1980

Bacterial meningitis in children

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BACTERIAL MENINGITIS IN CHILDREN

By

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B.A., University of Montana, 1978

Presented in partial fulfillment of the requirements for the degree of

Master of Communication Sciences and Disorders

UNIVERSITY OF MONTANA

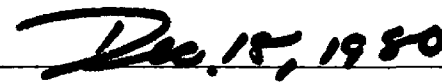1980

Approved by:

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Dean, Graduate School

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Date

UMI Number: EP38102

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UMI EP38102

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1-14-81

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Chapter 1

OVERVIEW

Introduction

During my externship at the Denver Children's Hospital, I was exposed to a great deal of information about childhood diseases and injuries and their possible long-range effects on hearing, speech and language development, and learning. In my estimation one of the most interesting of these childhood diseases, one with possibly profound and long reaching sequelae, is bacterial meningitis.

This paper reviews the topic of bacterial meningitis with respect to incidence, etiology, long-term sequelae with special emphasis placed on hearing, and treatment. It also presents some of the more interesting children encountered during my externship who were victims of bacterial meningitis.

Incidence

Bacterial meningitis has been recognized since 1887, when bacterial organisms were first isolated from cerebrospinal fluid, as a serious, often fatal disease. Cerebrospinal fever was described by Vieusseaux in 1805, but it was not until 82 years later that the bacterial etiology was established.

Early estimates of the incidence of bacterial meningitis are

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difficult to find; however, in 1926 Neal, et al.[24] reported 654 cases in New York during a 15 year period from 1909 to 1925. This figure indicates an annual incidence of approximately 3.5 cases/100,000/year. Carpenter and Petersdorf[4] found an incidence of five cases/100,000/year in a five year survey of bacterial meningitis in King County, Washington. In 1976 Feigin and Dodge[6] noted that, "rather than diminishing in incidence, bacterial meningitis has increased in frequency during the past several decades." Current estimates of incidence lie between six to seven cases/100,000/year. In children under five the annual attack rate is estimated to be one case in 2,000/year.

Smith[35] noted that admission to the Pittsburgh Children's Hospital due to *Hemophilus influenza* increased 400 percent from 1950 to 1975 while total hospital admissions increased 50 percent. Reasons for this increase are unclear. It is possible that early in the century the actual number of cases was much higher and that few were reported. It is also possible that many died before reaching a hospital or that meningitis of bacterial origin was not diagnosed in many cases. That more virulent strains of the bacteria, which commonly cause meningitis, have developed over the last few decades is another interesting possibility. It is also possible that natural immunity to infection has been altered due to the increased use of antibiotics in minor diseases such as respiratory infection.

Distribution of Cases According to Age and Sex

Table 1 shows the distribution of cases of bacterial meningitis according to sex in four studies plus in a review of 58 cases of

Table 1

Distribution of Meningitis by Sex in Five Studies

Sex	Study				
	Neal, et al.[24] 1926	Sproles, et al.[36] 1969	Lindberg, et al.[19] 1977	Keane, et al.[14] 1979	Denver Children's Hospital 1979-1980
Male	376	22	51	59	30
Female	278	18	31	41	28
TOTAL	654	40	82	100	58
Ratio m/f	1.35/1	1.2/1	1.64/1	1.44/1	1.09/1

bacterial meningitis at the Denver Children's Hospital from July 1979 to June 1980. All studies reviewed showed a male to female predilection of approximately 1.1/1 to 1.7/1. Mandell, et al.[20] found that nearly 60 percent of all children who present with invasive diseases caused by *H. influenza*, a common meningitic pathogen, are males. As is true of many other disease entities, the males of the human species appear to be more susceptible than females.

Keane, et al.[14] proposed an interesting possible explanation for the increased incidence of bacterial meningitis in boys. They suggested that there is a locus on the X chromosome for synthesis of immunoglobulins, proteins capable of acting as antibodies against invading microorganisms. Females, by virtue of the heterozygosity of this locus (double X chromosome) may be more adaptable immunologically and, therefore, they are better equipped to fight off disease.

Not only is there a difference in the distribution of cases according to sex, there is a definite difference in distribution among age groups. Table 2 summarizes the findings of four studies regarding the prevalence of bacterial meningitis in various age categories. Figure 1 compares age distribution of meningitis between an early study in 1900 and a review of recent records at the Denver Children's Hospital.

These data illustrate that young children primarily in the first two years of life are more susceptible to bacterial meningitis. This seems logical because young children do not possess mature immunological systems and, therefore, they are more likely targets for bacterial invasion than are older children and adults.

Table 2

Prevalence of Meningitis by Various Age Categories

Study	Findings
Carpenter and Petersdorf[4] 1962	209 total cases. *Hemophilus influenza* most common in children 5 years old. *Neisseria meningitidis* seen in children and adults; rare in those > 50. *Diplococcus pneumoniae* rarely seen in patients between 2 and 30 years of age.
Feigin and Dodge[6] 1976	Risk for children developing bacterial meningitis by age 5 is between 1 and 400 and 1 in 2,000.
Keane, et al.[14] 1979	100 cases: 50 developed meningitis in the first year of life; almost 80% of the cases were between 3 months and 3 years of age.
Mandell, et al.[20] 1979	35-50 cases/100,000/year *H. influenza* meningitis in children < 5 years: 40% *H. influenza* meningitis in children 3-24 months and 46.9% meningococcal meningitis in children < 4 years.

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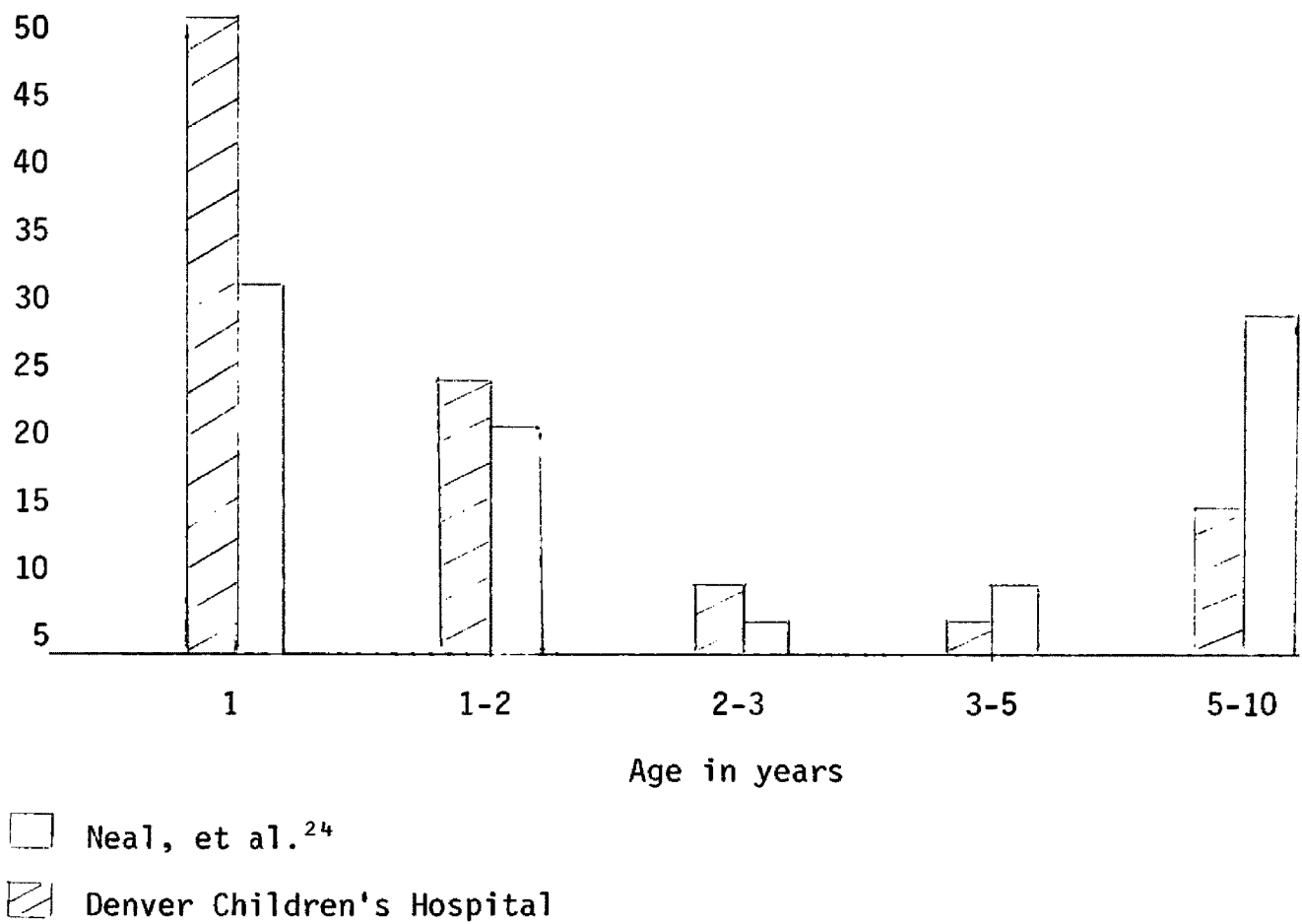
Figure 1

Percent of Total Cases

Pathogens

Meningitis is defined as an inflammation of the meninges, the three membranes that cover the brain and spinal cord: the dura mater, the pia mater, and the arachnoid. Bacterial meningitis means that this inflammation is the result of invasion by bacteria.

Most bacterial meningitis is caused by three primary microorganisms: *Hemophilus influenza, Neisseria meningitidis,* and *Diplococcus pneumoniae.* Certain age groups appear to be more susceptible to infection by one pathogen than another. Children under five years of age are more likely to be infected by *H. influenza.* Meningitis in adults is often caused by *N. meningitidis* and pneumococcal meningitis is more prevalent in the very young and the elderly.[4,14] In spite of the preponderance of cases attributed to these three bacteria, many other microorganisms may cause meningitis. For instance, in neonates coliform bacteria (e.g., *Escherichia coli*) are a common causative pathogen as well as Group B streptococcus.[7] The three more common bacterial agents are discussed herein with respect to incidence and pathogenicity.

Table 3 presents the incidence of meningitis caused by various pathogens. The information is from three studies plus a review of cases at the Denver Children's Hospital. The Carpenter and Petersdorf[4] data comprise all ages; the three other studies primarily involve children.

H. influenza is the most common meningitic culprit in young children. Smith[35] reported that 85 percent of the cases of meningitis

Table 3

Bacterial Pathogens

Study	Pathogens				Total
	H. influenza	*N. meningitidis*	*D. pneumoniae*	Other	
Carpenter and Petersdorf[2] 1962	35	53	63	58	209
Sell, et al.[32] 1976	15	5	5	0	25
Keane, et al.[14] 1979	67	9	13	11	100
Denver Children's Hospital 1979-1980	42	8	2	6	58

in children two months to three years of age are caused by *H. influenza*. This bacteria is an exclusive parasite of humans; it requires blood in order to grow, thus the name *Hemophilus*. This small gram negative bacteria may take on many shapes and it may or may not be enclosed by a polysaccharide capsule. The encapsulated strains are designated type b. They appear to be more virulent than nonencapsulated strains. The increased pathogenicity of the type b strains seems to be directly related to the capsule which inhibits destruction by phagocytes, special cells that destroy invading particles (e.g., white blood cells).[20, 35] As many as 90 percent of the strains of *H. influenza* that cause disease in humans are type b.

It is interesting that *H. influenza* can be cultured from the nasopharyngeal area in approximately 80 percent of otherwise healthy adults. Mandell, et al.[20] stated that at least 50 percent of children have one *H. influenza* infection in the first year of life and that "essentially all are infected by age 3." The vast majority of these infections are much less serious than meningitis, which is estimated to occur in 35-50 cases/100,000/year in children less than five years old.

Early symptoms of *H. influenza* meningitis are quite similar across cases. Several medical sources list six common symptoms: moderate and irregular fever, vomiting, loss of appetite, headache, irritability, and lethargy. Later, more serious symptoms include convulsions, delirium, coma, and signs of cardiovascular collapse.

A review of the admission summaries of 20 children admitted to the Denver Children's Hospital with *H. influenza* meningitis yielded the

information in Table 4. This information is compared to a study by Smith.[35]

Certain neurological signs are also common in *H. influenza* meningitis. Reflexes are often heightened, paresis of cranial nerves II, IV, VI, or VII is sometimes seen as is a positive Kernig's sign (contraction of the hamstring muscles upon extension following flexion). Neck stiffness is also seen in most cases.

N. meningitidis was first isolated as a cause of meningitis in 1887. *N. meningitidis* is a gram negative coccus which, like *H. influenza*, produces a polysaccharide capsule. As with *H. influenza*, this bacteria is frequently present in the upper respiratory tracts of healthy individuals. *H. meningitidis* is more likely to cause meningitis in infants and young children (< 4 years old) than in any other age group. In 1975, 1475 cases of meningococcal meningitis were reported to the National Center for Disease Control in Atlanta, Georgia. Of these, 333 (22.5%) occurred in infants under 1 year of age and 358 (24.4%) occurred in children between one and four years old. Meningococcal meningitis is also fairly common in adults, but it is rarely seen in individuals over 50 years of age.

Meningococcal invasion may present in a variety of clinical situations ranging from upper respiratory infection through meningococcemia (a condition wherein the organisms and their toxins are present in the blood) to full-fledged meningitis wherein the organisms are present in the cerebral spinal fluid. Symptoms of meningococcal meningitis are somewhat different than in *H. influenza* meningitis. According to Mandell,[20] low grade fever and vomiting may often be the

Table 4

Symptoms Demonstrated Prior to Admission

| Study | Total cases | Symptoms | | | | |
		Vomiting (%)	Fever (%)	Anorexia (%)	Irritability (%)	Stiff neck (%)
Smith[35] 1976	156	37	82	18	22	51
Denver Children's Hospital 1979-1980	20	45	75	30	35	80

only early symptoms. A patient may lapse into a coma before symptoms are thought to be serious enough to warrant medical attention. The so-called classic meningeal symptoms of headache and stiff neck were found by Mandell and his associates to appear in less than one half of 53 patients. (Note: stiff neck occurred in 16 of 20 Denver Children's Hospital patients diagnosed as having *H. influenza* meningitis.) Seizures are also less comonly seen in *N. meningitidis* meningitis, but many patients are in a state of shock and, in some instances, they are cyanotic.

The third most common pathogen that causes meningitis is *D. pneumoniae*. It is a gram positive encapsulated microorganism more typically associated with diseases in young children and the elderly. Meningitis of this sort often occurs concurrently with or as an extension of lobar pneumonia. It is generally accepted that pneumococcal meningitis is more serious and a greater threat to life at all ages than meningitis caused by *H. hemophilus* or *N. meningitidis*.[4,20] The disease process involved with pneumococcal infection is toxemia or poisoning produced due to absorption into the tissue of bacterial products.

Symptoms are quite similar to those seen in menigococcal and *H. influenza* meningitis; however, as previously stated, pneumococcal meningitis often accompanies pneumonia or other respiratory infections. Signs of neurological disruption, such as hyperreflexia, or seizures are common.

Routes of Infection

Some authors [6], [21], [34] feel that the primary route of infection is via the bloodstream--that microorganisms invade the venous system and are spread throughout the body. These produce a state of septicemia (presence of bacteria or bacterial toxins). The bacteria are taken into the body via the nasopharynx.

Meningitis may also occur following direct invasion of micro-organisms from paranasal sinuses or the ear. In this mode of invasion, intervening bone and membrane must actually be destroyed in order for bacteria to reach the meninges. It is sometimes seen that untreated or poorly treated chronic suppurative otitis media may sufficiently destroy the bony structures of the middle ear and mastoid bacteria may actually reach the meninges.[13] It was felt at one time that meningitis was primarily caused by invasion of the meninges via the ear.[10] Mawson and Ludman[21] stated that "meningitis now principally arises from chronic otitis media which spread to the meninges." This contention is not, however, supported in the literature. Nadol[23] found no correlation between presence of acute or chronic otitis media and meningitis. Richer and associates[28] found only five cases of otitis media among 97 of meningitis. Among 58 cases reviewed at the Denver Children's Hospital, only six presented with otitis media in addition to meningitis. Smith[35] stated that "meningitis is an uncommon complication of otitis media, but potentially the most serious, and physicians must bear in mind the small but definite risk."

The final route of infection may be via a preexisted

malformation in bony structure of the sinuses or ear allowing leakage of cerebrospinal fluid and a path of invasion for bacteria. These malformations may be congenital or caused by trauma, such as fracture.

Pathophysiology

When organisms invade the meninges, they cause inflammation. They may result in vasculitis (blood vessel inflammation) and reduced cerebral blood flow. A combination of reduced blood flow, vasculitis, and the presence of debris caused by infection alters cerebral metabolism which, discussed in Chapter 2, may have profound neurological effects especially in children.[6, 32, 35]

Treatment

Prior to 1900 there was little that could be done medically for persons afflicted with bacterial meningitis. As a result, many (most) died from the disease. In 1905 a group of British researchers discovered that healthy individuals could carry *N. meningitidis* in their systems without showing any signs of disease. This prompted the development of a serum taken from healthy carriers which acted as an antigen against *N. meningitidis*. The serum was injected into persons who had meningitis. The treatment was not extremely successful; however, meningitis was less often fatal.

The discovery of antibiotics was, of course, the key to successful treatment of bacterial meningitis. For years, penicillin was used along with sulphonamide and chloramphenicol. In the early 1960s ampicillin was introduced to the treatment picture. It was shown to be

very effective.[12]

Currently, ampicillin and chloramphenicol are the drugs of choice. Often both will be given to a patient when the diagnosis of bacterial meningitis is made; one may subsequently be discontinued depending on sensitivity studies of the organism involved.[9, 35]

Often, if antibiotic treatment is begun early in the course of the disease, supportive medications may not be indicated. When the course of the disease is severe, however, complications resulting from cerebral edema such as seizures, coma, and deteriorating respiration may result. In these cases supportive therapy, such as anticonvulsants (e.g., phenobarbitol), steroids, and osmotic agents (e.g., glycerol) to reduce cerebral edema, has been advocated.

Chapter 2

SEQUELAE OF BACTERIAL MENINGITIS

Mortality

As previously mentioned, the actual incidence of bacterial meningitis has been increasing over the last 30 to 40 years. The number of deaths reported each year as a result of the disease has, however, drastically decreased. In the early part of this century the cause of the disease was so serious and the prognosis so gloomy that Grant[33] was prompted to say, in 1913, that "of the various intercranial complications . . . there is not one which at this time is more difficult to diagnose and up to the present more disappointing in its treatment than meningitis." He seemed to be reflecting the mood of the day by asking, "What is the use of discussion upon a disease which when diffuse and purulent is invariably fatal?" The reasons for this fatalistic view are clear in light of reports of up to 90 percent mortality in the early 1900s. With the advent of the antibiotic era, the mortality rate significantly dropped. In their 1962 study, Carpenter and Petersdorf[4] found a mortality rate of almost 40 percent. Sell, et al.[32] reported a death rate of 11 percent in a study conducted in Nashville, Tennessee between 1960 and 1964. Lindberg, et al.[19] reported three deaths among 82 children (3.6%) treated for *H. influenza* meningitis in Gotenberg, Sweden between 1968

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and 1975. At the Denver Children's Hospital during a 12 month span, there were four deaths among 58 patients treated for bacterial meningitis (6.9%).

Among neonates, unfortunately, the mortality rate tends to be much higher. Fitzhardinge, et al.[7] found that the death rate was as high as 58 percent during a 10 year study conducted at the Montreal Children's Hospital. Feigin and Dodge[6] estimated that bacterial meningitis is responsible for about four percent of the total number of neonate deaths.

Sequelae of Meningitis

Although the mortality rate attributed to meningitis has decreased, a great many post meningitic children retain long-term sequelae as a result of the disease. Many studies have found neuromuscular disorders such as seizures, paralysis or paresis, spasticity, hydrocephalus, tremor, and cranial nerve damage.[4, 19, 24, 32] Others show intellectual impairment[33, 36, 41] and learning problems.[7, 17, 41] It is interesting that Kresky, et al.[17] and Lawson, et al.[18] found that, on measures of intelligence, post meningitic children as a group were within the normal range but that 20 to 30 percent of these children demonstrated marked difficulty at school. As an extension of the Kresky, et al. and Lawson, et al. studies, Wright and Jimmerson[43] found that there were significant differences between post meningitic children and controls on tasks involving visual-motor perception and abstract thinking abilities. The learning disabilities literature is replete with descriptions of children who

manifest symptoms of what is known as "minimal cerebral dysfunction syndrome."[3], [22], [25] Many post meningitic children demonstrate some of these symptoms. These include impairments in perception especially visual-motor, poor abstract reasoning, soft neurological signs, slow language development, disorders of motor functions, memory problems, distractibility, poor impulse control, and motor or verbal perseveration.

Some of the more interesting and possibly more subtle sequelae are those dealing with emotional disturbance. A survey by Degin[5] of 986 post meningitic individuals found that 109 were described by the survey informant as "less emotionally stable." Descriptions included depression, irritability, excitability, nervousness, or having a poor disposition. Vernon[40] found that many post meningitic children demonstrated abnormally aggressive behavior, bizarre behavior patterns, or were "out of touch with reality." Other authors[7], [33], [38] also described behavior problems among post meningitic children. While many of the neurological and intellectual sequelae may be directly attributable to damage sustained from meningitis, the cause of the emotional disturbances described is open to speculation. Because some of these appear in children who demonstrate other neurological sequelae, it is difficult to decide if these emotional symptoms appear in reaction to other handicaps or if they are further evidence of cerebral disruption.

Hearing loss is a common sequela of meningitis. This is discussed later. Vestibular disruption, manifested by dizziness and poor balance, is sometimes seen following meningitis.

Overall estimates of the prevalence of sequelae are high, ranging from 18 percent reported by Neal, et al.[24] to 57 percent reported by Sell, et al.[32] Other studies[7, 19, 36] reported that 30 to 35 percent of the survivors retained sequelae. A personal review of 23 cases of youngsters admitted to the Denver Children's Hospital with bacterial meningitis revealed nine cases of obvious sequelae (39%). Four children had hearing losses, two had seizure disorders, two demonstrated neuromuscular sequelae, and one had hydrocephalus.*

In the past, several authors[17, 23, 39, 42] tried to devise systems for predicting children who were at risk for developing long-term sequelae to meningitis. Kresky, et al.[17] found a positive correlation between the presence of sequelae and the duration of symptoms prior to admission. There was also a correlation re length of hospital stay. Trolle[39] found a disproportionate number of sequelae in children under five years of age. Nadol[23] found significantly more hearing losses in children who had shown signs of neurological disruption (i.e., coma or seizures) during or prior to hospitalization. Wright[42] reviewed many studies. He found that five common variables correlated with the development of sequelae: seizures, duration of symptoms prior to admission, length of hospitalization, age at onset, and presence of bacteria in the cerebrospinal fluid.

The prediction system with which I am most familiar was

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*
These children do not represent a subsample of the 58 cases referred to in Chapter 1.

Table 5

Sequelae to Meningitis*

Major sequelae	Minor sequelae
Blindness Hydrocephalus Institutionalization Microcephaly Quadriplegia Retardation Seizures	Ataxia Hearing loss Hemiparesis Hyperactivity Peripheral facial palsy Subdural effusions

*Adopted from Herson and Todd.[11]

developed at the Denver Children's Hospital in 1977 by Herson and Todd.[11] They divided sequelae into two categories: major and minor. These are listed above in Table 5.

The records of 73 patients were reviewed and their admission status was compared with the final outcomes to determine factors that predicted the development of sequelae. Those factors which most highly correlated were (from high to low) coma, hypothermia, seizures, shock, age, cerebrospinal fluid, white blood cell count, CFS glucose, and duration of symptoms. From this review, Herson and Todd[11] constructed a scoring system for predicting meningitic sequelae (see Table 6).

Children who, upon admission to the hospital, obtained a score of 4.5 points or above were considered to be at high risk for the development of sequelae. In an unpublished study at the Denver Children's Hospital in 1980, Gary, et al.[9] found that this predictive

Table 6

Method for Predicting Post Meningitic Sequelae*

Admission factor	Points
Coma	3
Hypothermia	2
Seizures	2
Shock	1
Age (less than 1 year)	1
CSF white blood cell count, 1,000/cu mm	1
CSF glucose, 25 mg	0.5
Symptoms more than 3 days	0.5

*Adopted from Herson and Todd.[11]

method was effective in identifying those patients at risk for major sequelae. It did not identify children who later showed minor sequelae.

The Gary, et al.[9] study further compared a high risk group that had received supportive medical care in the form of steroids and osmotic agents with a high risk, no additional therapy group. They found that, of 15 high risk patients studied, the majority of long-term handicaps were present in those who did not receive additional therapy. Significant handicaps were present in 17 percent of the treated group versus 78 percent of the untreated patients.

Reference was made earlier in this chapter to a retrospective review of 23 children admitted to the Denver Children's Hospital. Nine of these children demonstrated sequelae following bacterial meningitis. Admission summaries were also reviewed and each child was

assigned a risk score according to Herson and Todd's[11] predictive method. The 14 children who did not show any obvious sequelae had scores of less than 4.5 points. They were, according to this method, at low risk for sequelae. The nine children who did show sequelae (and their risk scores) are listed in Table 7.

Table 7

Risk Scores of Nine Children Demonstrating
Obvious Sequelae

Child	Herson and Todd[11] score	Observed sequela
E. S.	1.0	Moderate hearing loss
C. V.	0.5	Moderate low frequency hearing loss
J. S.	0.5	Mild hearing loss
J. R.	4.5	Ataxia, right hemiparesis
K. M.	2.0	Mild to severe hearing loss
K. B.	4.5	Seizure disorder
C. L.	3.5	Ataxia, subdural effusion
A. I.	5.5	Seizure disorder
A. H.	5.5	Hydrocephalus, significant developmental delays

According to this scoring method, four of the 23 children would have been placed at high risk for sequelae upon admission. Three of these children developed what Herson and Todd[11] categorized as major sequelae. Of the six children who developed minor sequelae, only one was a high risk child. None of the children who developed hearing losses were identified by this method.

This information agreed with the Gary, et al.[9] finding that the Herson and Todd[11] predictive measure was highly effective in

identifying children at risk for major long-term problems following bacterial meningitis.

Meningitis and Hearing Loss

Possibly one of the most fascinating and, according to Rosenhall, et al.,[30] one of the most frequent sequela of meningitis is hearing loss. Authors[14, 23, 38] have described meningitic hearing loss as generally bilateral, severe to profound, and irreversible. In reviewing the literature and from personal experiences, however, it is clear that hearing impairment as a result of meningitis may take on many faces. In a study of 100 cases in which audiometric data had been obtained during hospitalization, Keane, et al.[14] found six cases of hearing losses in which nine ears had severe or profound losses while two ears showed mild losses. The Keane, et al. data show that one child who initially demonstrated severe loss bilaterally realized improvement in one ear to the mild hearing loss range.

Rosenhall, et al.[30] found a somewhat higher incidence of meninogogenic hearing loss, citing 15 cases from a sample of 83 children. Three cases had severe to profound losses bilaterally. Nine children demonstrated severe to profound loss in one ear with three showing mild or moderate impairment in the other ear and six had a normal hearing ear. Three other children had mild hearing losses: one bilateral and two unilateral. Teng, et al.,[38] in a study of 337 patients with hearing loss as a result of meningitis, found that 95 percent were bilaterally impaired and that 268 of

the 320 with bilateral losses were profoundly impaired. Sixty-nine patients showed some residual hearing with losses ranging from mild to severe unilateral and bilateral.

Nadol[23] presented an in-depth study of hearing loss as a sequela of meningitis. He reviewed 236 cases of bacterial meningitis and found that approximately 30 percent of the survivors had hearing losses. Twenty-three of those over two and one-half years of age were found to have sensorineural hearing losses. Seventy-seven percent of these were bilateral: 30 percent of the children showed profound impairment. Information is extremely sketchy for those patients less than two and one-half years of age, but he stated that 5 percent of these children had "recognized" losses. Regarding the lack of conclusive data from this age group, he made a rather curious comment that "behavioral audiometry is difficult or impossible" in this age group. Personal experience suggests that the use of visual reinforcement audiometry in this age group provides highly reliable results.

Unfortunately, Nadol[23] did not provide follow-up data on the younger age group on his study; the reader is left not knowing the actual incidence of hearing loss.

In a review of the Denver Children's Hospital records, four cases of hearing loss were found in 23 total cases (17.4%). One child had a moderate to severe loss bilaterally, two demonstrated moderate symmetrical losses, and one child had a mild unilateral loss.

From these studies, as well as others,[16, 27, 30] it is clear that hearing loss caused by meningitis, while always sensorineural in nature, can vary greatly in severity.

Some of the more interesting and useful information in the Nadol[23] study concerns correlation between hearing loss and other clinical findings. He found that *N. meningitidis* caused proportionately more losses than *H. influenza* or *D. pneumoniae*. This information may be skewed because the study lacked conclusive evidence on children less than two and one-half years old. As has been shown, *H. influenza* is the most common pathogen in this age group thus, if adequate audiometric data and follow-up had been done, more losses might have appeared in this category.

As discussed earlier, Herson and Todd's[11] predictive method was unable to identify children at risk for hearing loss in one study and in a review of the Denver Children's Hospital records. Nadol[23] and Keane, et al.,[14] however, found positive correlations between some of the items on the predictive scale and the ultimate presence of hearing loss. These included the duration of symptoms prior to hospital admission, seizures, coma, and a low glucose level (< 25 mg/100 m). Unfortunately, as with hearing loss itself, the appearance of symptoms in hearing impaired children is highly variable as is evident in the comparisons made between the Keane, et al. data and the Denver Children's Hospital records (Table 8).

Koide, et al.[15] presented some fascinating information which may, in some way, relate to the finding that the CSF glucose level appears to be related to hearing loss. They found reduced cochlear microphonic response in hypoglycemic cats; however, the response recovered following glucose injection. This information should be viewed cautiously due to the unclear relationship between serum glucose and

Table 8

Comparison of Clinical Findings in Hearing
Impaired Children

	Study	
Clinical finding	Keane[4] 1979	Denver Children's Hospital 1979-1980
Coma	4/6	0/4
Seizure	4/6	1/4
CSF glucose, < 25 mg	?	3/4
Duration of symptoms more than 3 days	5/6	0/4

cerebrospinal fluid or endolymph glucose levels.

Several authors[8],[13],[16],[19],[27],[28] studied hearing loss in relation to various antibiotics used in the treatment of meningitis. Gamstorp and Klockhoff[8] found that, of 10 children with hearing losses, seven had been treated with ampicillin, one was treated with chloramphenicol, and one was treated with chloramphenicol, sulphonamide, and penicillin (triple therapy). Jones and Hanson[13] found an increase (although not significant) in cases of deafness following ampicillin therapy. These studies raised a question of possible ototoxicity. Richner, et al.[28] also found an increased incidence of hearing loss in children treated with ampicillin. Lindberg, et al.[19] found an increased incidence of long-term sequelae, including hearing loss, in a group of children treated jointly with ampicillin and chloramphenicol. To add to the confusion, Raivio and Koskiniemi, et al.[16] found no relation between hearing loss and antibiotic treatment.

Most children reviewed at the Denver Children's Hospital were given ampicillin and chloramphenicol as soon as bacterial meningitis was diagnosed. One or the other of these was frequently discontinued, depending on bacterial sensitivity--usually the chloramphenicol. It is difficult, therefore, to comment re the appearance of sequelae in relation to antibiotics.

There appears to be a relation between deafness as a result of meningitis and the appearance of other handicaps. Vernon[40] presented an excellent overview of meningogenic deafness in children and its physical, psychological, and educational implications. He found that, of 1,400 applicants to the California State School for the Deaf, 10 percent had been deafened as a result of meningitis (most within the first two years of life). Of these children, 40 percent demonstrated multiple handicaps: intellectual, physical, or emotional. Vernon found that post meningitic children as a group had lower IQ scores. They educationally achieved at about one half the rate of normal hearing youngsters. They also demonstrated poor writing skills in comparison to groups of children deafened by other causes.

Of particular interest to speech-language pathologists is the finding that almost 20 percent of the children in Vernon's[40] study demonstrated symptoms of aphasia, such as word retrieval difficulties and poor symbolic processing abilities. Other studies[5, 7, 36] reported aphasiclike symptoms in nonhearing impaired post meningitic children. This suggests that aphasia or aphasiclike characteristics in those deaf children may reflect generalized cerebral disruption rather than reduction in language skills as a result of deafness.

Improvement in Hearing

An interesting and unusual characteristic of hearing loss due to meningitis is the occasional improvement in thresholds. Roeser, et al.[29] reported two cases of improvement in hearing sensitivity. Not only did pure tone thresholds improve, speech discrimination ability also improved in both cases. Rosenhall, et al.[30] reported 10 cases of hearing improvement. They stated that "approximately 25 percent of all patients with meningitic hearing loss do recover partially or completely bilaterally or unilaterally."

During the course of my externship, several children who presented with severe hearing losses following meningitis were treated with steroids *after* their conditions stabilized. Hearing was often seen to improve. Two of these cases are presented in Chapter 3.

The exact reasons for improvement in hearing with or without treatment with steroids is unclear. The mechamism at work in causing hearing loss is, however, better understood. Many authors[14, 23, 27, 28, 30, 38] agreed that the main cause of hearing loss subsequent to meningitis is labyrinthitis, infection or inflammation of the inner ear (usually the cochlear and vestibular sections[1]).

Infection of the labyrinth by bacteria is called suppurative labyrinthitis. It may arise in the middle ear and mastoid or in the meninges. In meninogogenic suppurative labyrinthitis, microorganisms are thought to reach the inner ear via the cochlear aqueduct or internal auditory canal from the subarachnoid space.[26, 31]

It is generally agreed that, when the suppurative process involves

destruction of the inner ear, complete deafness results. In later stages, possibly after several years, ossification of the labyrinth may be observed. There is another type of labyrinthitis called serous or toxic in which fluid or bacterial toxins are present in the labyrinth but bacteria are not present. This condition may precede suppurative labyrinthitis. Hearing may be impaired but not always markedly. This condition is not followed by a permanent loss of vestibular or cochlear function.[21]

It is reasonable to assume that suppurative and serous labyrinthitis could occur in response to bacterial meningitis. The presence of suppurative labyrinthitis may explain why in some cases, despite appropriate treatment, permanent hearing loss remains.

If the cause of initial hearing loss is serous or toxic labyrinthitis, early and appropriate treatment may prevent the development of suppurative labyrinthitis and, thus, prevent permanent cochlear damage and hearing loss. As time and the healing process continue, hearing may gradually return.

In addition to labyrinthitis, cranial nerve VIII may be somehow involved in the disease process. While the site of lesion appears most often to be the cochlea, Keane, et al.[14] stated that, according to studies he reviewed, from three to nine percent of the hearing losses involved cranial nerve VIII. Permanent destruction of the nerve, or part of it, may occur due to the suppurative process. Temporary neural involvement may be induced by inflammation due to the bacterial toxins or increased intracranial pressure. In the latter case, return of hearing is expected--at least partially.

That steroids may, in some cases, induce hearing to improve, presents interesting possibilities. Steroids act to reduce cerebral edema which may help restore partial nerve function. Steroids may also act to speed the amelioration of serous labyrinthitis which may, in turn, show hearing improvement. That some hearing losses remain after steroid therapy may indicate that a suppurative process was responsible. Unfortunately, there appear to be no conclusive answers at this time. Because suppurative and serous labyrinthitis present similar clinical pictures, definite proof that a suppurative process has occurred is not available until tomograms show ossification of the labyrinth.[2]

In summary, hearing loss related to meningitis appears to be a variable and somewhat mysterious entity; the occurrence cannot be effectively predicted.

Chapter 3

CASE STUDIES

During my three month audiology externship I had an opportunity to be involved in testing several children who were victims of meningitis. In those months I assisted in obtaining acute audiometric data on 15 inpatients ranging in age from five weeks to four years. In addition, I was involved in the follow up of several children who had diagnosed hearing losses as a result of meningitis. The three case studies reported herein represent the more interesting hearing impaired children tested. A fourth case study may be of interest to a speech-language pathologist because the child, although not hearing impaired, manifested significant language problems as a result of meningitis.

Case 1: M. T.

This was an extremely interesting and, at times, controversial case. A three-year-old boy, M. T., contracted *H. influenza* meningitis in May 1980. The hospital admission data revealed that the youngster was lethargic but responsive. Symptoms prior to admission included vomiting, headache complaints (three days prior to admission), fever, and stiff neck (hours before admission). According to Herson and Todd's[11] predictive method, M. T. would have been assigned a score of 0.5 (CSF glucose < 25 mg), putting him at low risk for the development of sequelae.

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Antibiotic treatment was instituted soon after admission: ampicillin and chloramphenicol. Culture of the CSF produced *H. influenza* which was resistant to ampicillin; the ampicillin was discontinued.

Audiometric data were obtained on day 10 of hospitalization. M. T. was found to have a profound loss in the right ear and a moderate loss in the left ear (Fig. 2). Tympanograms were normal: Acoustic reflexes were absent. Steroid therapy was instituted immediately and continued for two weeks. Figure 3 shows the configuration of loss following two weeks of steroids: a significant improvement was noted in the left ear along with a fairly good speech discrimination ability. One previous audiogram, not included here, demonstrated similar results.

Performance while wearing a mild gain hearing aid was evaluated with good results. It was suggested that a trial rental of an aid might be warranted. M. T. was seen again two and one-half weeks later with improvement in the left ear thresholds to near normal 1k, 2k, and 4k. Speech discrimination ability was excellent. The decision to try amplification in the left ear was postponed due to near normal hearing. Figure 4 is another audiogram with now normal thresholds in the left ear, 2k and 4k. The final audiogram, Figure 5, shows further improvement. M. T.'s thresholds to date remain stable at the levels shown in Figure 5.

A speech-language evaluation was conducted four months after the onset of meningitis. Results of this evaluation showed that M. T. functioned at or above age level in receptive language, expressive language, and nonverbal abilities.
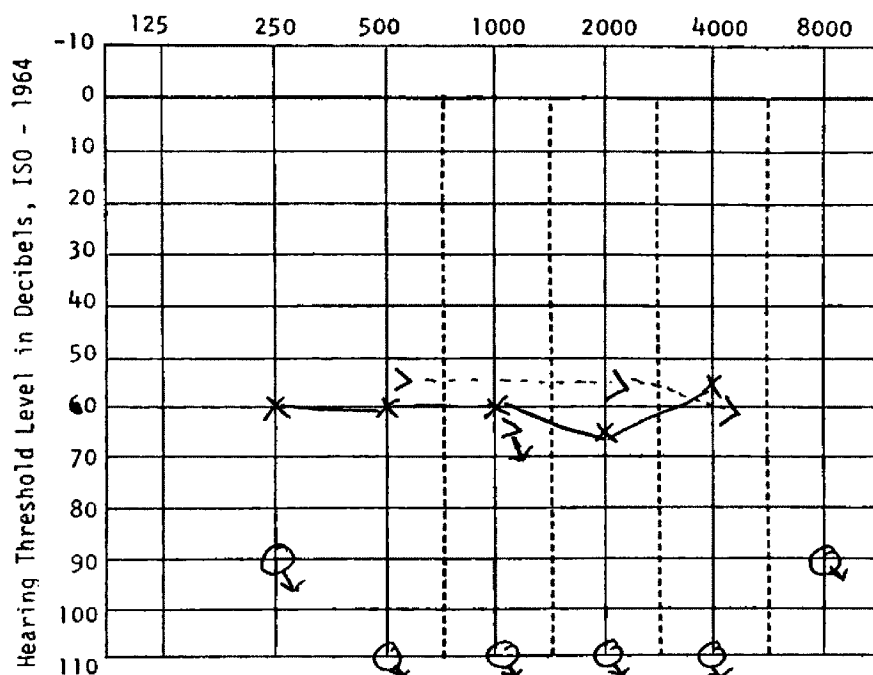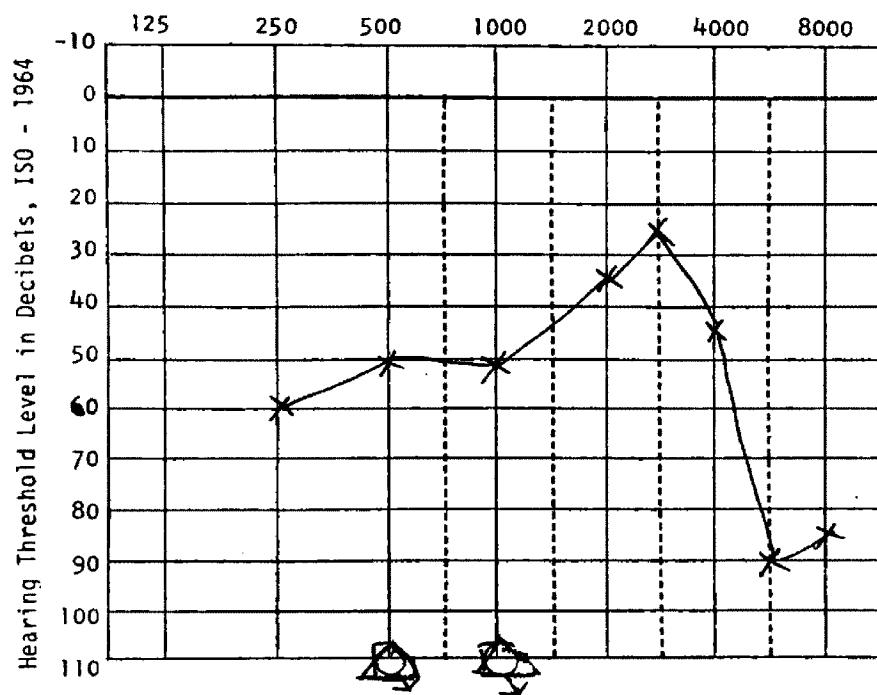
Figure 2

Audiogram 1 of Inpatient M. T., Age Three Years

Discrimination (WIPI)
Left ear 88% @ 70 dB
Sound field 84% @ 50 dB

Figure 3

Audiogram 3 of M. T. Following Two Weeks of Steroid Therapy

Δ = masked air conduction, right ear
Discrimination (WIPI)
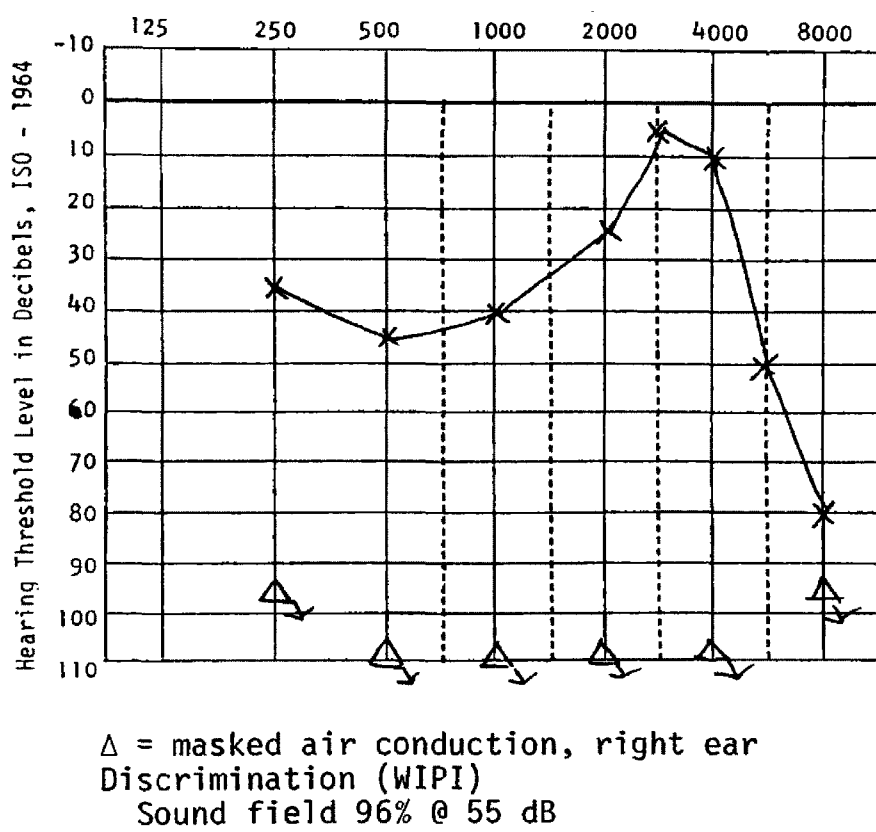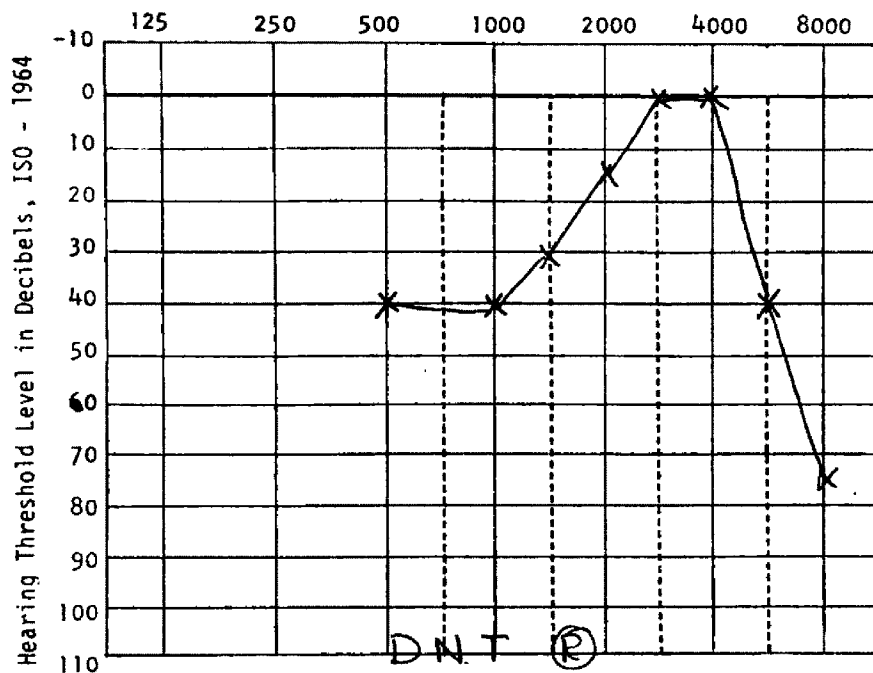   Sound field 96% @ 55 dB

Figure 4

Audiogram 5 of M. T. Two Months Following Meningitis

SRT, left ear, 20 dB
Discrimination (WIPI)
  Sound field 92% @ 50 dB

Figure 5

Audiogram 7 of M. T. Four Months Following Meningitis

Although M. T. had a moderate low frequency hearing loss in the left ear, the use of amplification was contraindicated by the presence of normal thresholds at 2k, 3k, and 4k Hz. An interesting development occurred following the completion of my externship. M. T.'s otologist felt that, due to the hearing loss in the left ear, M. T. should wear a hearing aid. The otologist was adamant that a hearing aid evaluation be conducted. Attempts were made to obtain an aid with a low frequency response made especially for the configuration of M. T.'s loss. The audiologist in practice with M. T.'s doctor performed the evaluation with a primary pediatric audiologist serving as a consultant. M. T. performed no better on speech audiometry with the aid than without. These results, coupled with the reports of good comprehension and expressive language abilities, raised questions regarding the need for amplification. M. T.'s general development, specifically in the speech-language area, is being closely monitored. Should problems arise, the need for therapy or a reevaluation of a need for amplification will be considered.

M. T. was an amiable, cooperative child with a good attention span and age appropriate language skills. M. T. demonstrated other mild sequelae to meningitis over and above the hearing loss: ataxia and mild left-sided weakness.

Case 2: C. V.

C. V. also presented an interesting history of fluctuating hearing loss; however, the hearing ultimately became poorer. C. V. was admitted to the Denver Children's Hospital following two days of

symptoms including low grade fever and lethargy. C. V. presented with serous otitis media in the right ear. Culture of the cerebrospinal fluid yielded *H. influenza*. This was treated with ampicillin and chloramphenical. Early in the course of his illness, C. V. developed hypertonicity and athetoid movements. C. V.'s Herson-Todd[11] score would have been 0, putting him at low risk for sequelae.

Audiometric data obtained during hospitalization was not conclusive, but the examiners felt a mild hearing loss could not be ruled out (Fig. 6). C. V. was again seen one month later; hearing was found to be within normal limits. Figure 7 shows that localization responses were observed using visual reinforcement audiometry at levels indicating normal hearing. Another evaluation performed at the Denver Children's Hospital one year later showed that responses were similar to those in Figure 1. It was recommended that C. V.'s hearing be reevaluated in one year.

The picture then changed dramatically. Approximately 18 months later, C. V.'s hearing was rechecked in Laramie, Wyoming. He was found to have a mild low frequency loss in the left ear and a moderate low frequency loss in the right ear (Fig. 8). Figure 9 shows a moderate low frequency mixed loss bilaterally. Tympanograms revealed significant negative pressure. The conductive component, which was not related to meningitis, resolved leaving stable thresholds resembling those in Figure 8. No plans have been made to date for possible amplification due to the problems encountered in fitting this rising configuration. The case illustrates the importance of routine audiologic follow-up of post meningitic children.
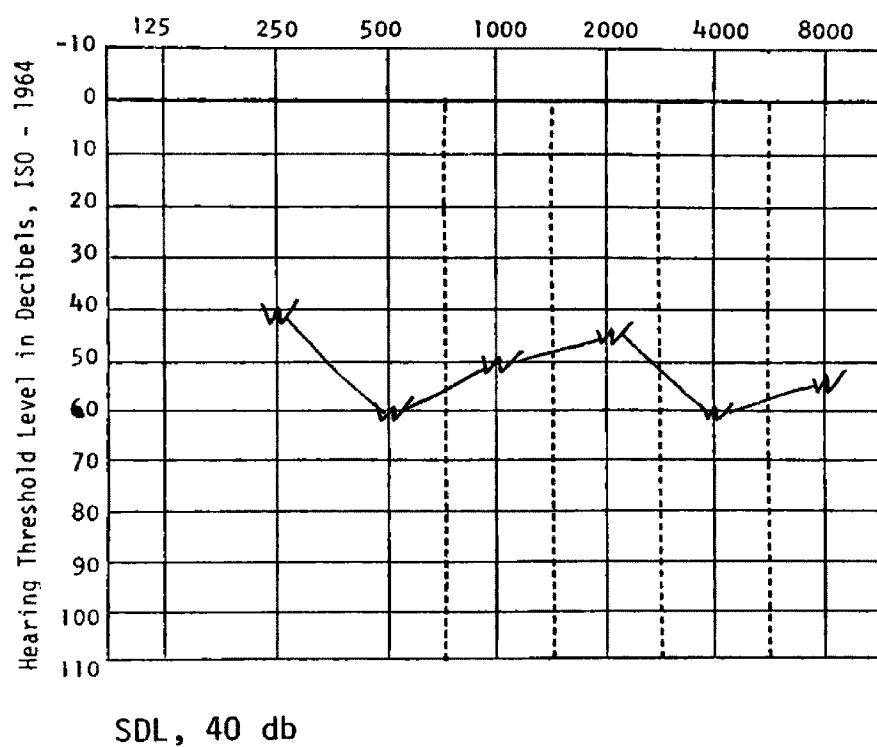
SDL, 40 db

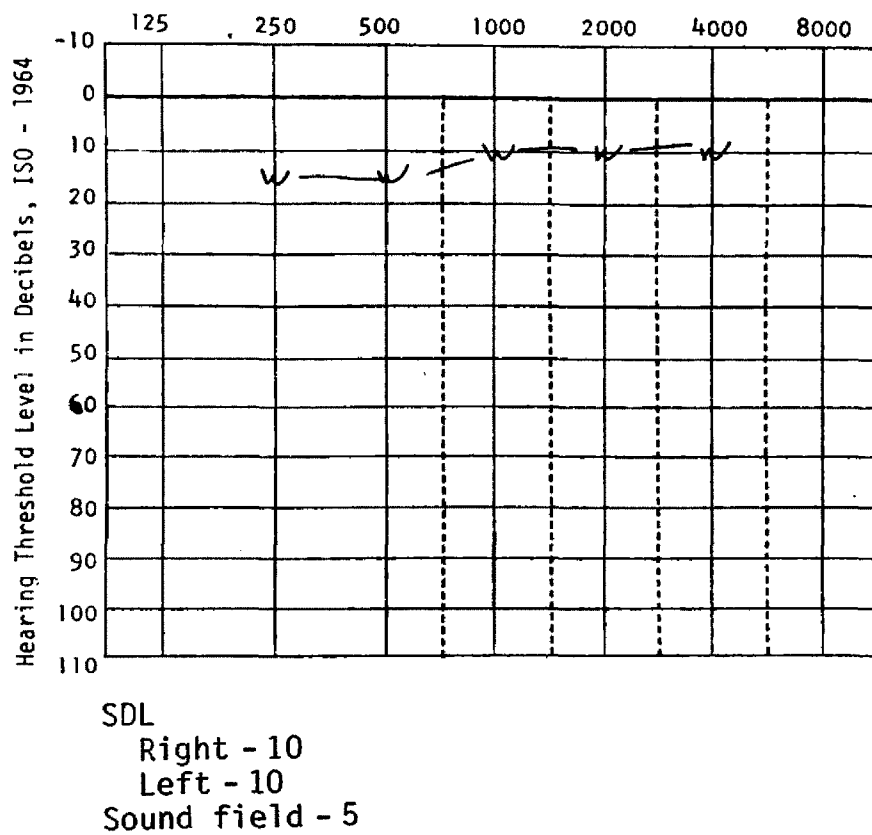Figure 6

Audiogram 1 of Inpatient C. V., Age 1-3

SDL
   Right - 10
   Left - 10
Sound field - 5

Figure 7

Audiogram 3 of C. V. Six Months After Menningitis

SRT
  Right 25
  Left 25
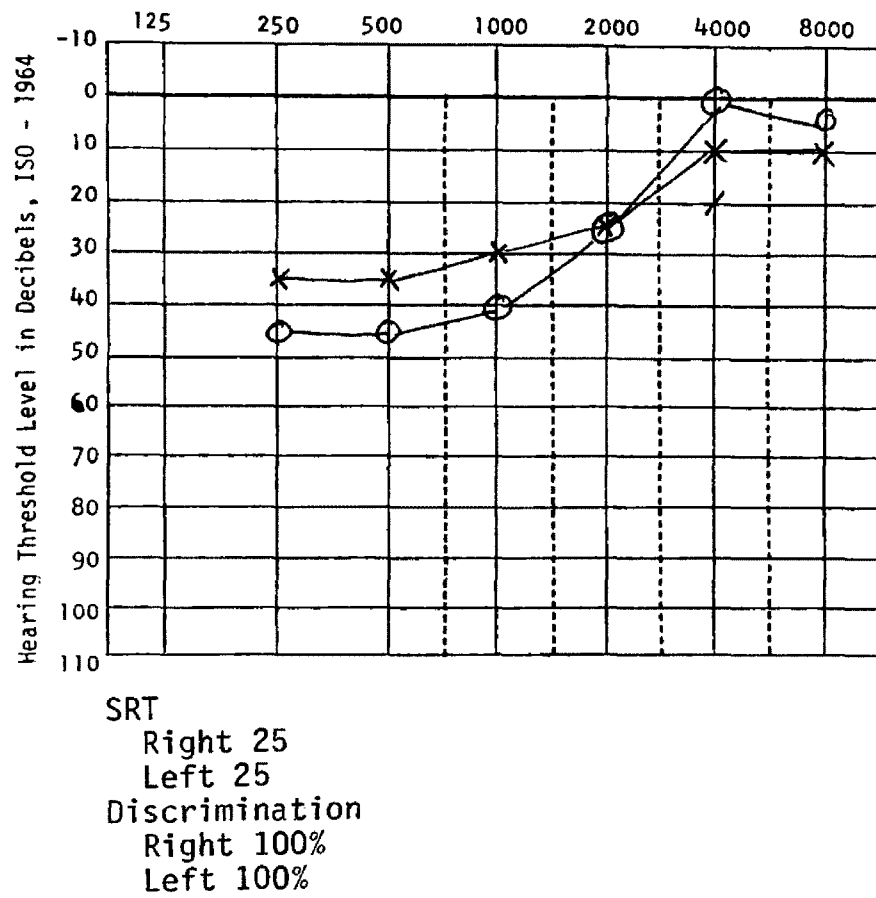Discrimination
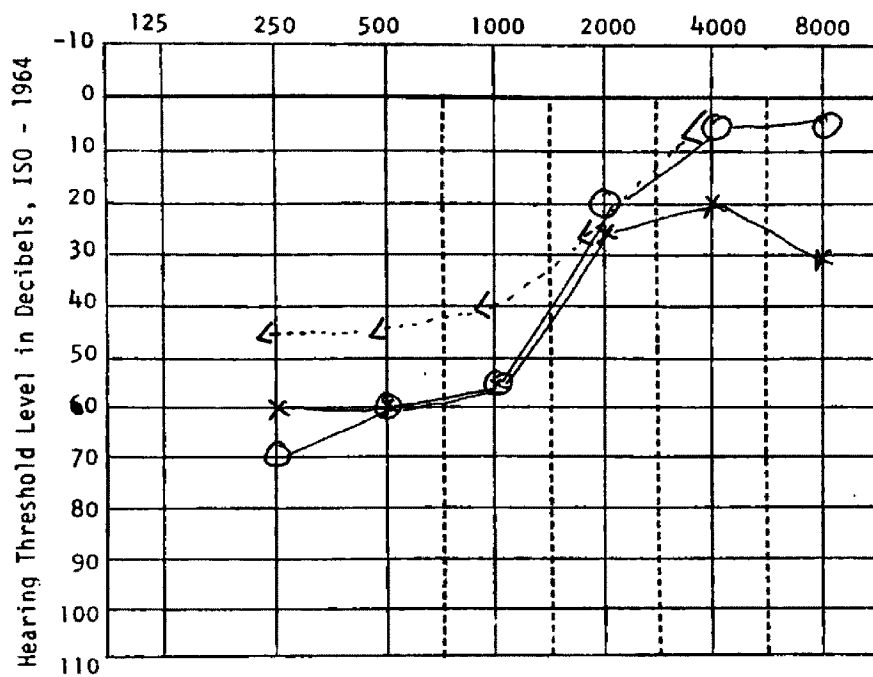 Right 100%
  Left 100%

Figure 8

Audiogram 5 of C. V. Three Years After Meningitis

SRT
 Right 30
 Left 35
Discrimination
 Sound field 84% @ 50 dB

Figure 9

Audiogram 6 of C. V. Three Years After Meningitis

C. V. had a speech-language evaluation in this department three months following meningitis at the age of 18 months. This evaluation revealed delays in receptive and expressive language as well as nonverbal abilities. C. V. also showed significant motoric delays-- he was not yet walking. It was recommended that a home language stimulation program be instituted along with occupational and physical therapy.

C. V., again evaluated at two years and seven months of age, was found to be functioning at age level in all language areas. In spite of the significant gains in the language area, C. V. retained neuromuscular sequelae including seizures and ataxia.

Case 3: R. L.

R. L. a two-year-old boy, was admitted to the Denver Children's Hospital three days after the onset of initial symptoms of nausea, vomiting, and fever. He had been admitted twice to another Denver area hospital but released. One of these admissions was prompted by the appearance of what the parents called "jerking." This was diagnosed as a febrile (fever caused) seizure. R. L. was treated for fever and released. Upon admission to the Denver Children's Hospital, he was described as lethargic but arousable; neurological signs were intact. Ampicillin and chloramphenicol therapy was initiated along with phenobarbitol and valium to control the seizures. Culture of the CSF produced *H. influenza* which was resistant to ampicillin; this antibiotic was discontinued.

R. L. would have been assigned a Herson-Todd[11] predictive

score of 2.5, constituting a low risk categorization. R. L.'s hospital course was described as difficult; he showed extended periods of reduced consciousness and neurologic problems such as seizures and ataxia. Acute audiometric data were obtained on hospital day nine. Localization responses to visual reinforcement audiometry indicated a profound hearing loss bilaterally. Recommendations included an ENT consult, thus steroid therapy was initiated on hospital day 10 for two weeks.

After one week of steroid therapy, R. L. was seen for audiologic reevaluation. No responses were obtained at the limits of the equipment. This was felt to reflect a high activity level and poor attention. R. L. was evaluated one week later. Responses were similar to those in Figure 10; they reflected a profound loss. Because hearing had stabilized, a hearing aid evaluation was begun. Figure 11 shows the results at six weeks' post meningitis. Hearing had improved to the moderate to severe category in at least the better ear (localization responses in found field). Responses one month later showed that hearing had remained essentially stable (Fig. 12). R. L. was fitted with high powered hearing aids and aural rehabilitation therapy was initiated with the department teacher of the hearing impaired. Figure 13 shows R. L.'s most current audiogram.

It is interesting that, in the three cases presented, the children displayed a rising configuration to their hearing losses. This does not coincide with study findings cited in the body of this paper which stated that hearing losses are generally flat and symmetrical.
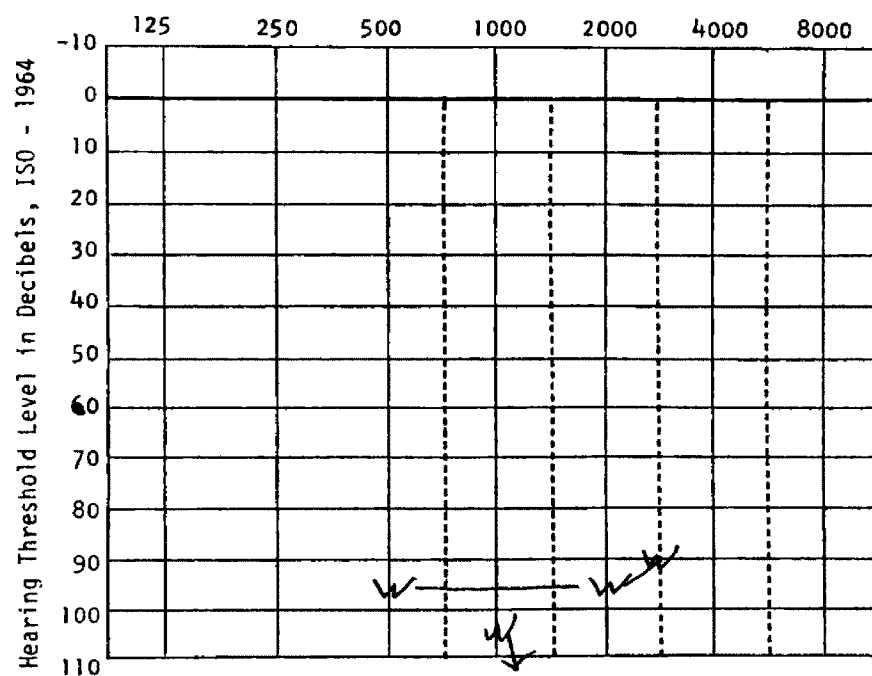
Figure 10

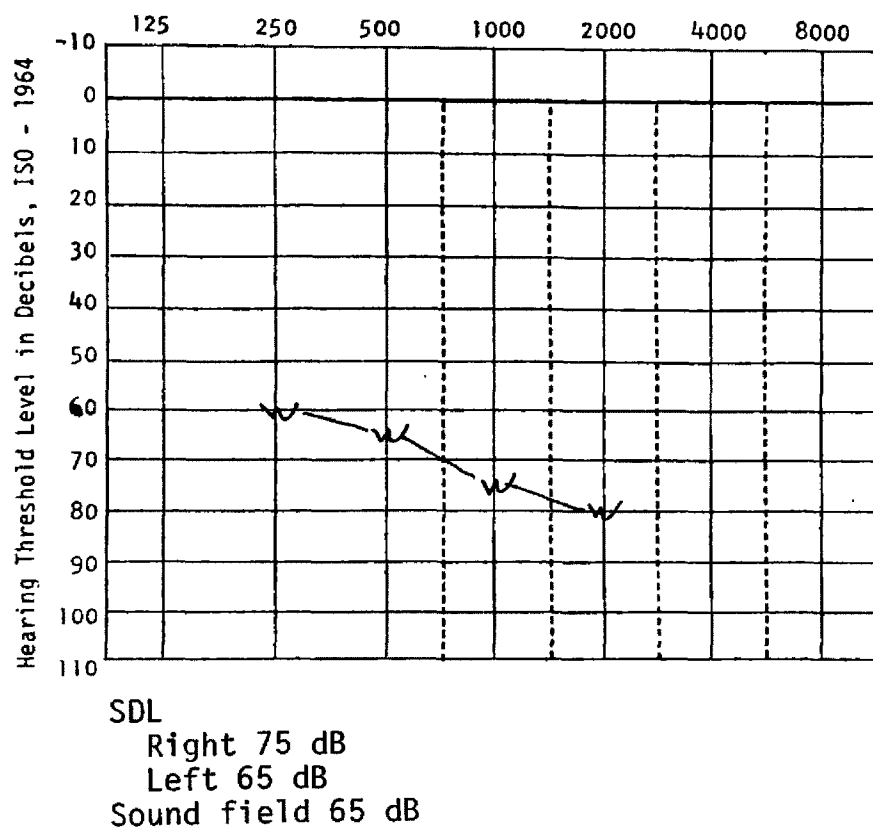Audiogram 1 of Hospital Day Nine for R. L., Age 20 Months

Figure 11

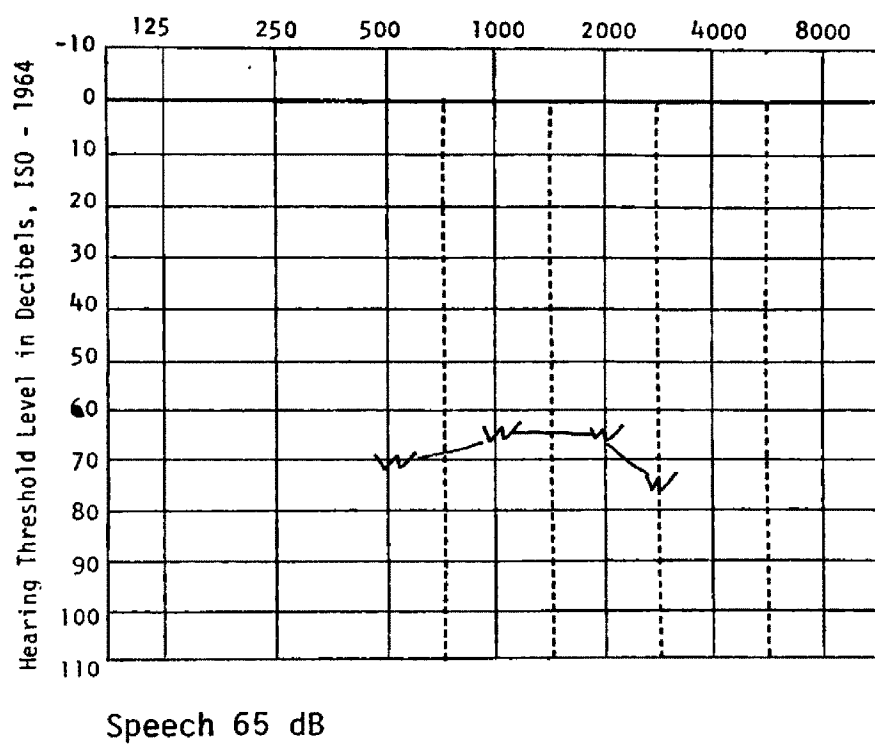Audiogram 4 of R. L. Six Weeks Following Meningitis

Speech 65 dB

Figure 12

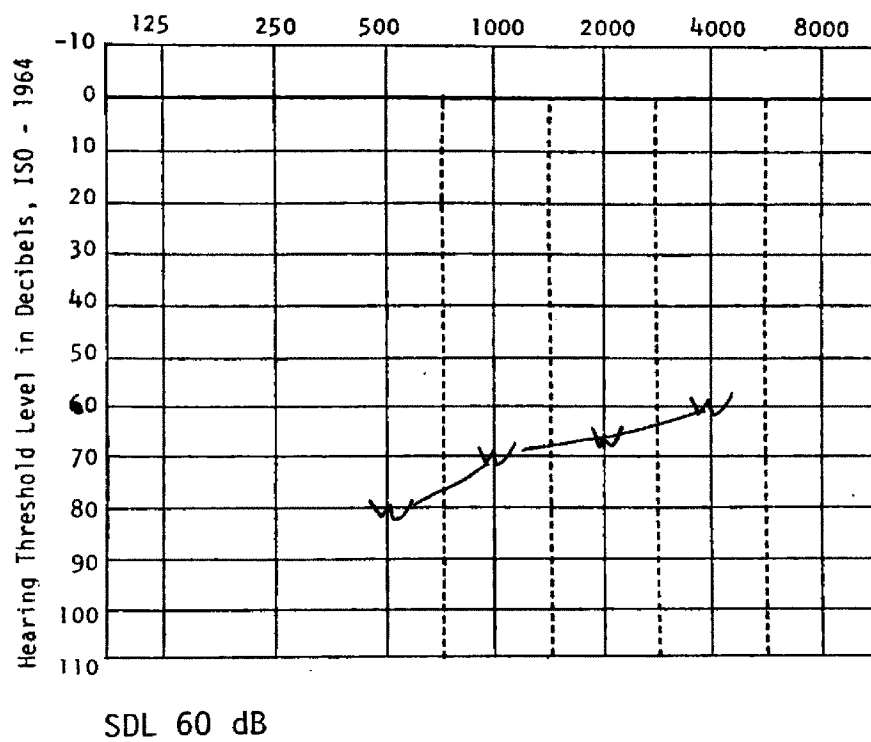Audiogram 5 of R. L. Two Months After Meningitis

SDL 60 dB

Figure 13

Audiogram 7 of R. L. Five Months After Meningitis

R. L. has also been seen in occupational therapy and physical
therapy. He demonstrated ataxia and subtle right-sided signs.
The most interesting aspect of the case was behavior. R. L. was
extremely distractible, impulsive, and his attention varied. Some-
times his attention was good and sometimes he was completely unable
to concentrate on an activity for even short periods of time. R. L.
has been described as hyperactive. He continues to receive medica-
tion for seizures.

It is difficult in R. L.'s case to say that some of these
symptoms were present prior to meningitis or that they were a
reflection of the hearing loss or that they represented symptoms of
minimal brain dysfunction. The behavior patterns resembled those
discussed in Vernon[40] and the literature re learning disabilities
common to children who have minimal brain damage.

R. L. is currently being seen for aural rehabilitation
therapy in the Speech Pathology and Audiology Department. His
therapist has also described the behaviors listed above as extremely
variable in their expression. R. L.'s language abilities are poor
for his age. They appear to cluster around the nine month level.
He wears binaural hearing aids with a dichotic fitting and he seems
to be adjusting well to them.

Case 4: J. H.

J. H., a six-year-old boy, was referred to the speech
pathology department by a speech-language pathologist in Texas.
J. H. had pneumococcal meningitis at the age of seven months.

The parents were subsequently told that J. H. had mild brain damage.

Developmental milestones appeared normal prior to meningitis. The parents reported that delays in speech-language and other areas became apparent at three years of age. J. H. is currently enrolled in special language therapy in Texas, but the parents have not felt the program was adequate; they decided to seek a second opinion.

I evaluated J. H.'s hearing and found it to be within normal limits bilaterally. The method employed was play audiometry. J. H. displayed significant trouble conditioning to the task and maintaining a conditioned bond. He was distractible.

The speech-language pathologist who evaluated him found that J. H. was distractible to internal and external stimuli. His language was characterized by perseveration and echolalia. Memory skills were also poor and there were questions of slow auditory processing. Receptive and expressive language abilities were found to be significantly delayed and nonverbal conceptual abilities were borderline normal.

This is a rather severe example of language problems as sequelae to meningitis. H. H. exhibited many of the aphasiclike characteristics spoken of by Vernon.[40] It is interesting that some of the behavior problems noted in this child--distractibility, inability to concentrate, and poor attention--were present in Case 3, a child with a hearing loss. This lends support to the contention that these patterns appear as a result of cerebral disruption due to meningitis rather than the handicapping condition of deafness.

Chapter 4

SUMMARY AND IMPLICATIONS

Bacterial meningitis has been recognized for years as a serious disease of children. The disease was almost always fatal in the early part of this century. The advent of the antibiotic era, however, has drastically reduced the mortality rate associated with meningitis. In spite of the decreased death rate, many children now present with serious, long-term sequelae as a result of bacterial meningitis. These may include neurologic residuals such as seizures, hydrocephalus, paralysis of paresis, and ataxia. Other sequelae may include hearing loss, blindness, and emotional and intellectual disturbances.

The variety of symptoms and sequelae associated with this disease are fascinating. Certain predictive methods appear to be useful in identifying children who are at risk for major sequelae, such as seizures or hydrocephalus, but they are not effective in predicting children who will ultimately present with a hearing loss and/or language and learning problems. These sequelae seem to be unpredictable in their selection of targets and extremely variable in severity across cases.

Hearing loss associated with meningitis has been described in the literature as generally sensorineural, bilateral, and profound. It has been my experience that there are exceptions to this rule. Hearing losses can vary from mild to profound and be unilateral or bilateral.

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The most interesting aspect of hearing loss is that it may fluctuate in severity for long periods of time following meningitis.

Although many authors cite cases in which hearing has improved, one child at the Denver Children's Hospital demonstrated a gradual decrease in hearing sensitivity. Evidence also indicates that steroids given after a child's condition has stabilized may induce hearing improvement. This raises questions re the relationship between the antibiotics used to treat meningitis and the occurrence of hearing loss.

My personal experience with children who have had meningitis and review of the literature raise additional questions that are worthy of further exploration.

1. Are there symptoms associated with meningitis which are predictive for so-called minor sequelae, such as hearing loss and learning disabilities? One of the more interesting possibilities may be cerebrospinal fluid glucose level.

2. In regard to hearing loss in particular, what is the actual pathology of the inner ear as a result of meningitis? Why do some children show improvement in hearing while others do not? Is it possible that children whose hearing improves have serous rather than suppurative labyrinthitis?

These questions raise some possibilities for long-term studies of children who have or have had hearing loss due to meningitis. The studies should include X-ray analyses of the inner ear as well as assessments of the vestibular system.

3. As an adjunct to question 2, why are steroids seemingly

effective in improving hearing in some cases but not in others?

There are, of course, more questions that could be answered. It is hoped that, in light of the variable nature of meningitic sequelae, all health care personnel will follow post meningitic children carefully. At least annual evaluations of language skills, perceptual skills, and learning appears appropriate. Case study 2 stresses the need for periodic audiologic follow-up for *all* post meningitic children. Hearing loss as a result of meningitis may fluctuate greatly. It may occur after the disease. Meningitis is an interesting and sometimes mysterious disease. The possibilities for research in this area are vast.

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