal tubular cells.

7.8.2 **Auditory system**

No inner ear abnormalities were described.

Hearing

Progressive sensorineural hearing loss was first noticed in the 4th decade in 9 of 13 affected members. In one patient progression to severe hearing loss occurred within 7years. No audiometric findings were described.

Vestibular system: No vestibular function tests were reported.

7.8.3 **Treatment and prognosis**

Anticonvulsant medication for epilepsy, hearing aid for the hearing loss may be used. Prognosis appears to be rather good until the onset of mental deterioration which portends death within a few years.

7.9 **Myoclonic epilepsy, ataxia and sensorineural deafness**

In 1968, May and White reported a kindred in which six members in four generations were affected by this syndrome.

7.9.1 **Characteristics**

1. Autosomal dominant transmission with variable expression.
2. Myoclonic and grand mal epilepsy beginning in the teens and occurring in about half the cases.
3. Slowly progressive cerebellar ataxia beginning in adolescence.

7.9.2 **Auditory system**

No inner ear abnormalities were reported.

Hearing: Hearing loss was first noted in early childhood or in early adult life. It was slowly progressive, resulting in severe loss in the later years of life.

Vestibular system : No vestibular testing was described.

7.9.3 **Treatment and prognosis**

Anticonvulsants for controlling epilepsy and hearing aid for the hearing loss is essential.

7.10 Myoclonic epilepsy and congenital sensori-neural deafness

This combination of symptoms was described in five of eight sibs by Latham and Munro (1937).

7.10.1 **Characteristics**

1. Autosomal recessive transmission
2. Myoclonus and grandmal epilepsy with onset at 10 to 12 years of age.
3. Terminal neurologic deterioration.

7.10.2 **Auditory system**

No inner ear abnormalities were reported.

Hearing: Bach of the affected persons was congenitally deaf and none of them developed speech. Audiometric testing was not described.

Vestibular system: No vestibular tests were mentioned.

7.10.3 **Treatment and prognosis**

Treatment was not described. Anticonvulsant medication is recommended in these cases.

7.11 Sensory radicular neuropathy and progressive sensorineural deafness

This combination of symptoms was first described by Hicks (1922). Denny-Brown (1951) restudied this kindred,isolated cases were described by Van Bogaert (1953) Hallpike (1967) and Stanley et al (1975).

7.11.1 Characteristics

1. Autosomal dominant transmission.
2. Progressive sensory loss and lightning pains that involve the distal extremities and begin in the second or third decade.
3. Loss of dorsal root ganglia, particularly in the lower thoracic and lumbar areas.
4. Perforating ulcers of the feet.

7.11.2 Auditory system

Inner ear : Sections of temporal bone in an

affected member showed severe atrophy of the stria vascularis and loss of hair cells in the organ of corti and the limbus (Hallpike 1967).

Hearing: Progressive early onset moderate to severe sensorineural hearing loss was reported in the affected persons (Hicks 1922, Van Bogaert 1953, Hallpike 1967). No other audiometric findings were reported.

Vestibular system: No vestibular tests have been reported.

7.11.3 **Treatment and prognosis**

Treatment is symptomatic, and in general, is unsatisfactory. Sensory loss and hearing loss was progressive accompanied by recurrent ulceration of the feet.

7.12 Progressive sensory neuropathy, absent gastric motility, small bowel diverticulitis and Sensorineural deafness

Hirschowitz, Groll and Ceballos (1972) reported this syndrome in three female sibs.

7.12.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Progressive sensory neuropathy without tropic changes.

3. Small bowel diverticulitis
4. Progressive loss of gastric motility
5. Tachycardia
6. Acanthosis migricans.

7.12.2 **Auditory system**

Inner ear: Examination of the temporal bones showed collapsed Reissner's membrane and destruction of the organ or corti.

Hearing: Progressive childhood profound sensorineural deafness. The ages of onset of bilateral sensorineural deafness were 8, 3 and 9 years of age respectively, at 10, 5 and 18 years respectively the deafness became total.

Vestibular system: Vestibular function was found to be normal in all three sibs.

7.12.3 **Treatment and prognosis**

Vitamin A acid is effective in the treatment of acanthosis migrans. Gastrointestinal abnormalities requires medical treatment. Prognosis is poor because of the progressive nature of the disorder.

7.13 **Multiple neurofibromatosis (Von Recklinghausen's disease)**.

Neurofibromatosis is a generalized disease characters.

by multiple neoplasms of the peripheral nerves, pigmentary abnormalities and connective tissue dysplasia.

The disease known today as multiple neurofibromatosis was first described by Tilesius in 1793, and Virchow in 1847 pointed out its familial nature. Von Recklinghausen coined the term "neurofibroma" and delivered his classic treatise on the subject in 1882. His eminence in the medical world led to the association of this disease with his name.

The average age of onset is 20 years (Rosenberg et al 1974). Males and females are equally affected. The incidence is estimated to be one in 2,000 to 3,000 live birhhs (Brasfield and Gupta 1972). It has been reported in all races and is found world wide (Wander and Dasgupta 1977).

In some patients bilateral nerve tumors are the only or principal manifestations of this disease. Familial bilateral acoRstic neuromas have been reported by many authors (Gardner and Frazier, Lee and Abbott 1969, Young et al 1970). About 4 percent of persons having acoustic neuromas have this syndrome.

7.13.1 **Characteristics**

1. Autosomal dominant inheritance with 80% penentrance.
2. Palsies of the 5th, 6th, 7th, 9th and 10th cranial nerves due to encroachment on the adjacent cranial nerves by the acoustic neuroma.

3. Severe headaches and progressive visual loss due to increased intracranial pressure.
4. Muscular dystrophy and partial albinism in some cases.
5. Spinal root neuromas, ependymomas, astrocytomas, or meningcomas have also been found.

7.13.2 **Auditory system**

Neurofibromas may occur in the external auditory meatus, on the pinna and on the surrounding tissue. Hallpike (1960) described a neurofibroma causing stapes fixation and conductive deafness. Autopsy findings have been described in several patients (Gardner and Frazier 1930, Gardner and Turner 1940). Each showed bilateral (acoustic tumours showed interlacing bundles of elongated cells forming palisades, characteristic of acoustic neuromas (Nager 1964, Perez De Moura et al 1969).

Hearing: Hearing loss was first noted in the 2nd or 3rd decade and consisted of progressive bilateral neural hearing loss, resulting in total deafness within 5 to 10 years. Hearing loss was the first symptom in 50 percent of patients. Audiograms generally show no or slow puretone change, progressive loss of discrimination and more marked at higher frequencies (Histelberger and Hughes 1968, Perez De Moura et al 1969).

Vestibular system: Vestibular abnormalities are characteristic (Gardner and Frazier 1930; Young et al 1970).

7.13.3 **Treatment and prognosis**

Surgical removal of the tumor is the therapy of choice. Patients live an average of about 20 years (with a range of 2 to 44 years) after the onset of symptoms.

7.14 Bulbopontine paralysis with progressive Sensorineural hearing loss

This syndrome was described in three sibships (Vialetto 1936, Van Laere 1986, Boudin et al 1971). Several sporadic eases have been described (Van Laere 1967, Arnould et al 1968; Trillet et al 1970).

7.14.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Childhood onset of slowly pngressive bulbar paralysis with weakness of facial muscles, lips, tongue, larynx and muscles of mastication.
3. Dysphagia and dysarthria.

7.14.2 **Auditory system**

No inner ear abnormalities were described.

Hearing: A progressive bilateral sensori-neural hearing loss was frequently the first of this disease, beginning between 10 and 35 years of age. Two patients had auditory hallucinations (Vialetto 1938).

Vestibular system :Caloric vestibular tests on four patients showed hypoactive or absent vestibular responses.

7.14.3 **Treatment and prognosis**:

Therapy is symptomatic and is of little help. Prognosis is poor because of the progression of the disorder.

-oOo-

C H A P T E R VIII

Genetic hearing loss with metabolic abnormalities

There are many types of metabolic abnormalities which are associated with deafness. The most common of these is pendred syndrome, characterized by Goitre and deafness. The other types include micopolysaccharidoses (Hunter-Hurler syndrome), elevated protein bound Iodine (PBI) and elevated growth harmones.

The associated hearing loss is mostly sensorineural in nature.

8.1 Pendred Syndrome (Goitre + deafness)

Pendred syndrome, defined as a clinical triad consisting of perceptive hearing loss, goitre and abnormal perchlorate test was originally described by Vaun Pendred (1^896). Since then, it has received little attention except for occasional sporadic reports (Brain 1927; Johnsen 1958; Me Girr etal 1959; Fraser et al 1960 etc).

Srivatsa dn Mehrotra (1963) reported 3 affected moslem brothers from India. Varalakshmi and Kanna (1969) described 2 affected mothers in another family. Atleast over 300 cases have reported so far.

Pendred syndrome possibly accounts for as much as 10 percent of the cases of congenital deafness (Batasakis and Nishiyama 1962).

8.1.1 **Characteristics**

1. Autosomal recessive transmission.
2. Goiter developing prior to adolescence.
3. Positive perchlorate discharge test.

8.1.2 **Auditory system**

External and middle ear were reported to be normal.

Inner ear: Temporal bone pathology was described by Huidberg-Hansen and Balslev-Jorgensen (1968) and Kiar et al (1972). The changes were characteristic of Mondini defect.

Hearing: Although variation in hearing loss occur, audiometric testing usually shows a congenital bilateral 40 to 100 dB sensorineural hearing loss, more severe in higher frequencies (Arnvig 1955, Von Harnaeck et al 1961, Okamato et al 1978). It is severe in 50 percent of cases. The average age at which deafness is detected is 2.2 years (Thould and Scowen 1964). The hearing loss progresses slightly during childhood. Rarely the hearing loss will be minimal; hearing in one ear may be relatively normal (Fraser 1965).

Recruitment tests suggest that the auditory defect is in the organ of corti (Nilsson etal 1964, Fraser 1965, Okamato et al 1978).

Vestibular system: Caloric vestibular tests generally show depressed vestibular function (Johnsen 1958; Fraser 1965), although normal vestibular responses have been found in some cases (Deraemacker 1956; Von Harnack et al 1961).

8.1.3 **Treatment and prognosis**

Various surgical procedures and harmone therapy have been used to treat goiter. If therapy is started early, the goiter may regress, hearing does not improve however. (Kitlak and Gebert 1968). Hearing loss remains stable with little change over the years, if there is some residual hearing, hearing aid may be of use.

Patients have normal life span, with adequate thyrorune therapy, even though the hearing does not improve, atleast the goiter does not enlarge.

8.2 Goiter, elevated protein bound iodine (PBI) stippled epiohyses and congenital sensori-neural deafness

This syndrome was described in 3 of 6 sibs by Refetoff and colleagues (1967, 1972).

8.2.1 Characteristics

1. Autosomal recessive transmission.
2. Stippled epiphyses.
3. Bird like faces
4. Winged scapulae
5. Goiter with abnormally high PBI.

8.2.2 **Auditory system**

No external, middle or inner abnormalities were reported.

Hearing: Congenital severe bilateral sensorineural deafness was present in all the three sibs. The deafness was more marked in higher frequencies.

Vestibular system: No vestibular studies were reported.

8.2.3 **Treatment and prognosis**

Treatment of deafness was ineffective because of the severity of the loss.

The disorder was non progressive.

8.3 Mucopoly Saccharidoses

The mucopoly Saccharidoses are inherited disorders of mucopoly Saccharide metabolism. Defective activity of various genetically controlled pathways of lysosomal degradation lead to intracellular storage of undegraded acid mucopolysaccharides and to relatively similar clinical and skeletal changes. The Phenotype is most pronounced in the Hurler and Maroteaux syndromes and less severe in other mucopolysaccharidoses (McKusick 1972, Spranger 1972).

A. Hurler syndrome (MPS I-H)

First described by Hurler (1919) is the classic prototype of mucopolysaccharidoses.

Characteristics:

1) Autosomal recessive inheritance.

2) Growth failure after infancy.

3) Marked mental retardation.

4) Progressive coarsening of facial features beginning toward the end of the first year of life.

5) Corneal clouding.

6) Chronic nasal discharge and repeated upper respiratory infections.

7) Hernias

8) Progressive lack of mobility of joints.

9) Hepatosplenomegaly.

10) Biochemical evidence of intracellular storage and extensive urinary excretion of acid mucopoly Saccharides.

Death usually occurs before 10 years of age from pneumonia and/or cardiac failure.

Auditory system

Virtually no hard data is available on the deafness in many types of mucopoly Saccharidoses.

No external or inner ear abnormalities were reported.

Middle ear: Keleman (1966) reported temporal bone findings. The air cells of the tegmen and epitympanum were filled with reticular mesenchymal tissue. The mucous membrane of the middle ear was high and papilomatous, blocking the niches of the oval and round windows.

The deformed nasopharynx and increased susceptibility to upper respiratory illness lead to middle ear infection.

Hearing: Probably most Hurler syndrome patients have some degree of progressive conductive deafness. No audiometric data is available.

Vestibular system: No vestibular tests were described.

A. Scheie syndrome (MPS I-S)

It is an allelic form of Hurler syndrome.

Characteristics:

1. Autosomal recessive inheritance.
2. Facies is somewhat coarsened and shows mandibular prognathism and downturned oral commisures and broad nose.
3. Progressive corneal clouding beginning in early life.
4. Stature is mildly retarded, intelligence is normal.
5. The hands and feet are broad, and the fingers and toes are fixed in a claw like position.
6. Mobility of all joints is limited.
7. Most affected individuals have aortic regurgitation.

Auditory system:

No external/middle/inner ear abnormalities were mentioned.

Hearing : A systematic audiometric study has nat been carried out. Possibly not more than 10 to 20 percent exhibit hearing loss which is not severe in the middle age (Konigsmark and gorlin 1976). Although not adequately documented, the hearing loss is probably mixed type (Koskenoja and Suvan to 1959, Murray 1959, Scheie et al (1962).

Vestibular system: No studies were reported.

C. **Hunter syndrome (MPS - II)**

Originally described by Hunter (1917), this syndrome occurs in 2 forms, mild type (type A) and severe (Type B).

Characteristics: 1. X linked inheritance.

2. In type A, intelligence is mildly impaired, stature is less severely retarded than in MPS I-H. These patients usually survive to adulthood.

3. Type B patients suffer rapid psychomotor deterioration and usually die before puberty.

4. Hepato splenomegaly.

5. No gross evidence of corneal clouding.

Auditory system

No external ear abnormalities were mentioned.

Middle ear: Wolff (1942) found no joint cavity between the malleus and incus and irregular bony nodules in the round window window area, protruding into the lower most portion of the scala tympanum. Zechner and Altman(l968) found the middle ear mucosa to be edematous and to contain

large foamy PAS positive cytoplasm. Malleus and incus contained large hyperemic narrow spaces. PAS positive cells were inside the mastoid air cells. Otosclerotic foci were noted near the oval and round windows.

Inner ear: Wolff (1942) found certain changes in the organ of corti, but there appeared to be postmortem artifacts. Zekhner and Altman (1968) found normal organ or corti, and the cytoplasm of the spiral and vestibular ganglia was engorged with foamy PAS positive material. Beneath the stria vascularis a broad PAS positive zone was noted. In the semicircular canal region, numerous blue mantles were seen.

Hearing: Deafness is seen in 50% of the cases. Hearing loss is usually not severe (Lerpy and Clocker 1966). Many researchers have reported sensorineural deafness (Konigsmark and Gorlin 1976) based on their experience suggest that hearing loss is more often mixed. Kittel (1963) illustrated mixed hearing loss in his patient. No other audiometric data is available.

Vestibular system: Vestibular testing on one patient showed reduced caloric response bilaterally.

D. **Sanfillo Syndrome (MPS III)**

This occurs in two aonallelic forms.

Characteristics

1. Autosomal recessive inheritance.
2. The faces is far less marked than in MPS I-H.
3. The corneas are clear.
4. Height is almost normal.
5. Children become agressive and restless prior to school years.
6. Death usually occurs in the second decade.

Auditory system:

No external/middle/inner ear abnormalities were reported.

Hearing: Deafness has rarely been reported. It was evident in only 10 of 10 patients documented by Spranger et al (1967) and in 3 of 8 patients studied by Rampuri (1969). However agressive nature and lack of co-operation has made audiometric testing difficult to impossible. Sparse evidence suggests that, when present the hearing loss appears at about 6 to 7 years of age and becomes progressive.

Vestibular system: No studies were conducted.

E. **Morquio syndrome (MPS IV)**

This syndrome occurs in 1 out of 40,000 births.

Characteristics

1. Autosomal recessive inheritance.
2. Marked growth failure after the first year of life.
3. Short neck
4. Pigeon breast.
5. Progressive spinal deformity.
6. Other skeletal anomalies such as knock knees and flat foot. Extremeties appear disproportionately long.
7. Facies is normal.
8. Excessive joint mobility.
9. Intelligence is nearly always normal.

Auditory system

No external/middle/inner ear abnormalities were reported.

Hearing: Most patients exhibit mixed deafness. It has its onset during the second dacade, and in most cases it is not severe (Robins et al 1963, Von' Roorden et al 1968). Reidner and Levin (1977) suggested by the end of first decade of life most of the cases may be expected to have either mixed or sensorineural hearing loss. It is unknown whether the conductive hearing loss is due to ossicular chain malformation The mechanism for onset of sensorineural loss is not clear.

Vestibular system: No studies were reported.

F. **Maroteaux- Lamy syndrome (MPS - VI)**

Patients exhibit a sever Hurler like appearance but have normal intelligence. There are 2 forms - mild and severe.

Characteristics:

1. Autosomal recessive inheritance.
2. In the mild form the first changes appear around 6 years of age when small stature and spinal alterations are noted. These patients survive to adulthood.
3. The severe form is identified in early childhood by several facial and skeletal changes severely impaired vision and cardiac defects that lead to death in adolexcence.

Auditory system:

No external/middle/inner ear abnormalities were reported

Hearing: About 25 percent of patients exhibit deafness, probably conductive, which appears at about 6 to 8 years of age and results from frequent bouts of% otitis media (Liebenan 1938, Stoeckel 1941, Maroteaux et al 1963, Sarrowy et al 1965, Fallis et al 1968, Spranger et al 1970).

Vestibular studies were not reported.

Treatment and prognosis (in general)

No satisfactory long term therapy has been devised for the mucopoly Saccharidoses. Treatment when considered is symptomatic.

Prognosis is variable depending on the type of mucopoly Sacharidosts. In MPS I, MPS-III & MPS VI death usually occurs by 2nd decade because of cardiac defects.

8.4 **Mannosidosis**

Mannosidosis was described in 1967 by Ockerman. Autio et al (1973) described several other cases. Booth et al (1975) and Farriann et al (1975) reported three affected sibs. Spranger et al (1976) studied 12 children. Other cases were reported by Loeb et al (1963), Beaudet and Nichols (1975), Tsay et al (1974) and Pererman et al (1975).

8.4.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Coarse facies and short neck.
3. Recurrent respiratory infections.
4. Kyphoscoliosis, mild hypotonia, protuberant abdomen, linguinal and/or umbilical hernia.
5. Progressive mental retardation
6. Mild dysostosis multiplex.
7. Reduced mannosidase activity in liver, plasma and leukocytes.
8. Vacuolated lymphocytes.

These symptoms become evident only after the first few years of life.

8.4.2 **Auditory system**

No external/middle/inner ear abnormalities were described.

Hearing: Severe high frequency sensorineural deafness is a frequent feature (O'ckerman 1967, Loeb et al 1969, Booth et al 1975, Spranger et al 1976).

Vestibular system : No vestibular studies have been reported.

8.4.3 **Treatment and prognosis**

Treatment is symptomatic.

The children succumb to respiratdry infections.

The deafness and cental retardation are progressive.

8.5 Prenatal dwarfism, elevated growth hormone levels, Mental retardation and congenital deafness.

This syndrome was first reported in two male sibs by Van Gemund, Laurent de Angulo and Van Gelderen (1969).

8.5.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Prenatal dwarfism.
3. Mental retardation.
4. Elevated serum immuno teactive growth harmone and end organ unresponsiveness.

8.5.2 **Auditory system**

No external/middle/inner ear abnormalities were reported.

Hearing: Both sibs were congenitally deaf, and neither achieved any facility of speech. The deafness was not otherwise described.

Vestibular system: No studies were reported.

8.5.3 **Treatment and prognosis**:

Anabolic steroid therapy may be initiated to promote growth.

Although the disorder is not life threatening prognosis is poor since treatment is ineffective

S.6 **Aplasia of nasal alae, hypothyroidism, growth RETARDATION, Malabsorption. absent permanent teeth and sensorineural deafness**

Johanson and Blizzard (1971) and Park, Johanson, Jones and Blizzard (1972) described this syndrome in three unrelated female children. Morris and Fisher (1967) and Townes (1972) reported less well documented cases in females.

8.6.1 **Characteristics**:

1. Limitation largely to females with possible lethacity in males.
2. Absence of nasal alae
3. Somatic and mental retardation
4. Cretinism

5. Urogenital abnormalities like single urogenital orifice, double vagina and bicornuate uterus.
6. Malabsorption due to proteolytic and lipolytic deficiency.
7. Absence of permanent teeth.

8.6.2 **Auditory system**

External and middle ears were,normal.

No inner ear abnormalities were described.

Hearing: The deafness was congenital, profound and sensorineural in all patients.

Vestibular system: No studies have been reporte

8.8.3 **Treatment and prognosis**

Rhinoplasty may correct the nasal defect.

Cretinism may be treated with thyroxine.

While growth improvex muscular hypotonia and intelligence do not

The outlook for these patients is poor.

The mental retardation is marked and death may results from heart failure.

8.7 Chronic Lactic acidemia, metabolic myopathy Growth retardation and sensorineural deafness

Hackett, Bray, Ziter, Nyhan and Creer (1973) describe two sisters with this apparently unique syndrome.

8.7.1 **Characteristics**

1. Autosomal recessive inheritance
2. Muscle weakness with insidious onset at 6 to 8 years of age.

3. Growth retardation
4. Possible retarded sexual maturation
5. Chronic lactic acidemia.

8.7.2 **Auditory system**

No external/middle/inner ear abnormalities were described. Both sisters exhibited moderate sensorineural deafness, otherwise uncharacterized.

Vestibular system: No vestibular function tests were carried out.

8.7.3 **Treatment and prognosis**

Therapy consists of treatment of lactic acidosis as indicated.

Prognosis apparently not good, the lactic acidosis resulted in death in one sister.

8.8 Hypothalamohy pophysical dwarfism and sensorineural deafness

Winkelmann et al (1972) reported two sisters with the above combination of symptoms.

8.8.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Somatic and sexual infantilism due to deficiency of growth harmone and gonadotropius.
3. Normal intelligence
4. Growth retardation.

8.8.2 **Auditory system**

No external/middle/inner ear abnormalities were reported.

Hearing: Sensorineural hearing loss, which progressed rapidly was noted at approximately 6 to 8 years of age. 8y 12 years of age both the sisters were totally deaf.

Vestibular system: No studies were reported.

8.8.3 **Treatment and prognosis**

It should be possible to treat such patients with growth harmone or with anabolic steroids. Prognosis for treatment of deafness is poor, Harmonal therapy for the dwarfism should be effective.

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C H A P T E R IX

Genetic hearing loss associated with chromosomal disorders

Hearing loss may occur as a part of syndromes resulting from chromosomal abnormalities. In addition to deafness there are various multiple congenital malformations. Mental retardation appears to be a common feature in all these syndromes. In 1959, Lejeune, Gautier and Turpin described the first abnormality of human chromosomes, the association of .47 chromosomes with Down's syndrome. The prevalence of chromosomal abnormalities in live born infants is about 1:200.

There are 23 pairs of chromosomes in each human cell. Of these 22 pairs are autosomes, whereas one pair is sex chromosome containing XX chromosomes in females and XY chromosome in males. Thus the chromosomal disorders are of two types. Autosomal syndromes resulting from the abnormality of autosomes and sex chromosome syndromes resulting from abnormal sex chromosomes.

According to Denver classification (1960) the autosomes are divided into 7 groups and are numbered from 1 to 22, based as nearly as possible in the order of descending length. Designating the groups as A to G, the 22 pairs of autosomes are divided in this way.

Pairs 1-3 are group A, 4 and 5 are group B, 6-12 are group C, 13-15 are group D, 16-18 are group E, 19-20 are group F and 21 & 22 are group G. The X chromosome is in group C and the + chromosome in group G.

Modification of these nomenclature was added at Paris conference in 1971. The presence of one additional chromosome (Trisomy) is indicated by a plus (+) followed by the letter or number identifying the chromosome, absence of one chromosome by a minus (-). for eg. 45XX1-13, indicates a female missing chromosome l3, 47XY1 + 21 indicates a male with trisomy 21. The long arm of the chromosome is designated by the letter "Q" and short arm by "P".

Three facts emerged out of the extensive chromosomal analysis on new borns and handicapped individuals.

1. Many children with chromosomal abnormalities can't be easily detected clinically in infancy because they don't have any distinguishing physical characteristics. Infants with autosomal abnormalities can be more easily identified at birth, than sex chromosome syndromes (Lubs and Ruddle 1970).
2. As more patients with the same chromosomal abnormalities have been detected, it has been evident that wide phenotypic variability is the rule and not the exception.

3. One should note that no single anomaly is pathognotmomic of any syndrome. The symptoms of various syndromes overlap a great deal. Therefore, it is the total pattern of anomalies rather than a single anomaly which may indicate the correct clinical diagnosis of a specific chromosomal abnormality syndrome.

The most common disorder under this category is Down's Syndrome.

9.1 **Trisomy 21 or 47 XX, + 21 (Down's Syndrome)**

Since the clinical description by Langdodon Down in 1866, Mongolism or to use the preffered term, Down's syndrome has become a familiar clinical syndrome. In 1959, Lejenne, Gautier and Turpin first identified its association with an extra chromose in the 21-22 group, which by custom is referred to as a number 21. Subsequent studies have shown the Down's syndrome to be the most common autosomal abnormality with a frequency of about 1:700 newborns (Fabia 1969). The incidence of this disorder is found to Increase with Increasing maternal age.

9.1.1 **Characteristics**

The symptoms are too numerous. The important ones are:

1. Brachy caphaly with prominent forehead, shortening of anteroposterior diameter and flattening of the occipit.

2. Flat nasal bridge epicanthic folds, palpebral fissures that slant upwards.
3. Iris abnormalities.
4. Protruded tongue.
5. Short and broad neck, hairline reaches farther down the back than normal.
6. Abdomen is protuberant umbelical hernia is common.
7. Varying degrees of mental retardation.
8. Abnormal dermato glyphics with a characteristic simans crease.
9. Marked hypotomia in early infancy.

9.1.2 **Auditory system**

External ear: Ears were usually small and simple in appearance often having an over-folded upper helix, poor antihelix development and a small lobe.

Middle ear: Wright (1969) described inflammatory changes in the middle ear with thickened mucosa and exudate. Igarshi et al (1977) found deformity of stapes supra structure and incus under developed pyramidal eminence.

Inner ear: Igarshi et al (1977) in their temporal bone study found that the spiral reconstructions showed cochlear length to

be slightly shorter, cochlear modiolus was under developed with grossly deficient spiral ganglion population. The spirallin cochlear shell showed partial deficiency of the inter-scaler septum between the middle and apical coils. The cochlear duct was shorter than normal, the organ of corti was normal. Wright (1969) found no inner ear abnormality.

Hearing: There is little documentation available on the frequency of deafness in this condition. Glovsky (1966) in a study of 38 children with trisomy 21, found 50 percent with sensorineural hearing loss, 20 percent with mixed loss, and 3 percent with conductive deafness. In contrast Fulton and Lloyd (1963) found conductive deafness in 20 percent, mixed loss in 10 percent, and sensorineural hearing loss in 10 percent.

Vestibular system: No vestibular tests were described.

Johnson (1971) reported that the lateral bony semicircular was malformed and there was stenosis of the membranous semicircular duct. Igarshi et al (1977) found no structural abnormality of the vestibular system except for the degeneration and reduction of the scarpas ganglion cells and nerve fibers.

9.1.3 **Treatment and prognosis**

Educational programme is planned based on the severity of retardation. Use of 5-hydroxy-tryptophan in improving muscle tone has resulted in varied success.

About 25 to 30 percent die during the first year of life and about 50 percent during the first five years. The most frequent cause of death is respiratory infections and congenital heart disease.

9.2 **Chromosome 13-15 trisomy (Patacis Syndrome or D Trisomy)**

Patan et al (1960) described the first patienR with trisomy 13. Since then more than 150 patients with this syndrome have been identified. The incidence of this disorder in newborn was estimated as 1:7600 (Taylor 1968). According to Sando & Wood (1971) the incidence is 0:45 in 1000 births.

9.2.1 **Characteristics**

1. Microcephaly
2. Mental retardation
3. Multiple eye anomalies
4. Peculiar faces
5. Hypertelorism
6. Cleft palate/lip.

7. Webbing of the neck
8. Cardiac anomalies
9. Abnormal palm prints, simian creases and a hyper-convexity of finger nails, polydactyly.

9.2.2 **Auditory system**

External ear: Low set, poorly differentiated pinna, preauricular tags and atresia of the external auditory canal have been reported.

Middle ear: The documented middle ear anomalies have included a deformed stapedial supra structure, absence of incudostapedial joint, absence of the stapedius muscle and tendon, persistance of stapedial artery, obtuse geniculate turn of 7th cranial nerve (Black & Sando 1971, Kos et al 1966, Maniglia et al 1970, Sando, Baker 1972).

Inner ear: Temporal bone studies have been reported by Kos et al (1966), Black and Sando (1971) Saito et al (1974), Sando and Baker (1972), Sando et al (1975) Zev et al (1978). They have revealed a variety of inner ear abnormalities including aplasia, of organ of corti and stria vascularis, displacement and encapsulation of tectorial membrane, collapsed cochlear duct with Reissners membrane lying on the organ of corti.

Collapsed saccular wall, incomplete development of the Saccular macula and its otolictic membrane communicating scalae, under-developed modiolous large patent cochlear acqueduct.

Kos et al (1966) reported scherbes type of abnormality while Maniglia et al (1970) described Mondini or Modini Alexander type.

By contrast Mottel and Jensen (1965), Kelmen et al (1968) found no anomalies of the inner ear.

Hearing: 85 percent of infants with 13-15 trisomy have apparent deafness; Deafness may be conductive,sensorineural or mixed in nature. The degree of hearing loss is not specified.

Vestibular system: No studies were reported.

9.2.3 **Treatment and prognosis**

Treatment is of no avail.

The life span is severely limited, approximately half of the affected infants lived upto one month, one-third to 3 months and ll/12th of infants lived to 3 years of age (Magenis et al 1968).

9.3 **Trisomy 18 (Edwards Syndrome or E Syndrome)**

In 1960, Edwards and his associates reported a female infant with a peculiar facias, webbing of the neck,

congenital heart disease, neonatal hepatitis and many minor abnormalities in association with an extra 3 group chromosome. Since then more than 150 patients with this syndrome have been identified. The incidence in newborn was estimated as 1:6800 (Taylor 1968).

9.3.1. **Characteristics**

1. Scaphocephaly
2. Prominent occipit
3. Ptosis of the eyelids
4. Micrognathial
5. Cleft palate
6. Psycomotar retardation.
7. Hypertonta
8. Seizures
9. Cardiac anomalies and failure to thrive.

9.3.2 **Auditory system**

External ear: The reported abnormalities include low set ears, poorly differentiated pinna, overfolding of the helix and absence of the external auditory canal.

Middle ear: Histopathologic studies of the ears have been documented only in few cases (Kelemen 1966, Kos et al 1966, Sando et al 1970, Gacek 1971, Miglets et al 1975, Saito et al 1977).

Middle ear abnormalities have varied:- abnormal form of ossicles, malformations of the stapes, fusion of the incus and malleus, absence of the stapedial tendon and pyramidal intratympanic course of facial and chorda tympani nerves.

Inner ear: Inner ear anomalies have included poorly decreased or absent spiral ganglion cells. Under developed stria vascularis, communicating scalae, absence of semicircular canals and cristae, absence of endolymphatic duct and sac, widely patent cochlear aqueduct.

Wolf et al (1965) found no significant changes in the inner ear.

Hearing: 70 percent of affected individuals have apparent deafness. Hearing loss is mostly mixed in nature. No audiometric data is available,

Vestibular system: No studies were described.

9.3.3 **Treatment and prognosis**:

Treatment is of no avail.

In a survey of 153 patients, the mean survival was 71 days (Taylor 1968). In another survey of 101 patients by Weber et al (1964), half of the patients survived for 2 months, one third for 3 months and only one for 10 years*

9.4 Chromosome 18 long arm deletion(18q-) Syndrome

In 1964, de Grouchy et al reported a deaf microcephalic and mentally retarded girl with deletion of a portion of the long arm of a number 18 chromosome. Subsequent descriptions of more than 25 patients have shown that a fairly consistent phenotype is to be expected, (de Grouchy 1969, Wertelecki and Gerald 1971, Insley 1967, Kushmck and Matsushita 1968, Stewart 1970).

9.4.1 Characteristics

1. Microcephaly.
2. Short stature
3. Psychomotar retardation
4. Muscular hypotonia.
5. Midfacial hypoplasia.
6. Hypertelorism.
7. Epicanthal folds.
8. Spindle shaped fingers with increased number of fingertip whorls.
9. Congenital heart disease.

9.4.2 Auditory system

External ear : The pinnae are often dysplastic with prominent antihelix and antitragus. In over 50 percent of the cases atresia or stenosis or hypoplasia of the external auditory canal was found (Kunze et al 1972, Bergstorm et al 1974).

Inner ear: No inner ear abnormalities were reported.

Hearing: Deafness was reported in about 65 percent of cases (Wertelecki and Gerald 1971, Kunze et al 1972), Bergstrom et al (1974) reported conductive hearing loss due to atresia or hypoplasia of the external auditory canals in 3 of their 4 patients. The degree of hearing loss was not specified.

Vestibular system: No vestibular studies were described.

9.4.3 **Treatment and prognosis**

Treatment is of no avail.

This disorder is not life threatening.

9.5 **XO syndrome (Turner syndrome or Gonadal Dysgenesis)**.

In 1938, Henry Turner reported a syndrome consisting of shortness of stature, sexual under development, short webbed neck in 7 girls aged 15-23 years. In his opinion this syndrome was brought about by pituitary insufficiency. Subsequently, a number of patients with these clinical features were shown to be chromatic -ve and to have a 45 X karyotype.

The frequency of this syndrome in newborns is about 1:3300 (Court Brown 1969). However this may not indicate the true incidence as stuHies of early spontaneous abortuses have shown that abott 3-5 percent have a 45 X karyotype and &hat 97 percent of conceptions die in utero.

9.5.1 **Characteristics**

1. Short stature
2. Sexual infantilism
3. Streak gonads
4. Elevated urinary gonadoteopin levels.
5. Various physical stigmata such as cubitus vulgus, osteoporosis and increased cutaneous nevi.
6. Flat nasal bridge, hypertelorism, epicanthal folds, ptosls, pitting edema of hands and feet.

9.5.2 **Auditory system**

External ear: 1.6% of cases show some deformity of the pinna and external auditory meatus (Stratton 1965). The deformaties include large prominent ears and stenosis or atresia of the auditory canals (Szpunar et al 1968).

Middle ear: There is increasingly greater frequency with which repeated acute or chronic middle ear inflammations were found in these cases (Stratton 1965,

Engel and Forbes 1965, Goldberg et al 1968, Anderson etal 1969, Szpunar et al 1968). X ray studies revealed marked hypocellularity of acellularity of mastoid (Szpunar et al 1968).

Inner ear: Anderson et al (1969) suggested the possibility of defect in the outer hair cells in the organ of corti in the upper part of the middle coils of the cochlea. But no temporal bone studies were reported.

Hearing: Hearing loss is mostly conductive or mixed in (Ferguson-Smith et al 1964, Ehgel and Forbes 1965, Goldberg et al 1968, Anderson et al 1969) some cases.

Lindstein (1963) and Anderson et al (1969) found bilateral sensorineural hearing loss with recruitment and a dip in audiogram centered about 2000 Hz.

Severe deafness was noted only in about 10 percent of cases. There was no striking progress of hearing loss with older age.

9.5.3 **Treatment and prognosis**

Estrogen therapy after the age of expected puberty is recommended to promote feminization and social acceptibility enjoy good health.

9.6 XX Gonadal dysgenesis and Sensorineural deafness

9.6.1. XX gonadal dysgenesis refers to individuals of female phenotype whose height is greater than 152 cm, and who exhibit sexual infantilism, primary amenorrhea and eunuchoid habitus. They are often tall and slender with increased arm span and absence of Turner syndromelike features. Streak gonads, hypoplastic Fallopian tubes and uterus, elevated urinary gonadotropins, decreased estrogen encretion are the other abnormalities. A high proportion of cases of XX gonadal dysgenesis may be due to a single autosomal recessive gene; parental consanguinity has also been noted (Christakos et al 1969, Pelez-Ballester et al 1970, Simpson et al 1971).

9.6.2 **Auditory system**

No external/middle/inner ear abnormalities were described.

Hearing: In a few cases severe congenital sensorineural deafness was noted (Josso et al 1963, Christakos et al 1969, Perez - Ballester et al 1970).

Vestibular system: No studies were described.

9.6.3 **Treatment and prognosis**

Harmone treatment may be useful.

This disorder is not life threatening.

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C_H_A_P_T_E_R X

Miscellaneous Syndromes Associated with Genetic Hearing Loss

In this chapter, those syndromes which did not quite fit into any of the precious chapters will be considered. It includes deafness associated with cardiac defects, dental abnormalities.

10.1 Slectrocardiographic abnormalities, fainting spells and sudden death with congenital sensoryndural hearing loss:-

(Jarvell and Lange-Nielsen Syndrome, Cardio-auditory syndrome, Surdocardiac syndrome).

Jarvel and Lange-Nielsen (1957) first described association of abnormal EKG and deafness in 4 siblings. Since then over 50 cases have been described by several authors (Levine and Woodworth 1958; Fraser St al, 1964; Jarvell et al, 1966; Lisker and Finkelstein, 1966; Kalljelz, 1968; Saahez Cascoset al, 1969; Van Bruggen et al, 1969; Fanchier et al, 1969; Athanasion and Welner,1972).

This syndrome may account for one percent of hereditory deafness (Fraser et al 1964).

However, Sanchez cascos et al,(1969) found only one case among 511 deaf children. Fay et al; (1971) found one example among 1100 deaf children.

10.1.1 **Characteristics**:

1. Autosomal recessive transmission.
2. Prolonged electrocardiograph QT intervals.
3. Recurrent strokes - adams attacks beginning in early childhood and occasionally resulting in sudden death.

10.1.2 **Auditory system**

No external or middle ear abnormalities have been reported.

Inner ear: Temporal bone changes have described by Friedmann et al (1966, 1968). The most unique change was the accumulation of PAS-Positive hyaline aggregates in an atrophic stria vascularis. There was almost complete degeneration of the organ of corti and loss of sensory cells. The tectorial membrane was shrunken and tetracted and Reissner's membrane was adheraat to the basilar membrane, practically obliterating the cochlear duct. The sensory epithelium of the utricle and saccule was atrophic and the cristae were disorganized. There was moderate loss of ganglion cells. These findings closely resemble those of Sicbenmann and Bing (1907).

Hearing:All patients demonstrated congenital bilateral severe sensorineural loss with higher tones maximally involved and with some retention of hearing in lowtones.

Vestibular system: Vestibular findings have not been described in any case.

10.1.3 **Treatment and prognosis**:

A hearing aid may be of some help for minimizing the hearing loss, Electrocardiographic abnormalities require, medical treatment. Hearing loss is not progressive. Affected persons have a variable number of syncopal attacks. In about half of the cases, the patient has died by the age of 15 years, few patients older than 21 years have been identified.

10.2 Progressive Lipodystrophy of the face and arms, multiple bone cysts and conduction deafness

Van Leeuwen (1933) described this syndrome in three adult sisters.

10.2.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Progressive lipodystrophy of face and arms, beginning in the first decade.
3. Multiple bone cysts.

10.2.2 **Auditory system**

No external/middle/inner ear abnormalities were reported.

Hearing: All the three sisters manifested conduction deafness at about 5 to 6 years of age. Although the degree of deafness was not stated, it was implied that it was severe.

Vestibular system: No studies were reported.

10.2.3 **Treatment and prognosis**

Stapedectomy could be performed to correct deafness.

One sister died of osteosarcoma, which had metastasized to the lung.

10.3 Otodental dysplasia

Levin and Jorgenson (1972; 1974) and Jorgenson et al, (1975) described a syndrome of dental abnormalities and sensorineural deafness in two large kindreds.

10.3.1 Characteristics

1. Autosomal dominant inheritance
2. Dental changes including globoid posterior teeth and taurodontism.

10.3.2 Auditory system

External ear: The pinnae were described as outstanding in some affected individuals (Jorgenson et al 1975). No middle or inner ear abnormalities were reported.

Hearing: Bilateral high tone sensorineural hearing loss to about 65 dB was noted in 28 of 30 affected individuals. The age of onset ranged from early childhood to middle age.

Vestibular system: Caloric tests were normal.

10.3.3 **Treatment and prognosis**.

A hearing aid may be employed.

Prognosis, is good. This disorder does not interfere with normal life.

10.4 Oligodontia and Sensorineural deafness

Glass and Gorlin (1979) described a new syndrome of oligodontia and congenital profound deafness in two sibs aged 7 and 9 years. Levin and Kopstein (1978) earlier reported a variation of this syndrome characterized by sensorineural hearing loss, dizziness and hypodontia.

10.4.1 **Characteristics**

1. Autosomal recessive inheritance.
2. Digodontia

10.4.2 **Auditory system**:

No external/middle/inner ear abnormalities were reported.

Hearing: Congenital profound sensorineural hearing loss was described in both the sibs.

The 9 year old boy had no residual hearing beyond 1000 Hz on audiometric testing. The other sib showed profound, but slightly less severe &ensorineural hearing loss.

Vastibular system: No studies were reported

10.4.3 **Treatment and prognosis**:

Patient should be referred to a dental surgeon. Usefulness of hearing aid is questionable because of the severity of loss.

10.5 Sickle cell disease and sensorineural hearing loss .

Sickle cell disease is a relatively common haemoglolanopathy of blaeks. It has been estimated that amout 7 to 9 percent of American blacks are heterozygotes (Hemoglobin strait). Thus about one in 400 would be homozygous.

10.5.1 Characteristics

1. Homozygotes may initially exhibit only anemia and little or no splenomegaly.
2. Patients develop recurrent attacks of weakness, fatigue, abdominal pain anoremia, jaundice and pallor.
3. With age there may be enlargement of the heart, leg ulcers, aseptic necrosis of the hip and hematuria.

10.5.2 Auditory system:

No external ear abnormalities were mentioned.

Middle ear: Within the ossicles the marrow was hyperplastic and erosive.

Inner ear: Temporal bone studies showed degenerative changes in the organ of corti and the stria vascularls consistent with ischemia (Morgenstein and Manance, 1969). Toold et al (1973) postulated that hearing loss resulted from a thromboembolic process. Serjeant et al, (1975) ruled out narrowing of the auditory canal as an etiologic factor.

Hearing: Mild to moderate bilateral sensori-neural hearing loss more marked in higher frequencies was reported in the affected members (Morgenstein and Manance, 1969; Todd et al, (1973). Onset was insiduous and males and females were equally affected (Todd et al 1973).

Vestibular system: No vestibular studies have been reported.

10.5.3 **Treatment and prognosis**

Treatment is symptomatic.

The general outlook for the patient is not very good.

10.6 Di George Syndrome (3rd and 4th pharyngeal pouch syndrome).

Di George syndrome is one of the important ummuno-deficiency syndrome causing otitls media. Congenital

absence of thymus and parathyroid glands is characteristic of this syndrome which results in congenital primary hypothyroidism and deficiency of cellular immunity.

10.6.1 **Characteristics**

1. Etiology is unknown, it is though to result from an embryonic maldevelopment of structures derived from pharyngeal clefts.
2. Neonatal tetany.
3. Craniofacial anomalies including characteristic facies hypertelorism, shortened lip philtrum, nasal clefts.
4. Congenital heart disease.

10.6.2 **Auditory system**

External ear: Various malformations of the pinna and external auditory meatus have been reported (Adkins & Gussen 1974, Black et al, 1975).

Middle ear: Authors have reported extensive middle ear abnormalities and otitis media in many patients.

Inner ear: Temporal bone findings in a 7 week old child revealed bilateral cochlear ahomaly (Adkins, 1974).

Hearing: Hearing loss is mostly conductive. In some there may be cochlear involvement also. Hearing was apparently present in one patient, whereas hearing was anatomically impossible in the other patient; out of the two cases reported by Black et al 1975. No other audiometric data are available.

10.6.3 **Treatment and prognosis**

Some reports suggest successful treatment of this disorder with thymic transplants. If the congenital heart disease is compatible with survival, they usually die of overwhelming infection before 3 years of Age.

10.7 **Otosclerosis**

Otosclerosis is one of the major causes of hearing loss in the elderly. It has been the subject of over 1000 publications (Steinberg and Neumann, 1973).

Guild (1944) studying 1100 pairs of temporal bones found that 5% had histologic evidence of otosclerosis. A somewhat higher incidence was found by JØrgensen and Kristensen (1967) in Denmark. Among 237 temporal bones in general 11 percent showed otosclerosis; among patients above 60 years old, 18 percent had otosclerosis.

10.7.1 **Characteristics**

1. Autosomal dominant transmission with about 40 percent penetrance.
2. Gradual onset of hearing loss in the early decades of life.
3. Slow progressive, conductive or mixed symmetrical hearing loss of varying severity.
4. Normal vestibular response.

10.7.2 **Auditory system**

Otolpaic examination

Pathology: Careful examination of the stapes footplate shows 'bridge formation' from the footplate to the oval window. This formation - begins as a thickening of a portion of the footplate, progressing to involvement of the entire oval window. (Gussen 1969, Kelemen and Linthicum 1969, Lindsay 1973). Histologically, otosclerosis consist of a focalspongy overgrowth of bone involving the bony labyrinth, usually beginning near the oval window. This spongy bone contains numerous blood vessels and marrow and is sharply demarcated from surrounding normal bone. The otosclerotic change may spread from the oval window toward the round window and basal turn of the cochlea, and sometimes it may spread inward toward the posterior canal and cochlea (Nager and Fraser, 1938; Wolff and Bellucci, 1974).

Hearing: Although hearing loss from oto-sclerosis can be initiated in childhood, it usually begins in the second or third decade of life. In about 90 percent of

patients, symptoms are first noted between 15 and 45 years of age. The onset is insidious. Audiometric testing shows a conductive or a mixed sensorineural and conductive hearing loss, somewhat more marked in the higher frequencies. In some cases the sensorineural component may be quite marked with patients showing no response at higher frequencies to air or bone conduction (Myers et al 1963). Speech discrimination, tone decay and SISI testing are generally normal.

Vestibular system: No vestibular abnormalities have been described in patients with otosclerosis.

10.7.3 **Treatment and prognosis**

A hearing aid will help most patients with otosclerosis. In some cases, surgical therapy with stapedectomy may be carried out. The hearing loss is slowly progressive and is usually only moderate in degree. Pregnancy may accelerate the hearing loss.

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C H A P T E R XI

SYNDROMES ASSOCIATED WITH N0NGENETIC HEARING LOSS

11.1 INTRODUCTION

Nongenetic hearing loss refers to hearing loss acquired due to extraneous factors other than genetic causesoperating either before, during or after birth. The extraneous factors may be inflammatory, toxic, metabolic or traumatic in nature or it may be due to unknown causes.

Approximately half of all congenital deafness is acquired as a result of RH incompatibility, infection with rubella during embryonic life, ototoxic drugs, prematurity injury and various diseases. Any infection to the mother during gestation period would result in damage to the fetus causing various deformities including the auditory system.

Another common cause of acquired congenital deafness is prematurity. Davis and Stewart (1975) in a study of low birth weight or preterm birth children found hearing loss to be significant. Lindsay (1973) reported deafness in cases of breech presentation with the cord round the neck which resulted in anoxia or severe hypoxia. He

also reported the incidence of deafness among premature babies, otherwise apparently normal to be higher than in full term births.

Other deafness which can occur in early infancy are those secondary to infection and trauma. Most common among these types of deafness which can occur in infants are those secondary to mumps, and meningitis and otitis media. There is also the possibility of skull fracture and head injury causing either unilateral or bilateral deafness.

According to Fraser (1969), the nongenetic factors account for 46% of profound childhood deafness. He has grouped the causes of acquired hearing loss into 3 categories namely prenatal, perinatal and postnatal.

Prenatal: The prenatal causes may be due to Rubella, Syphilis, Tonoplasmosis, other viral and bacterial infections, metabolic and harmonal disturbances or due to the usage of ototoxic drugs. About 6% of childhood deafness can be attributed to these factors.

Perinatal : Perinatal causes are the factors operating at birth. Infections, asphymia, kernicterus, toxic drugs, prematurity might result in profound congenital deafness approximately in about 10%.

Postnatal: Infections diseases like measles, mumps, meningitis and trauma may result in deafness during infancy.

In addition to the above mentioned factors, deafness can be still acquired in later due to various factors like vascular, neural, viral or of unknown etiology. In such eases deafness may be the primary defect, or may be a part of a more generalized disorder/disease, eg. Menleres syndrome, Ramsay Hunt syndrome, Cogan's syndrome. Usually the acquired or nongenetic hearing loss is bilateral and profound in nature. In most of the cases, the inner ear is involved. The hearing loss may be progressive or nonprogressive. In some cases, the hearing loss improves with advanced medical treatment, while in others it is non reversible.

11.2 **Deafness acquired during prenatal life**:

The first 28 days of fetal life form a crucial time of very rapid growth and development during which more than 70% of long term neurological handicaps originate (Hardy 1973). A significant portion of these handicaps appear to begin with fetal infection acquired, during pregnancy. There have been well documented instances of fetal infection and disease following maternal infection with Rubella, congenital cytomegalovirus tonoplasmosis, Syphilis.

The fetal infection occurs by one or more of the following routes:

1. Transplacental passage, (2) Extension up the birth canal with infection of the membranes, (3) Direct contact or contamination during the birth process. The maternal infection may be clinically evident or subclinical with atypical characteristics or it may not be apparent at all.

The deafness in these cases may be caused either by the lack of development of one or more parts of the auditory system, or an interruption at any stage of the process of development, or due to degeneration of the partly or wholly developed auditory mechanism (Ormerod 1960).

The resulting deafness is usually profound, and bilateral and sensorineural in nature.

The most common types of prenatally acquired deafness are Rubella, Congenital syphilis (MV infection and congenital toxoplasmosis.

11.2.1 **Rubella syndrome**

One of the most commonly encountered diseases associated with acquired deafness is German measles (Rubella). In 1941, Gregg reported the high incidence of congenital

defects in infants whose mother had a Rubella infection in early pregnancy. Rubella was first reported as a cause of congenital deafness by Carruthers in Australia in 1945 and since then been amply confirmed.

11.2.1.1. **Characteristics**

1. Cardiac defects characterized by an atrial and/or ventricular septal defect or patent ductus arteriosus in 50% of cases.
2. Mental retardation with gross brain injury in 40% of cases.
3. Visual defects including cataracts and/or retinal degeneration in 30% of cases.
4. Microcephaly.
5. Bony abnormalities
6. Neonatal hepatp splenomegaly and thrombocytopenia.

11.2.1.2 **Auditory system**:

No external ear abnormalities were reported. Middle_ ear: Congenital fixation of stapes, otitis media with effusion was reported by many authors (Richards, 1962).

Inner ear: Significant changes in the ear were reported by Carruthers (1945), Gray (1959), Lindsay (1973),

Bordley et al; (1969), Friedman and Wright (1966), and Ward et al; (1968). The pathologic features were similar to so called congenital sacculo-cochlear degeneration of scheibe.

Hearing: Hearing loss occurs in more than 50% of the affected individuals (Rendle-Short 1964; Firiedman and Wright, 1966). Hearing loss was most frequent in children whose infection occurred during the first trimester, among whom 68% are deaf. Infection in second trimester causes deafness in 40% of cases (Bordley and Hardy, 1969).

The deafness in most of the cases is sensori-neural, in about ¼ of the cases there was conductive element due to otitis media or stapes fixation.

Hearing loss was moderately severe to profound more marked in higher frequencies. Hearing loss may be unilateral or bilateral. Audiograms were described as having characteristic asymetrical loss between two ears with a flat audiometric pattern (Bar and Lund-strom, 1961).

11.2.1.3 **Treatment and prognosis**

Prevention is better than cure. Passive immu-nization of the threatened mother immediately after

exposure to infection or termination of pregnancy may be considered. Handicap of deafness can be overcome by early diagnosis and skilled speech and auditory training.

Prognosis is variable. At one end of the broad spectrum as amany as 15% of the first trimester infections may end in spontaneous abortions. At the other end, many inputs have only defects not readily detected in the new born period. Later the acquisition of Rubella during pregnancy, slighter the risk of the child becoming severely handicapped.

11.2.2 **Congenital cytomegalovirus (CMV)**

Only during the past 20 years intrauterine infections due to CMV have been recognized. Cytomegalovirus is the commonest known microbiological cause of brain damage in infancy (Stern et al, 1969). CMV infection is especially common during pregnancy and becomes progressively more common from trimester to trimester (Reynolds et al, 1973).

11.2.2.1 **Characteristics**

1. Microcephaly
2. Hydrocephaly
3. Spasticity
a. Mental retardation
5. Chorioretlnitis
6. Jaundice
7. Petechiae
8. Enlargement of liver and spleen.

11.2.2.2 **Auditory system.**

No external or middle ear abnormalities were reported.

Inner ear: The temporal bone findings are those of an endolymphatic labyrinthitis secondary to Viremia via tie stria vascularis, Inclusion of bearing cells are seen in the superficial lining cells of the stria, Reissner's membrane, the limbus spiralis, Saccule, utricle and semicircular canals. Increased labyrinthine fluid and hydrops has been reported in the cochlear utricle and Saccule.

Hearing: Hearing impairment has been reported in 50% of 13 children, ages 21 to 77 months, with subclinical congenital infection (Dahle et al, 1974). The hearing loss ranged from a slight high frequency impairment to a profound unilateral loss. Dahle et al,(1974; 1979) noted that both the incidence and severity of hearing impairment increased with age.

Vestibular system: No studies were reported.

. 11.2.2.3 **Treatment andprognosis**

Treatment is symptomatic.
Prognosis depends on the severity of the disease.

11.2.3 **Congenital Syphilis**

Syphilis is caused by Trepanomapallidum and may be acquired sexually or non sexually or as a congenital infection via the placenta. Deafness may occur in both congenital and acquired forms.

11.2.3.1 **Characteristics**

Congenital syphilis: The course of infection resembles that of secondary and late stages of acquired syphilis except that lesions develop more quickly in patients with congenital infection. This occurs in two clinical forms Early and late forms. Early form is associated with menigoneuritis of 8th cranial nerve, meningoneurolaby-rinthitis or otolabyrinthis or meningo neurolabyrinthitis, skin lesions, saddle nose deformity, mental deficiency, seizures, painful pseudoparalysis. In late form, the onset is between 8th and 20th year. It is characterized by triad of "Hutchinson" - i.e. labyrinthitis,intersti-tial keratitis and notched teeth.

Acquired syphilis: It occurs in 3 stages, namely primary secondary and tertiary stage.

Primary stage: is characterized by painless undurated ulcerating swellings on the lips, mouth, anus, genitals and fingers.

Secondary stage: It is characterized by malaise, head ache, Sore throat, irregular fever, cutaneous rashes, mucous patches, lymphadenopathy, meningitis and cranial nerve palsies.

Tertiary stage: It is characterized by gumma formation. Lesions may occur almost anywhere.

11.2.2.2 Auditory system

External ear: In syphilis of the external ear, a primary lesion is extremely rare. However secondary lesions of all types are more frequent. In tertiary syphilis there may be gummatous involvement of the canal wall with occa-
" sional necrosis of the bone. Cholesteatoma may also arise from the proliferation of the squamous epithelium during hearing process.

Middle ear: Syphilis of middle ear may be found in two froms. It may be sequelae to a secondary syphilitic lesion or a tertiary lesion (gumma) located in the naso-pharynx or at the orifice of the eustachian tube. Infla-mmation surrounds the lesion and ascends into the middle ear, producing an otitis media. Mastoiditis has been documented in such cases. Sometimes there is ankylosis of ossicles.

Inner ear: Productive periostitis, atrophy of organ of corti with round cell infiltration in the cochlea, mainly in the vascular stria, spiral ligament and 8th ner^e, vascular changes of obliterative character, extensive destruction of bony capsule of the labyrinth and semicircular canal has been reported by many authors (Fraser 1938, Goodhill 1939, Mayer 1985).

Hearing: There is a great evidence of abrupt bilateral sensorineural deafness (Weatherhill et al, 1965; Perlman, 1967). There is no specific type of hearing loss associated with syphilis (Bunch 1931, Ciocco 1937, Goodhill 1939).

It may be conductive or sensorineural or mixed in nature. Hearing loss usually begins suddenly in one ear and soon involves the other ear also. The progress of deafness may be extremely rapid or quite gradual, but the ultimate outcome of untreated will be a severe or total sensorineural deafness.

Sometimes cochleo vestibular dysfunction may occur as the only manifestation of late syphilis (Becker 1979).

Vestibular system: Abnormal vestibular findings have been reported by some authors.

11.2.3.3 **Treatment and Prognosis**

With early adequate medical treatment the hazardous effects of the disease can he overcome.

The disease is progressive. In syphilis of the inner ear, the hearing loss usually persists, while tinnitus and vertigo tend to disappear after complete destruction of the labyrinth.

11.2.4 **Toxoplasmosis**

Toxoplasmosis is being recognized increasingly as a common infection In man. Studies have shown the responsible organism is "toxoplasma gonadii" an protc-zoan parasite. This infection may be acquired by adults as well as children, but it is the congenital infection , that is handicapping.

About 33% of adults in England are affected. In pregnant women, an estimate of the incidence based on prospective serological studies is 4-6 per 1000.

11.2.4.1 **Clinical features**:

The most familiar form of congenital toxo-plasmosis present at birth is a generalized disease. The symptoms include jaundice, hepatosplenomegaly, anemia, skin rashes, pneumonitis, encephalitis, mental retardation and epilepsy, cerebral palsy and blindness in 80-90 percent, hydrocephaly or microcephaly in 20%.

In the adult, the parasite causes continuous pyrenia which may be associated with pulmonary lesions

or more commonly lymphaderitis. Calcification of the lesions is common and calcified foci may be recognized radiologically.

11.2.4.2 **Auditory system**

No external ear abnormalities were reported.
Inner ear: Sections of the temporal bones in one ear of a patient exhibited signs of otitis media, presence of calcareous deposits in the vasaular stria and spiral ligaments of the cochlea, while in the other patient, no abnormalities were seen. (Kelemen 1958).

Wright (1968) inoculated T. Gondii into the bulla of guinea pigs and concluded that it may cause acute inflammation but no cochlear lesion.

Deafness: The role of toxoplasmosis as a cause of deafness has attracted considerable attention. Ristow (1966) and Wright (1971) believe that toxoplasmosis does not represent a significant cause of congenital or infantile deafness.

11.2.4.3 **Treatment and prognosis**

Symptomatic treatment.
Prognosis depends on the severity of the disease and general condition.

11.3 **Deafness acquired during perinatal life**

Kernicterus and prematurity are by far the most important and common types of deafness acquired during birth.

Kernicterus: is a complication of haemolytic disease of the new born characterized by an increase in bilirnbin secondary to blood incompatability. This occurs most often in children whose patients have differing types of RH factors. The overall incidence of Kernicterus is about 1 per 200 births.

11.3.1.1 **Characteristics**

This condition was orignially described by gross anatomical findings - namely the icteric staining of certain 'Nuclei of the brain with microscopic evidence of necrosis of ganglion cells in the stained area. Most infants sustain brain damage which may be evidenced by; (l) Language disorders, (2) Cerebral palsy, (3) distractibility, (4) hyperactivity, (5) inconsistent behaviour, emotional lability, 6) temporal rigidity, (7) Lack of inhibition and/or corapulsiveness, (8) Retarded motor development, (9) mental deficiency, Neonatal jaundice is the characteristic feature.

11.3.1.2 **Auditory system**

No external or middle ear abnormalities were reported.

Inner ear and auditory pathway: Keleman (1956) has presented the only histological observation of the inner ear suggesting a inner lesion characterized by displacement of cochlear and vestibular sacs. Wolf( ) found some cytoplasmic changes in the spiral ganglion. The lack of valid documentation of inner ear lesions has led to the consideration of the central nervous system to be the site of lesion. Crabtree and Gerrard (1950) found kernecteric lesion occurring in the dorsal and ventral cochlear nuclei.

Carhart (1967) suggested that hearing loss in kernicterus was due to lesions within the cochlear nuclei which is characterized by generalized depopulation of neurones. These lesions disrupt the analysis of tonotopic (place) information more radically than they do analysis of time locked (volley) information.

Hearing: A high incidence of hearing impairment, usually of sensorineural type has been reported among affected individual. Marcus (1970) reported that about 10% of severe hearing loss is related to neonatal janndice, but Shimizu (1976) noted only a 1.5% Incidence. Hearing impairment was found in 4.2% of affected individuals (Hymen et al, 1969).

The hearing loss that results from kernicterus tend to fit a characteristic audiometric pattern (matkin's 1965). The audiometric configuration clearly shows a frequency dependent impairment. Most typically there is a plateau of mild loss (30 d3) from 250 Cps downward, a plateau of substantial loss (70 dB) from 2000 Cps upward and a fairly smooth transition between these plateaus, usually however the increase in loss is most abrupt in 250 - 1000 Cps and averages about 23.5dB. However variations in the pattern have been reported by many authors.

The measurement of cochlear microphonics and neural responses from auditory nerve in thirteen patients suggested that the hearing loss is due to auditory nerve damage while the hair cells are spared (Chisin, Perlman and Sohmer, 1979).

Vestibular system: No studies were reported.

11.3.1.3 **Treatment and prognosis.**

Current methods of early detection and medical management have greatly reduced the proportion of kernicterus due to Rh imcompatibility. Marriage counselling and blood examination of every pregnant mother is essential.

Prognosis is variable depending on the severity of the various aspects of the problem.

11.3.2. **Prematurity**

Another common cause of acquired congenital deafness is prematurity. Many children born prematurely have mental retardation, cerebral palsy and significant hearing loss.

Deafness: Davies and Stewart (1975) in a study of low birth weight of pre-term birth children found the hearing loss to be significant. Lindsay (1973) reported the incidence of deafness to be higher among premature babies than full term births.

Pathology: The pathology underlying this deafness is not known. The temporal bone studies of infants who died from asphyxia neonatorum by (Hall 1964) revealed normal ears with loss of central nervous system components of the auditory pathways. The loss of cells in the central nervous system was correlated directly with the length of time the child was affected by asphyxia neonatorum. Thus it was concluded that the deafness associated with prematurity may be central.

Buch studied(3uch, 1963)the temporal bones of 73 new born infants and suggested that traumatic procedures experienced during birth played an important role in the etiology of inner ear haemorrhage.

Another type of deafness associated with prematurity is that which is acquired through drugs used to treat infections

in the premature infant. Usually Kanamycin and neomycin are used which are ototoxic and destroy the hair cells in the membranous portion within the cochlea resulting in sensorineural deafness. Thus a premature child may also have been subjected to ototoxic drug (Elchenward, 1966).

11.4 **Deafness acquired in later life**

Deafness can be acquired later in life due to a variety of factors namely vascular diseases, neurological diseases, viral infection, endocrinal disturbances etc. 3ut in most of the conditions, the exact cause is not known. The most important type of deafness under this category is Meniere's syndrome. The other types Include RamSay Hunt Syndrome due to Herpes Zoster affecting the geniculate ganglion, Oogan's syndrome affecting the eye and the ear, Costens syndrome due to disturbed temporo mandibular joint function and Vogt Koyanagi Haroda syndrome.

In majority of cases, the onset of hearing loss is sudden and it is progressive. Very little information is available regarding the audiometric findings in most of the cases. Barlier the detection of the disorder and initiation of treatment, better are the chances of either preserving or improving the existing hearing.

11.4.1 **Meniere's syndrome**

This syndrome derives its name from the Paris physician prosper Meniere who first described it. Meniere(1861)

drew attention to the inner ear as the seat of a syndrome characterized by proxymal attacks of vertigo associated with unilateral deafness and tinnitus. On post mortem evidence he believed the symptoms to be due to haemorrhage into the labyrinth. Hallpike and Cairns (1938) demonstrated endolymphatic hydrops and proposed that the syndrome be known as Meniere's disease.

It occurs at any age but 65% of patients have their first attack of vertigo before the a?e of 50 years. The youngest recorded case was 4 year old. There is slight preponderance of incidence in males over females.

11.4.1.1 **Aetiology**

There is no one primary cause of Meniere's syndrome. It is accepted that endolymphatic hydrops is the most significant change in the inner ear, but the problem of the causation of thehydrops remains undetermined. Various theories have been put forward to explain the etiology. Wright believes the condition to be due to bacterial intoxi-cation of the labyrinth and describes it as focal labyrin-thitis.

Crowe ascribes the condition to a disorder of the normal conditions of pressure and chemical constitution of the endolymph.

Atkinson (1946) suggested that the primary cause lay in increased permability of the cappilaris forming the

stria vascularis resulting from infection, allergy, avitaminosis, histaminic sensitivity or nutritional damage following vasospasm.

Lempert et al (1952) postulated that rupture of the subepithelial vesicles liberated toxic fluid into the endolymph and that the symptoms of Meniere's disease could be explained as a result of contamination of the endolymph by this vesicular fluid.

The theory first discussed by Lermoyez (1919) that the underlying aetiology to be due to paroxymal vasomotor imbalance was fully supported and elaborated by Seymour(1960). He believed that paroxymal autonomic imbalance resulted in spasm of the internal auditory artery and/or its branches of distribution and this resulted not only in impairment of sensory function of the sensory epithelium of the cochlea and vestibular end organs, but interfered with secretion of endolymph. Autosomal dominant or recessive transmission of the disease has been suggested by Brown, 1949 and Bernstern, 1965.

11.4.1.2 **Pathology**

Temporal bone of two affected persons showed a gross distention of endolymph system together with degenerative changes in the sensory elements (Hallpike and Cairns,

1938).

Histologically, the major change commonly encountered is the gross dialation of the scala media and saccule. Reissner's membrane bulges into the scala vestibuli and may eventually rupture allowing the perilymph to mingle with endolymph. After rupture the pressures are equalized and the membrane may proceed to repair itself (Lawrence and Mc Cabe, 1959).

11.4.1.3 **Clinical features**

Meniere's disease is characterized by attacks of vertigo associated with deafness, tinnitus and vomiting. The attacks may occur at any time with or without warning. Sometimes, the attacks occur singly with an interval possibly of months or years, or there may be a series of attacks occuring over a period of weeks or months which is followed by a long period of complete freedom. Between the attacks, there may be feelings of insecurity and vague anxiety. The head or affected ears feel full. Hearing is reduced and distorted. Dizziness may result from changes of position of head. Tinnitus is loud and persistant. As an active phase gives place to a quiescent phase the feeling of pressure disappears, hearing improves, tinnitus diminishes.

In 50% of cases the onset of vestibular and cochlear symptoms occur together. In 25% vertigo precedes deafness.

Vertigo: Vertigo is typically rotational in type. The patient is suddenly seized with a sensation of severe imbalance either with himself or the surroundings. At the time, the chief desire is to lie prostrate and still, after a variable period of usually few hours to few days, the patient staggers to his feet and begins to resume activity with support.*

Vestibular test usually reveals a reduced response to caloric stimulation.

Tinnitus: Tinnitus is present in 80 percent of cases, usually as a constant background noise with a rumbling or hissing quality. It varies in intensity and tends to increase and change in character before an attack. Tinnitus may be especially distressing after the vertigo wears off.

Deafness: Deafness is present in 90% of cases and is typically sensorineural in nature. It begins by being unilateral. In early stages recovery in hearing loss is seen. At the later stages hearing loss is permanent.

Puretone audiometry typically reveals in early cases, a greater loss of hearing to low tones as compared to hightones. As the disease progresses, hearing loss becomes more equally distributed.

Patients usually obtain high SISI scores, tone decay -ve, Bekesy type II and IV tracings, reduced speech discrimination score, Weber test lateralizing to the better ear, suggestive of cochlear lesion.

In severe cases, there may be additional vagal symptoms of abdominal pain, brady chardia, Pallor, Sweating, headache, nausea, vomitting, diarrhea.

11.4.1.4 **Treatment and prognosis**:

The continuing absence of knowledge of exact causation, unpredictable onset and periods of remissions and encerbations make it Impossible to determine for certain whether the apparent benefit is attributable to the treatment or to a coincidental natural remission. Nevertheless the management may be guided by some well tried and accepted principles and treatment may be given by which the majority of patients can be helped significantly. Treatment may be medical or surgical.

Medical treatment:consists of treatment of Frustenburg, antivitamins, antibiotics, vasodialators, multivitamins, sedatives, streptomycin are found to be effective.

Surgical treatment: may be conservative and radical conservative surgical treatment attempts to modify labyrinthine behaviour without adversely affecting the hearing

loss. It follows 3 main direction, stellate ganglion block (Passe and Seymour, 1948), Labyrinth decompression (Portmann 1927), Cervical symphathectomy and selective destruction of vestibular end organs by ultra sonic beam (Arslan, 1953), Electro-Cogulation of lateral semicircular canal (Day, 1961).

Radical surgical treatment includes total destruction of labyrinth by injecting alcohol (Mollison, 1931) and membranous labyrinthectomy (Cowthorne, 1943), which has yielded excellent results.

In the early stages, the disease is reversible with adequate treatment as the disease progresses, the condition becomes irreversible.

11.4.2. **Lermoyez syndrome**

Marcel Lermoyez (1919), a French otologist first described the syndrome that bears his name in a patient who had symptoms resembling Meniere's disease but occurring in the reverse order. Lermoyez wrote the patients condition as "Le vertigo qui fait endendre", the syndrome consisting of progressive deafness apparently relieved by a sudden attack of vertigo. Lermoyez however did not regard the vertigo as the cause of

improvement in hearing, but only the witness to it.

The incidence of the Lermoyez syndrome is rare. Few cases have been described since the original. Bailie (1965) described 5 cases, Williams (1952) found only 3 cases in 500 cases diagnosed as Meniere's disease. Lermoyez syndrome is very closely linked with Neniere's disease and is possibly only a variant of it.

Kitamura (1976) noted that the difference between the two is that duration of the pre-existing cochlear symptoms of Lermoyez syndrome is relatively longer and it improve simultaneously at the beginning of the vertiginous spell in contrast to the gradual improvement of symptoms during vertiginous spell in Meniere's syndrome, Boenninghans et al (1967) reported that the symptoms in both diseases differ in the time relationship between the hearing and the equilibrium disturbances. In Lermoyez syndrome the disturbance is of the regulation of endolymph in the ductus cochlearis as opposed to an increase in the volums leading to the rupture of the system in Meniere's syndrome.

11.4.2.1. **Aetiology and Pathology**:

Atkinson (1946) considered that his histamine sensitive group represented the Lermoyez type, but 8aile (1956) found that it was not marked.

Lermoyez (1919) believed it to be due to intermittant vasospasm secondary to autonomic imbalance.

The symptoms result from the obstruction of the labyrinthine ducts which may be due to (1) deposits of salt or of normal mucopolysaccharide of the endolymph. (2) formation of solid substances in suspension in the endolymph and (3) ductal torsions of compressions(Ried,1973).

11.4.2.2. **Clinical features**

At the onset the patient complains of numbness, blockage or muffling of the ear, then definite increasing deafness usually with tinnitus. Suddenly an attack of vertigo with or without vomiting occurs and in a few hours the hearing recovers. Recovery may be partial or complete. The course of the condition resembles Menlere's disease in that periods of repeated attacks may be followed by periods of remissions. Vertigo is usually rotatory.

Hearing loss is of cochlear type. Recruitment is generally present during the deaf spells, speech discrimination is poor. Caloric tests reveal some abnormality in most cases.

11.4.2.3. **Treatment and prognosis**

The few reports indicate that in some cases, the attacks of vertigo tend to die out leaving some legacy

of deafness and that in others symptoms may be ameliorated by medical treatment.

On the supposition that Lermoyez syndrome is a variant of Meniere's syndrome, the roedical treatments described there may be considered for trial. Stellate ganglion block has proved beneficial in some cases, but most favourable line of treatment appears to be nicotinic acid in sufficient doses combined with an antihistamine such as promethazine hydrochloride (3ailie, 1956).

11.4.3 **Ram Say Hunt Syndrome**

(Herpes Zoster Otieus, Herpetic geniculate ganglio-nitis aural shingles).

Ramsay Hunt syndrome is a rare but a known clinical entity since 1870. The credit for bringing together the manifestations of geniculate ganglion herpes into a single entity belonged to the New York neurologist, J. Ram Say Hunt (1967). It is characterized by Otalgia, vesicular eruptions on pinna and external auditory canal with or without lower motar neurone seventh cranial nerve palsy and cochleovestibular disturbances.

11.4.3.1. **Aetiology and Pathology**

This syndrome probably develops from a viral meningitis with a predilection of Herpes Zoster virus for sensory ganglia and nerve roots. Some authors note the possibility of a I

viral infection which lies dormant for many years and is then reactivated by poorly understood circumstances to create the clinical syndrome (Hope-Simpson, 1965).

Although histologic material is rare, there is some evidence of inflammation in the ganglia and degeneration of the sensory nerve fibers (B1ackley et al, 1967).

11.4.3.2 **Clinical features**:

Hunt divided the syndrome into three clinical groups.

1. Herper auricularis
2. Herper auricularis with facial palsy.
3. Herper auricularis with facial palsy and auditory symptoms.

Herper auricularis: The onset is typically heralded by an uncomfortable, hot stiff feeling in the ear, soon becoming a dull ache punctuated by sharp pain. The preherpetic pain may be very intense and interfere with sleep and at this stage, the auricle, meatus or tympanic membrane may present a red swollen, erysiptlaid appearance until on the third, fourth or even as late as the 7th day, clusters of herpetic vesicles make their appearance. Malaise, Pyrexia and Swelling of lymphatic glands is usual at first, but in simple herper auricularis all tend to subside once the vesicles appear. The vesicles may appear on the concha,

the lobule, the tragus, helix and antihelix, within the auditory meatus or less commonly upon the tympanic membrane. In a few days the vesicles dessicate, the swelling and edema of the parts subside until at the end of a fortnight only a few small healed blemishes remain. Disturbances of sensation may persist much longer in the form of burning pains, itching and in the elderly sharp lancinating post herpetic neuralgia. Conductive hearing loss of mild to moderate degree is observed.

Herpes auricularis with facial palsy: To the herpes auricularis as described above is added a complete peripheral facial palsy on the same side as the vesicular eruption. In majority of cases the facial palsy appears on the 2nd or 3rd day, but may be delayed a week or longer.

Herpes auricularis with facial palsy and auditory symptoms:

This is the most severe clinical type with the extension of the inflammatory process to the adjacent 8th cranial nerve and its acoustic and vestibular ganglion. Occasionally there is menigial irritation in the form of fever, headache etc. The symptoms reflect disturbances of both hearing and balance. Tinnitus, deafness, displacusis, vertigo, nausea, vomiting and nystagmus may all be seen together with manifestations of type 1 and 2 (Morey, 1946).

Hearing loss is typically sensorineural which may he unilateral or bilateral.

The vertigo appears with deafness and slowly disappears. Tinnitus occurs in later stage, it may be low pitched or high pitched and disappears slowly.

Nystagmus may accompany a vertigo and produce a directional preponderance on caloric tests.

11.4.3.3. **Treatment and prognosis**

As it is caused by varicella, no effective prophylaxis is possible nor there is any definite curative measures.

Treatment is essentially symptomatic and subsequent. Physiotherapy or in severe case decompression of facial nerve or plastic surgery for facial palsy may be considered.

Prognosis is variable depending on the severity of the disorder. Although in severe cases the vestibular symptoms generally disappear completely, deafness and tinnitus can persist permanently.

11.4.4 **Cogan's syndrome**:

It is a rare affilication, affecting simultaneously the eye and the ear. David G. Cogan, an Opthalmologist described this condition in 4 patients in 1945. It consisted of non specific interstial keratitis, either

unilateral or bilateral accompanied or followed by rapidly progressive disturbances in vestibular and auditory functions. It tends to take a chronic course with multiple unpredictable recurrences. More than 40 cases have been reported in the literature since then.

Cogan's syndrome appears to be found primarily in young adults of either sex usually in the 2nd or 3rd decades of life, although it has been seen as early as 5 years of age and as late as 60 years.

11.4.4.1 **Aetiology**:

Aetiology is unknown. It is thought to represent a manifestation of a systemic disease most likely collagen. It could be a variant of periarteritus nodosa (Oliver 1953, Stevens 1955, Crawford 1957). It is found to follow a recent viral infection or vaccination. Antigen antibody reaction has also been postulated as the underlying mechanism of origin.

11.4.4.2 **Pathology**:

Autopsy findings of the temporal bone revealed changes confined to the inner ear and to a lesser extent the 8th cranial nerve. Spiral ligament revealed inflammatory

changes, degeneration of the organ of corti, spiral and vestibular ganglia, displacement of Reissner's membrane, edema of the cochlea and semicircular canals, demyelination of the 8th cranial nerve (Fisher and Hellstrom 1961).

Wolff et al (1965) found new bone formation which was discernible on temporal bone sections. Reissner's membrane was distended and a saccular rupture suggested labyrinthine hydrops. The spiral ganglion of the basal coil was atrophic.

11.4.4..3 **Clinical features**:

Symptoms consist of redness and burning of eyes, lacrimination, blurred vision and biepharospasm associated with tinnitus, vertigo, nausea, vomitting and diminished hearing which appear within a few weeks of each other.

Deafness :Rapidly progressive sensoriaeural hearing loss sudden onset occurs which becomes severe and permanent preceded by excerbations and remissions.

McNeill etal, (1952) described a patient who had lost all hearing except for lowest frequencies.

Smiths (1970) 62 year old patient failed to respond to any audiometric signal, but some sound awareness was present to loud sounds.

Mizuno and Komal Suzaki (1979) reported a 18 year old girl demonstrating bilateral sensorineural deafness.

Symptoms of vomitting and vertigo usually disappear as hearing loss occurs.

Caloric tests usually reveal absent or greatly diminished labyrinthine responses (Smith 1970, Mizuno and Komal Suzaki 1979).

11.4.4.4. **Treatment and prognosis**

No effective treatment is available. Becaase of the rapid development of symptoms, it is reasonable to assume that permanent degenerative changes occur early in the course of disease. Sven a few days delay account for permanent degenerative changes of eye and ear.

Therefore, the onset should be considered as a medical emergency, large doses of steroids if started immediately may produce some beneficial effects on hearing and eyes (Smith, 1970).

Beckwan and Trotsky (1970) found a dramatic gain in hearing on two occassions following oral administration of glycerin 1.5 gm/kg.

11.4.5 **Coaten's Syndrome**

In 1934, James Costen, an American Otolaryngologist from St.Louis first presented his syndrome of ear and

sinus symptoms dependent upon disturbed function of temporomandibular joint.

11.4.5.1 **Aetiology**:

Costen over the next 20 years expanded his views and pointed that the symptoms were due to one or more of the following:

1. Mandibular over closure with distal condylar displacement and compression of the eustachian tyt.be
2. Erosion of the roof of the glenoid fossa and tympanic plate.
3. Medial pressure on the condyle on chordatympani nerve.

But Brooks et al (1980) criticized this view and concluded that there is no direct aetiological basis to link temporomandibular joint dysfunction and other aural symptoms apart from otalgia.

11.4.5.3. **Clinical features**:

Symptoms consist of pain within and around the ears, neuralgia of the second or third divisions of trigeminal nerve, headaches, sinus pains, defective bite, stuffy sensation in the ears, impaired hearing, continuous or intermittent tinnitus, dizziness, pressure or ear blockage and occlusal disequilibrium.

Deafness: A slight conductive hearing loss of closed type, especially during chewing was noted in the affected patients. Hearing loss is greater on the affected side. In some cases, mild freauency loss was present (Borgo et al 1964).

Mild tinnitus occurs in the ear homolateral with the affected joint.

Vertigo of brief duration occurred among all patients.

Caloric tests revealed only mildly altered reflexes in few patients (3orgo et al 1964).

11.4.5.3 **Treatment and prognosis**:

Most of the pains were cured by dental treatment (Hankey 1962). Correction of the bite brings relief. In minority of patients who do not respond to dental treatment, empirical maniscectomy has given excellent results as far as relief of pain is concerned.

11.4.6 **Vogt Koyanagi Haradas syndrome (VKH syndrome)**

The VKH syndrome is a relatively rare multisystem disease. Through the years, the term dysacousia has been used with this syndrome, when there was associated auditory problems.

Vogt in 1906, is given credit for the first description of this condition. In 1929, Koyanagi reviewed the literature which composed of 16 cases, 4 of his own. In 1926, Harada described 5 instances of this syndrome with bilateral posterior uveitis with retinal detachment.

Koyanagi and Harda disease have been incorporated into VKH syndrome.

There is a wide spread geographic distribution with greatest number of cases being observed in Japan. It occurs more prevalently in 3rd decade of life. There is no predominance to sex. Social conditions do not seem to be a factor.

11.4.6.1 **Aetiology**:

Specific etiology is unknown. Endocrine allergy and viral causes have been most frequently incriminated.

11.4.6.2 **Clinical features**:

Symptoms consist of head ache, fever, bilateral anterior uvertis, dysacousia, hearing loss, tinnitus, vertigo, balance disturbances, retinal detachment, whitening of eyelashes, patchy alopecia of the vertex, vitiligo of face, neck and shoulders and poliosis.

Cowper preferred to classify the syndrome into 3 stages 1. Meninglal (2) Opthalmic and (3) Covalescent stage.

Meningial stage consists of signs and symptoms ranging from headache to paresis.
Following this is the opthalmic stage daring which uveitis vestibular and hearing problems occur.
Dysacousia, the least common of the syndrome is reported in 54% of Rosen's study and 50% of callaquillo's study.

Deafness: Hearing loss is bilateral sensorineural type and of acute onset occurring on simultaneously with or soon after the appearance of bilateral uveitis. The degree of hearing loss depends on the site and amount of damage in the cochlea. Hearing loss may be temporary or may persist permanently.

Of the 3 patients tested by Seals and Rise (1967), one had no testable hearing, 2nd had completely normal hearing, 3rd patient responded only at 50-80 dB. SISI was 100%,tone decay was -ve, Bekesy type II and IV tracings were obtaining suggesting cochlear involvement.

Caloric responses were absent or diminished.

11.4.6.3 **Treatment**

No effective treatment is available. Treatment is symptomatic and supportive.

11.4.7 **Fanconi Anaemia Syndrome** :

Fanconi Anemia syndrome is a rare, recently described syndrome consisting of multiple congenital anomalies and aplastic anemia. Skin pigmentation, skeletal deformities, renal anomalies and mental retardation are common. Typically, the anemia begins in early childhood and death occurs within 2 years aften due to acute leukemia.

The etiology is not exactly known.

11.4.7.1. **Auditory system**

Deafness or ear abnormalities or both were found in 12 of 111 cases reported by Ssparza et al (1966).

McDonough (1970) reported a rare case of Fanconi Anemia occurring in an adult with congenital middle ear disease.

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