THE COGNITIVE AND BEHAVIORAL SEQUELAE OF HEMOPHILUS INFLUENZAE MENINGITIS

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Abstract

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This study investigated the effects of Hemophilus Influenzae (H-flu) meningitis on the cognitive profile and behavioral functioning of normal survivors. In particular, the variables of age at onset of illness, time elapsed since illness, seizures, and treatment in relation to outcome were examined. Forty-three post-meningitic children diagnosed as normal by their physicians participated in the study. Twenty-one siblings served as controls. All children were assessed on the McCarthy Scales of Children's Abilities (MSCA), the Peabody Picture Vocabulary Test (PPVT), Conners' Short Form Rating Scale, and Peterson Problem Checklist. No significant differences were found in global IQ between post-meningitic children and their siblings. As a group, post-meningitic children did not differ significantly from their siblings in any of the cognitive and behavioral measures investigated. However, when the effects of language at testing and sex were eliminated post-meningitic children tested in English scored significantly lower than their siblings on the PPVT. Age at illness significantly predicted the performance of post-meningitic children on the Perceptual-Performance subtest of the MSCA. The younger the child at onset of illness the worse the performance. Time elapsed since illness, seizures, and treatment were not found to bear any relationship to outcome. These results suggest optimism about the outcome of H-flu post-meningitic children diagnosed as normal. At the same time they highlight areas of development that may be affected by the disease.

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Although the mortality rate due to H-flu meningitis has been drastically reduced by antibiotic treatment the morbidity is reported to range from 27 to about 50% (Lindberg, Rosenhall, Nylen and Ringner, 1977; Sell, Webb, Pate and Doyne, 1972; Sproles, Azerrad, Williamson and Merrill, 1969).

Research addressing the issue of sequelae with respect to specific cognitive and behavioral areas of functioning has been sparse. In particular, the variables of age at time of illness, lapse of time post-illness, seizures, and treatment as related to outcome have not been systematically investigated.

The present study was designed to assess the cognitive and behavioral functioning of "normal" survivors of H-flu meningitis as compared to non-meningitic siblings. "Normal" survivors, in the context of this study, were children who at discharge from the hospital and one year follow-up were considered to be neurologically, audiologically, and psychologically normal according to physician's examination. Cognitive and behavioral sequelae were studied with respect to age of the child at the time of illness, time elapsed since illness, presence or absence of seizures during the course of the disease, and treatment administered to the child.

In the following section an overview of the disease is presented.

Characteristics of H-flu Meningitis

H-flu meningitis is the agent most commonly isolated from bacterial meningitis in early childhood. This microorganism together with *Streptococcus pneumoniae* and *Neisseria meningitidis* accounts for 90% of the cases of meningitis in children over 2 months of age (Feigin and Dodge, 1976). The age of the children is the striking characteristic of the prevalence of H-flu meningitis. It is rare in children under 6 weeks of age, reaches

a peak at age one year, and then declines sharply. There are no definite clinical correlates which differentiate influenzal from pneumococcal or meningococcal meningitis.

An explanation for the age incidence of H-flu meningitis was attempted by Fothergill and Wright (1933). These authors documented an inverse relationship between the presence of bactericidal antibodies and the prevalence of meningitis. The rare occurrence of H-flu meningitis in neonates before the second month of age and in the adult (Snyder and Brunjes, 1965) coupled with the high incidence in children 3 months to 3 years of age, led Snyder and Brunjes (1965) to postulate an explanation in terms of bactericidal immunity. Accordingly, the neonate is protected from the disease because of the antibodies passively received from the mother which decline after the third month of life, and are actively acquired again in childhood and adulthood by active exposure to the infectious organisms.

Fothergill and Wright's (1933) postulated inverse relationship between H-flu meningitis and bactericidal antibody titer of the host has been questioned since then. Feigin, Richmond, Hosler and Shakelford (1971) conducted a study to determine the bactericidal antibody of H-flu in 289 patients whose age ranged from birth to 42 years. Their results indicated that a significant proportion of newborns, 30% exactly, had negligible quantities of or were totally lacking in bactericidal antibody, and about 35.5% of the non-medical adults studied from 17 to 42 years had no antibodies. On the other hand, only 18% of the children one month through 2 years of age were lacking of bactericidal antibody. Given the fact that the greater prevalence of H-flu meningitis occurs in the latter group, these results cast serious doubt on the postulated inverse relationship existing between H-flu meningitis and antibody

titer, and indicate that the amount of bactericidal antibody that the host possesses may be one cause predisposing to meningeal infection but it is not the unique one. Norden (1974) observed the highest frequency of immunization to occur among medical personnel and parents of children who had been afflicted with epiglottitis, a disease also caused by H-flu organisms. Thus, these findings seem to indicate that active exposure to the infectious agent is an important manner of acquiring immunization. Similarly, a continuous nasopharingeal carriage in the absence of the disease has been related to the appearance of defenses against H-flu meningitis (Sell, 1970).

It would seem that an important variable related to the virulence of the illness is polyribophosphate which has been shown (Smith, 1954) to be in greater amounts in the cerebro-spinal-fluid (CSF) of children whose course of malady was complicated than in those in which it was uneventful. Along these lines, Robbins (1973) found antipolyribosephosphate antibody to protect against H-flu meningitis <u>in vivo</u>. In this respect, Feigin and Dodge (1976) have emphasized the fact that only a negligible proportion of children younger than 17 months seem to develop this antibody. This would, to a certain extent, explain the higher incidence of residua of H-flu meningitis in the very young child.

There would seem to exist some racial variation in the prevalence of H-flu meningitis, blacks being more often afflicted than whites (Parke, Schneerson, & Robbins, 1972). Possible causes of the greater incidence of the disease in blacks may be overcrowding, deficient dietary regimens, or genetic predisposition such as occurs in sickle cell anemia (Tarr and Peter, 1978). This suggests that race and social class may be important variables to consider when assessing the outcome of the disease; they have often been neglected in past studies. Also, males are more often

afflicted than females in a ratio of about 1.7:1 (Feigin and Dodge, 1976).

In summary, H-flu meningitis is a disease entity that strikes children at a crucial developmental age afflicting more males than females and being more prevalent among blacks. The trauma due to the illness may have wide implications for development.

H-flu meningitis prior to the antibiotic era was often a fatal disease with a reported mortality rate of about 90 to 100% (Sproles et al., 1969). The introduction of antibiotics such as sulfonamides and streptomycin significantly reduced the mortality rate. These antibiotics were later abandoned because of their toxicity: specifically, streptomycin was found to produce damage to the eighth cranial nerve resulting in hearing loss. Ampicillin and chloramphenicol were substituted, have remained the drugs of choice in the treatment of the disease, and further reduced the mortality rate to about 3.4% (Lindberg et al., 1977). This reduction in mortality rate coupled with a recrudescence in the incidence of the disease (Michaels, 1971) and an unparalleled decline in morbidity have made the study of the sequelae of the illness a question of paramount importance.

In the ensuing section the literature pertaining to the variables under investigation in this study, that is age at illness, time elapsed since illness, seizures, and treatment received by the child will be examined, in particular with reference to the child who appears normal upon discharge.

The Relationship of Age at Illness, Time Post-Illness, Seizures, and Treatment to Outcome

The relationship of the variables: age at illness, time elapsed since illness, seizures, and treatment, to outcome of the disease is controversial and has not been systematically studied in "normal" survivors.

Crook, Clanton, and Hodes (1949) reporting on 101 patients with a diagnosis of H-flu meningitis, observed that the lowest recovery rates occurred in the younger patients. Bloor, Grant, and Tabris (1950) in a 5 months to 4 years follow-up study on 29 of 34 survivors of meningitis due to H-flu found that children who suffered the disease when younger than 9 months of age had the poorest prognosis in terms of death rates. These authors also reported a significantly higher incidence of seizures during the course of the illness in the group with the poorest outcome. Along these lines, Kresky, Buchbinder, and Greenberg (1962) described a negative correlation between age of the child at the time of illness and the number of neurological deficits exhibited at a 3 to 5 years follow-up.

On the other hand, Sell, Merrill, Doyne, and Zimsky (1972) found no correlation between IQ and age at onset of illness or length of hospitalization. Also, Lindberg et al. (1977) observed a similar incidence of residua in all groups investigated regardless of age at onset of illness.

In view of this controversy and the fact that, as will be later mentioned in the course of this introduction, these studies suffer from serious methodological pitfalls that obscure the interpretation of the results, more research seems warranted to elucidate the influence of these variables on the specific cognitive and behavioral functioning of post-

meningitic children.

Neurological sequelae such as quadriparesis and hemiparesis, which result from injury to the motor areas of the brain; blindness, and deafness have been found in certain cases of meningitis to disappear with time (Feigin and Dodge, 1976; Koeser, Campbell and Doyle, 1975; Tepperberg, Nussbaum, and Feldman, 1977). There is also evidence that delays in mental development observed in the early life of premature and anoxic children disappeared at 4 and 7 years follow-up respectively (Berges, Lezine, Harrison and Boisselier, 1972; 1973; Ernhart, Graham and Thurston, 1960). However, the effects of time on subtle cognitive and behavioral sequelae have not been investigated in post-meningitic children. More information on outcome is needed for discussing with parents and educators the long-term implications of the disease. It is to research concerning these issues that I now turn. The literature pertaining to treatment will be discussed in this context.

Sequelae of H-flu Meningitis. The residua of H-flu meningitis most commonly reported include, retardation, spastic hemiplegia, hydrocephalus, blindness, deafness, hemiparesis, ataxia, delayed speech, paresis, and hyperactivity (Bloor et al., 1950; Crook et al., 1949; Feigin and Dodge, 1976; Hutchison and Kovacs, 1963; Kresky et al., 1962; Smith, 1954; Sproles et al., 1969). According to Sell (1970) meningitis is the leading cause of mental retardation in the United States. However, the literature on the residuae of H-flu meningitis up to the 70's is plagued with methodological errors that make the interpretation of the results at best tentative. Among the most serious pitfalls are: (a) lack of

controls, (b) failure to describe the criteria for inclusion of subjects and outcome measures, (c) tendency to include various types of purulent meningitis which makes it difficult to disentangle the specific effects due to haemophilus influenzae meningitis, (d) failure to report patterns of abilities, (e) follow-up period of less than a year which may confound the results because of the neurological defects that have been shown to disappear within a year, (f) failure to relate treatment to outcome, which given the fact that antibiotics such as streptomycin produce damage to the eighth cranial nerve resulting in hearing loss, may have confounded the results in some past investigations.

The lack of control of treatment would appear to be no longer a problem since at present the standard therapy consists of either ampicillin or chloramphenicol. These two antibiotics have been shown to be comparable in terms of mortality, morbidity, and complications of the disease (Barrett, Taber, Norris, Stephenson, Clark, and Yow, 1972; Feigin et al., 1976; Lindberg et al., 1977; Schackelford, Bobinski, Feigin and Cherry, 1972; Schulkind, Altemeier, and Ayoub, 1971). However, when both antimicrobial agents are administered conjointly as may be the case in geographical areas in which resistance to ampicillin has been found, at least one report (Lindberg et al., 1977) has shown that the sequelae of the disease increases in the recipients of both drugs conjointly. These authors reported a 72.7% of sequelae including psychomotor delay, behavior problems, bilateral severe hearing loss, unilateral severe hearing loss, and slight bilateral or unilateral hearing loss in the recipients of both drugs conjointly, compared to only 12.5% residua in those treated only with ampicillin and 18.2% in those treated with only chloramphenicol. Hearing loss either bilateral or unilateral seems to be the complication

that increases in frequency in the recipients of both drugs as compared to those treated with only one antibiotic. Thus, 54.4% of the recipients of both drugs exhibited hearing impairment, while only 4.5% in the chloramphenicol group and 9.3% in the ampicillin group presented similar sequelae.

In terms of the author's interest in the frequency of cognitive and behavioral sequelae in those appearing normal, Lindberg et al.'s (1977) study shares with previous reports on the sequelae of bacterial meningitis, that weakness of an appraisal investigation of the survivors without controls with which to compare the results of the assessment. Also, psychological evaluations were performed only on patients with a history of behavior problems or delayed intellectual development, and only global functioning was reported.

Wright and Jimmerson (1971) conducted the first controlled investigation to assess the specific residua of H-flu meningitis in both global and specific areas of intellectual functioning. Their sample consisted of 10 post-meningitic children who had been diagnosed as cured and unscathed by the pediatrician at time of discharge from the hospital, the follow-up period was about 8 years, and the post-meningitic children were matched with the controls on the basis of age, sex, race, family income, and history of hospitalization. The controls had been hospitalized for bone fractures and similar problems. The instruments used to evaluate the cognitive functioning of these children were the Bender Gestalt, the Frostig Developmental Test of Visual Perception, and the Wechsler Intelligence Scales for Children (WISC). Their results showed no differences between the groups on the Bender and the six Frostig variables. However, a difference favoring the controls was obtained on

five WISC subscales, comprehension, similarities, picture completion, block design, and coding, as well as on Verbal, Performance, and Full Scale IQ.

According to these results it would seem that post-meningitic children have a depressed IQ resulting from verbal conceptual difficulties; as well as visual attention and analysis (Glasser & Zimmerman, 1967). However, the fact that no differences between the probands and controls was obtained on the Frostig and Bender is highly inconsistent with the lower scores of the probands on the WISC performance subtests which have a strong visual component (Glasser and Zimmerman, 1967).

Sell, Pate, Webb and Doyne (1972) conducted two controlled studies to investigate the aftereffects of H-flu meningitis. In the first study 21 post-meningitic children were compared to nonmeningitic siblings on the WISC. Results indicated the mean global IQ of the probands to be significantly lower. These results are consistent with those reported by Wright and Jimmerson (1971).

In Sell et al.'s (1972) second study, 25 post-meningitic children who had purulent meningitis due to H-flu, meningococcus, and pneumococcus, and who appeared normal, were compared to normal peers of school age on the Illinois Test of Psycholinguistic Abilities (ITPA) which measures the capacity to receive, integrate, and express language; the Frostig Developmental Test of Visual Perception, and the PPVT. Results showed the controls to be superior in mean psycholinguistic age score as measured by the ITPA, and in word knowledge as assessed by the PPVT. On the Frostig no differences between the probands and controls was obtained, except for the subtest measuring position in space. These results are consistent with the verbal deficits reported by Wright and Jimmerson (1971) and would seem to support the hypothesis that post-meningitic children are impaired in their verbal conceptual skills. It may be that

post-meningitic children have an adequate visual perceptual system but are impaired in central auditory processing which in turn handicaps their verbal conceptual skills.

Sell et al.'s (1972) studies do not report subtest scores which allow for an analysis of the findings with regard to specific areas of intellectual or language functioning that would help to elucidate the particular areas in which post-meningitic children are deficient. Also, since in their second study the effects of meningitis due to various bacterial organisms were investigated, the particular effects in the case of H-flu meningitis cannot be isolated.

Language development may be one of the deficient areas due either to hearing impairment, often reported as a side-effect of meningitis (Lindberg et al., 1977) or to more central language disturbances which may be of auditory nature. However, in view of the fact that Sell et al.'s (1972) subjects were audiologically normal, the latter hypothesis appears more tenable, and research along these lines may be fruitful. In this respect the research of Tallal and associates seems relevant.

Tallal and Piercy (1973) studied the ability of children diagnosed as suffering from developmental aphasia, but otherwise with no hearing, articulation, emotional or neurological handicaps, to perceive binary sequences of nonverbal stimuli in the auditory modality. Their findings indicated that performance was directly related to time available for processing of auditory information. Based on these findings, Tallal (1976) noted that a deficit in rapid auditory processing has its principal effect on the analysis of the rapid formant transitional information which is characteristic of particular phonemes regardless of the rate of speech. Aphasic children, however, have been shown not to differ

in performance from matched control children, on visual tests involving both rapid nonverbal perceptual processing and nonverbal serial memory (Tallal and Piercy, 1973). Similar difficulties in central auditory processing may account for the apparent language deficits of post-meningitic children reported by Sell et al. (1972) and Wright and Jimmerson (1971).

On the bases of the studies reviewed, it was predicted that the language of post-meningitic children would be deficient relative to their nonmeningitic siblings. Thus, their performance on verbal tests was expected to be lower than on performance tests. In addition, their vocabulary was also expected to be lower than that of their siblings. This pattern of abilities is often found in learning disabled children (Hulesman, 1970) and it is in agreement with reports on learning disabilities consequent to meningitis (Kresky et al., 1962; Lindberg et al., 1977; Sproles et al., 1969).

Also, it is not expected that the performance of affected children on visual tasks will be lower than that of their siblings.

With respect to behavior a higher rate of hyperactivity and conduct disorders is expected for post-meningitic children than for their sibling controls (Kresky et al., 1962; Sproles et al., 1969).

Based on Feigin and Dodge's (1976) findings which indicate that neurological deficits may improve with time or disappear altogether and on Kresky et al.'s (1962) results of a poorer prognosis for children who suffer the disease at a very young age, it is predicted that as a group the probands afflicted with the illness at a younger age and with the shortest follow-up period will be the most deficient, and those older

at the time of illness and with the longest follow-up period will be the least. Finally, children with seizures are expected to show the poorest prognosis (Bloor et al., 1950).

The present study attempted to test these hypotheses. We hoped to establish whether or not there is a profile of abilities specific to post-meningitic children so that remediation procedures and educational plans to suit their needs could be implemented as soon as possible. It was also expected that this study would serve to elucidate the influence of age at onset of illness, time elapsed since illness, seizures, and treatment on the cognitive and behavioral functioning of survivors of H-flu meningitis. Only "normal" survivors were studied in an effort to eliminate confounding environmental variables such as those resulting from the restricted experiences of children neurologically handicapped relative to those free from neurological handicaps.

Method

Subjects. The medical records from 1971 to 1977 at the Montreal Children's Hospital were surveyed for children with diagnosed meningitis due to H-flu, type B, organisms. Only those children who at the time of admission presented the characteristic symptoms of the disease, i.e., nuchal rigidity, fever, vomiting, etc. and whose laboratory analysis grew H-flu organisms in either the cerebro-spinal-fluid (CSF) or blood or both were selected.

For each child, data as to birth history and development prior to and post illness, socio-economic status (SES) assessed by Hollingshead's (1967) two-factor index of social position, severity of illness according to the criteria described by Wehrle, Mathies, Leedom, and Ivler (1967), EEG, and treatment, were collected from medical records and interviews with parents. The data form appears in Appendix A. Wehrle et al. (1967) classified the episode of meningitis as severe if coma, semicoma, significant hypotension, or definite shock were present; moderate if the child presented only with convulsions; and mild if none of the above symptoms applied.

Of the children with diagnosed meningitis only those who at discharge and one year follow-up appeared neurologically, audilogically, and psychologically normal to the pediatrician and whose age at the time of testing ranged from 2-1/2 to 8-1/2 years (due to test-instrument limitations) were included in the study.

Since some of the children were not followed by the Department of Infectious Diseases at the Montreal Children's Hospital but by their private practitioners, a letter and a check list were sent to these

physicians by the author and the Department of Infectious Diseases to be completed with data as to the neurological, developmental, and health conditions of the child at each of the periodic follow-up visits (usually 15 days, 3, 6, 12 months post-illness). The response rate was 90%. The data could not be gathered for 3 children and they were excluded from the study. For a sample of the letter and check list see Appendix A.

Names of 69 children were obtained by the above procedures. A letter was then sent to the parents informing them of the study and requesting their participation (see Appendix A). The letter was followed by a telephone call within one week which had the purpose of personally explaining the project to the parents and asking them information not contained in the medical records pertaining to siblings, academic performance of the proband if in school, and other developmental and sociological variables relevant to the study.

Only 46 of these children could be reached and of them 43 agreed to participate in the study. Twenty-one siblings served as controls. Sibling controls were utilized to control for variables such as family child-rearing styles and social class which after the age of 3 years shows a moderate correlation with intelligence (Koch, 1954). The controls were selected from among the siblings nearest in age to the probands, with the restriction that only one aibling per family participated. An attempt was made to match the control and experimental groups on age and sex. Characteristics of the samples of probands and sibling controls are presented in Appendix B.

Materials. The tests used were the McCarthy Scales of Children's Abilities, the Peabody Picture Vocabulary Test, the Peterson Problem Checklist, and the Conners' Short Form Rating Scale. For purposes of this

study French versions of the Peabody Picture Vocabulary Test, the Peterson Problem Checklist, and the Conners' Short Form Rating Scale were obtained from the English forms and used in the assessment of French speaking children (see Appendix C).

The McCarthy Scales of Children's Abilities (McCarthy, 1970) are similar to the Wechsler Scales in that they provide a profile of abilities (Verbal, Perceptual-Performance, Quantitative, Memory, and Motor). They are standardized for children ranging in age from 2-1/2 through 8-1/2 years. The General Cognitive index which results from summing the Verbal, Perceptual-Performance, and Quantitative indexes, has been found to correlate .71 with the WPPSI full scale score and .81 with the Standford-Binet. The reliability of the five scales and the General Cognitive index calculated for 10 age intervals (2-1/2 through 8-1/2 years) by the split-half method and test-retest when appropriate, ranged from .79 to .93 with a mean of .84. As it concerns its predictive validity the instrument was tested on a sample of 31 first grade children aged 6 to 6-1/2 using the Metropolitan Achievement Tests as the criteria. Results indicated that the General Cognitive, the Quantitative, and the Perceptual-Performance indexes effectively predicted achievement in mathematics and total performance. However, due to the small sample size (N=31) the investigators warn to interpret those results with caution.

The Peabody Picture Vocabulary Test (Dunn, 1965), appropriate for children ranging in age from 2.5 through 18 years, is a well known, well accepted, rapid to administer test of word knowledge. This test was included among the measures of this study because of the ease of administration and the fact that it has been used by previous investigators (Sell et al., 1972) which permitted a comparison of the results and, thus, could help to generalize findings across different populations.

The Peterson Problem Checklist (Peterson, 1961) is a 55 item behavior rating scale appropriate for children in kindergarten to sixth grade. It yields two factors: (a) a conduct disorder factor which refers to the expression of behaviors by the child which are bothersome to society (e.g. disruptiveness, fidgeting, irritability, etc.) and (b) a personality disorder factor which refers to those behaviors that the child inhibits and, thus, disturb him (e.g. anxiety, depression, aloofness, etc.). The correlation between the two scale scores, which are composed of items weighted 2, 1, or 0, was found to be .18. This finding indicates that both factors are reasonably independent. For purposes of this research, two scores, conduct and personality problems, were derived for each child according to the standard scoring of the test.

This scale, however, presents the problems inherent to similar instruments measuring behavior disorders which are the non-availability of norms and sparse research on its validity. This instrument was selected because: (a) it provides information on a variety of behavioral problems that have been reported to be possible side-effects of the illness; (b) it is the best researched instrument in the area, taking into consideration that it covers as adequately as any other available the age range of the children in this investigation; (c) the factors that this scale provides are independent of one another and have appeared consistently in a number of studies despite discrepancies in subjects, variables, and analysis techniques (Hewitt and Jenkings, 1946; Himmelweit, 1953; Peterson, Quay and Cameron, 1959).

The Conners' Short Form Rating Scale (Conners, 1970) consists of 10 items which deal with hyperactive behaviors. It is adequate for children ranging in age from 5 to 16 years. It is scored by assigning

a 0, 1, 2, 3 weight to the item when the "not at all", "just a little", "pretty much" and "very much" categories are selected respectively. These weights are added across the 10 items. In this manner a global score was obtained for each child in the study.

The purpose of using this scale was to supplement information about hyperactive disorders obtained through the Peterson Problem Checklist. It is also a practical instrument since it does not require much time to complete. The Peterson Problem Checklist and the Conners' Short Form Rating Scale are shown in Appendix C.

Procedure. Parents were requested to come to the Montreal Children's Hospital for 1-1/2 hour interview with the proband and, in some cases, with a near age sibling. Upon arrival parents were introduced by the receptionist to the experimenter and showed the testing rooms. All testing was conducted in the Emergency Department.

Parents, after signing a consent form (see Appendix D) were shown the test materials (McCarthy Scales of Children's Abilities, Peabody Picture Vocabulary Test, Peterson Problem Checklist, and Conners' Short Form Rating Scale) to be completed by them and their children. They were then instructed on how to complete the Peterson and Conners rating scales.

Two bilingual examiners, one of them blind as to the group membership of the child, administered the McCarthy Scales of Children's Abilities and the Peabody. Thus, in the case of a family in which the participation of a proband and a sibling control was required, only one visit of the family to the hospital was necessary, avoiding therefore travelling expenses and other inconveniences. Children whose mother tongue was not English or French were tested in either of these languages depending on the parental

report as to the language the child was most proficient in.

To control for any bias in the case of the examiner who, being the major coordinator of the study, was aware of the group membership of the children, a trained observer blind to the hypotheses and group membership, independently scored 12% (N = 4 probands, N = 4 siblings) of the test performance. This procedure made possible the calculation of interjudge reliability. Reliability calculated by correlating the scores assigned by the blind observer and investigator on four subtests of the McCarthy Scales of Children's Abilities (Verbal, Perceptual-Performance, Quantitative, and Memory) and the Peabody Picture Vocabulary Test ranged from .97 to .99 with a median of .98. Thus, the examiner did not appear to be biased in her assessment of the performance of the probands vs. sibling controls.

In the majority of the cases the parents stayed in the testing room for the duration of the assessment. At the end of the session the tests were corrected and some general feedback as to the performance of the children was given to the parents. In cases of severe problems, referrals to other departments (Speech Therapy, Neurology, Psychology, etc.) were made for further assessment.

Results

The scores of the total proband group (N=43), the probands who had a sibling participating in the study (N=21), and the sibling controls (N=21) on the cognitive measures (Verbal, Perceptual-Performance, Quantitative, Memory subtests of the McCarthy Scales of Children's Abilities and the Peabody Picture Vocabulary Test) and behavioral measures (Peterson Conduct problem, Peterson Personality problem, and Conners' hyperactivity score) were examined. Means and standard deviations are presented in Table 1.

Assessment of Predictors of Outcome. Step-wise multiple regression analyses were performed on each of the dependent measures separately to assess the degree to which the dependent measures were associated with the experimental variables (age at illness, follow-up period, seizures, and treatment) and control variables (sex, age at testing, SES, language at testing, language at home, number of siblings, birth order, and hospitalization length). The predictors of outcome within probands and sibling controls yielded by these step-wise multiple regressions analyses are shown in Table 2 and Table 3.

As shown in Table 2, age at illness contributed significantly to the prediction of performance on the Perceptual-Performance subtest. As expected, the younger the child at the time of illness the lower the performance.

Table 1

Means and Standard Deviation Scores of Cognitive and Behavioral Variables for Probands and Siblings

Variables	Probands (N=43) M	Probands (N=43) SD	Probands[a] (N=21) M	Probands[a] (N=21) SD	Siblings (N=21) M	Siblings (N=21) SD
Verbal Subtest Score	44.7	(10.8)	45.2	(11.6)	49.1	(11.8)
Perceptual-Performance Subtest Score	60.4	(12.3)	59.1	(14.3)	61.2	(12.2)
Quantitative Subtest Score	49.1	(10.7)	49.8	(12.3)	52.5	(11.7)
Memory Subtest Score	43.9	(12.9)	46.5	(14.3)	46.6	(13.1)
General Cognitive Index Score	101.7	(19.0)	103.1	(22.5)	107.5	(20.8)
Peabody Vocabulary Score	104.1	(16.9)	100.8	(15.1)	106.6	(18.1)
Conners' Hyperactivity Score	7.9	(6.3)	7.1	(5.2)	8.0	(6.1)
Peterson Conduct Problem Score	8.1	(6.9)	7.5	(5.2)	8.9	(6.6)
Peterson Personality Problem Score	6.5	(7.9)	5.7	(4.4)	5.4	(4.2)

[a]Probands who had a sibling participating in the study.

Table 2

Significant Experimental and Control
Predictors for Probands (N=43) on Dependent Measures

Criterion	Step	Significant Predictors	Multiple R	B Weights
Verbal Subtest	1	Language at Home	.43	-5.9 **
	2	Hospitalization Length	.51	- .3 *
	3	SES	.59	- .1 *
Perceptual Performance Subtest	1	Age at Testing	.39	.2 **
	2	Sex	.48	1.1 *
	3	Hospitalization Length	.59	- .5 **
	11	Age at Illness	.75	-7.2 **
Quantitative Subtest		None		
General Cognitive Index	1	Sex	.31	12.4 *
	2	Hospitalization Length	.46	- .8 **
Memory Subtest	1	Language at Home	.33	-5.5 *
Peabody Test Score	1	Age at Testing	.42	.3 **
	2	Language at Testing	.59	14.5 **
	3	Language at Home	.73	-9.6 **
Conners Hyperactive Score	1	Language at Testing	.34	4.4 *
	2	Birth Order	.46	- .9 *
Peterson Conduct Score	1	Language at Testing	.33	4.6 *
Peterson Personality Score		None		

* $p < .05$

** $p < .01$

Table 3

Control Predictors for
Sibling Controls (N=21) on Dependent Measures

Criterion	Step	Significant Predictors	Multiple R	B Weights
Verbal Subtest	1	Language at Testing	.68	-16.7 **
	2	Sex	.75	7.8 *
	3	Birth Order	.82	- 4.6 *
Perceptual-Performance Subtest	1	Sex	.51	12.4 *
Quantitative Subtest	1	Number of Siblings	.43	- 5.3 *
	2	Language at Testing	.62	-11.1 *
	3	Sex	.72	8.6 *
	4	SES	.80	- .2 *
General Cognitive Index	1	Sex	.49	20.4 *
	2	Language at Testing	.63	-17.4 *
	3	Number of Siblings	.75	- 8.9 *
	4	SES	.82	- .3 *
Memory Subtest	1	Language at Testing	.53	-14.5 *
	2	Language at Home	.68	7.9 *
Peabody Test Score		None		
Conners' Hyperactive Score	1	Language at Testing	.59	7.6 *
	2	Sex	.72	- 5.0 *
Peterson Conduct Score	1	Sex	.55	- 7.2 *
Peterson Personality Score	1	Language at Testing	.50	4.4 *

* $p < .05$

** $p < .01$

Hospitalization length significantly predicted performance of the probands on the Verbal, Perceptual-Performance, and General Cognitive indexes. The longer the hospitalization period the poorer the performance on the mentioned scales. The contribution of this variable is puzzling since contrary to expectations hospitalization length was not found to be related to severity of illness. A Kruskal-Wallis test for independent groups conducted on hospitalization length for the three ratings of severity of illness (mild, $M=14$, $n=35$; moderate, $M=13$, $n=6$; severe, $M=14.5$, $n=2$) indicated that the three groups did not differ significantly with respect to hospitalization length, $\chi^2 = 1.83$, $p > .05$. It might have been worth analyzing severity of illness as a separate variable.

Several control variables were also significantly related to outcome. Post-meningitic children who spoke languages other than English at home performed lower on the Verbal, Memory, and Peabody scales. Also, children tested in French scored lower than their counterparts tested in English on the Peabody and were reported to present more conduct disorders. These results raise questions about the validity of the French versions of the measures. Another possibility is that social class differences existent between the children tested in English and French were at the root of the observed differences in performance. However, a t-test for independent groups indicated that post-meningitic children tested in English and French did not differ significantly with respect to social class ($t(19) = .62$, $p > .05$).

In addition to the above, post-meningitic girls scored better than boys on the Perceptual-Performance and General Cognitive indexes. Older post-meningitic children scored better than their younger counterparts on the Perceptual-performance and Peabody scales.

Probands vs. Controls. To find out the strengths and weaknesses of post-meningitic children compared to their sibling controls and given the fact that the dependent variables were intercorrelated within cognitive and behavioral sets (see Appendix E), multivariate repeated measures analysis of variance for matched groups were conducted on the 21 pairs of post-meningitic children and sibling controls. Since previous factor analyses had shown two factors to underly the dependent measures separate multivariate analyses were conducted on the cognitive (N=5) and behavioral (N=3) variables.

The performance of post-meningitic children did not differ significantly from that of their siblings on the cognitive measures studied, multivariate F (5, 16) = .99, $p > .05$. Similar findings were obtained for the behavioral variables, multivariate F (3, 18) = .52, $p > .05$. In sum, in these overall analyses post-meningitic children did not differ cognitively or behaviorally from their sibling controls.

However, since the step-wise multiple regression techniques showed sex and language at testing to contribute significantly to performance on various variables (see Tables 2 and 3), the data for the children tested in English (N=13) and in French (N=8) were examined separately and sex was covaried out.

A multivariate repeated measures analysis of covariance for matched groups performed on the cognitive data of children tested in English was significant, multivariate F (5, 7) = 4.49, $p < .05$. The univariate F-tests which appear in Appendix F showed that post-meningitic children tested in English scored significantly lower than their siblings on the Peabody, F (1, 11) = 7.26, $p < .05$. Behaviorally, post-meningitic children tested in English did not differ from their controls, multi-

variate F (3, 9) = .26, $p > .05$. Means and standard deviations of cognitive and behavioral variables are shown in Table 4. A summary of the multivariate analyses of covariance is presented in Appendix F.

Probands tested in French (N=8) did not differ cognitively or behaviorally from their sibling controls, multivariate F (5, 2) = 15.9, $p > .05$, and multivariate F (3, 4) = .15, $p > .05$ respectively. These data are presented in Table 5 and the analyses of covariance are summarized in Appendix F.

A comparison of probands tested in English (N=13) and in French (N=8) and their sibling controls' performance on the General Cognitive Index (global IQ) showed no significant difference between the groups (see Table 6).

Table 4

Means and Standard Deviations of Cognitive and Behavioral Measures for Children Tested in English

Variables	Probands (N=13) M	SD	Sibling Controls (N=13) M	SD
Cognitive				
Verbal Subtest Score	47.9	(11.7)	54.6	(9.8)
Perceptual-Performance Subtest Score	60.0	(13.6)	60.9	(12.0)
Quantitative Subtest Score	54.2	(12.4)	55.0	(11.6)
Memory Subtest Score	50.8	(14.3)	49.6	(12.2)
Peabody Test Score	100.5	(13.9)	112.5	(12.0)
Behavioral				
Conners' Hyperactivity Score	4.0	(3.4)	4.6	(3.8)
Peterson Conduct Problem Score	5.0	(3.9)	6.4	(6.5)
Peterson Personality Problem Score	3.6	(3.1)	3.6	(3.2)

Table 5

Means and Standard Deviations of Cognitive and Behavioral Measures for Children Tested in French

Variables	Probands (N=13) M	Probands (N=13) SD	Sibling Controls (N=13) M	Sibling Controls (N=13) SD
Cognitive				
Verbal Subtest Score	40.8	(10.5)	40.2	(9.2)
Perceptual-Performance Subtest Score	57.7	(16.0)	61.7	(10.6)
Quantitative Subtest Score	42.7	(8.8)	48.5	(10.6)
Memory Subtest Score	39.5	(11.5)	41.6	(12.5)
Peabody Test Score	101.1	(18.0)	97.1	(20.8)
Behavioral				
Conners' Hyperactivity Score	12.5	(3.3)	12.5	(6.4)
Peterson Conduct Problem Score	11.5	(4.7)	11.6	(5.9)
Peterson Personality Problem Score	9.0	(4.4)	7.7	(4.6)

Table 6

Global Intelligence Test Results

Group	N	Mean IQ	SD	t-test
English				
Post-meningitic	13	108.4	(22.9)	-.51
Sibling Controls	13	112.1	(20.7)	
French				
Post-meningitic	8	94.5	(19.4)	-.68
Sibling Controls	8	98.7	(17.3)	

Discussion

Results partially supported the hypotheses of this investigation. Thus, children afflicted with hemophilus influenzae meningitis at a younger age performed lower than their older counterparts on the Perceptual-Performance subtest of the McCarthy Scales of Children's Abilities. In addition, for post-meningitic children tested in English it was found that their word knowledge, as evaluated by the Peabody Picture Vocabulary Test, was significantly lower than their sibling controls. Contrary to expectations, however, seizures, time elapsed post-illness, and treatment received in the course of the illness were not found to bear any relationship to either cognitive or behavioral outcome. Furthermore, post-meningitic children did not differ significantly from their siblings in the rate of conduct disorders.

The finding that age at illness predicted the score of post-meningitic children on the Perceptual-Performance subtest is in line with previous reports which indicated that the younger the children at onset of illness, the greater the impact of meningitis on their intellectual functioning (Cook et al., 1949; Lawson et al., 1965; Vernon, 1967; Wolff and Smallwood, 1952). In this study, however, age at illness was not found to predict overall cognitive performance and, also, as a group post-meningitic children did not differ significantly from their siblings on the Perceptual-Performance scale. The latter finding is incongruent with Wright and Jimmerson's (1971) results of significant differences favoring the controls on picture completion, coding, and block design. The attentuated and specific influence of age at onset of illness observed in this study may be due to the fact that only "normal"

survivors were investigated, or in other words to sample selectivity. It is also worth mentioning that Wright and Jimmerson (1971) did not study the effects of age at onset of illness. In accounting for the discrepancy with Wright and Jimmerson's (1971) findings of significant differences between probands and controls one should note that they studied only 10 children and thus, their findings could be the result of random fluctuations. Furthermore, these investigators did not observe any differences on the Frostig and Bender tests which, to a certain extent, is in agreement with present results.

The significantly lower word knowledge observed in the case of probands tested in English is consistent with previous reports (Sell et al., 1972) and, coupled with the observation of an almost significant difference in performance on the Verbal scale support the hypothesis that post-meningitic children considered "normal" may exhibit language deficiencies as a result of central auditory processing disturbances. However, similar findings were not observed for post-meningitic children tested in French. This could have been due to the inability of the French versions of the experimental measures used to detect subtle differences. An alternative explanation for the failure to find any significant differences on the cognitive performance of post-meningitic children tested in French may have been the small size of the sample used ($N = 8$) which did not allow for an optimum test of the hypothesis. Nevertheless it weakens the generalizability if these results and calls for further research using more homogeneous larger samples and more adequate assessment instruments.

That these observed differences in language development, for probands tested in English, were not predicted by any of the variables under investigation, i.e. age at illness, lapse of time post-illness, seizures, and treatment is puzzling. The explanation as to the cerebral site affected by the meningeal infection in relation to language disturbances and the variables affecting the outcome rests on further investigations.

The observation that post-illness time lapses longer than a year did not affect outcome appears to indicate that an assessment of post-meningitic children one year following the meningeal episode is likely to reveal any permanent sequelae or else a valid diagnosis of normality. This result supports current follow-up practices (15 days, 3, 6, and 12 months post-illness) at the Montreal Children's Hospital and suggests that longer follow-up periods are not warranted.

The observed lack of relationship between treatment received in the course of the malady and outcome agrees with published reports of comparability of ampicillin and chloramphenicol in terms of mortality, morbidity, and complications of the disease (Barrett et al., 1972; Feigin and Dodge, 1976; Lindberg et al., 1977; Schackelford et al., 1972; Schulkind et al., 1971). However, they are contrary to reports by Lindberg et al. (1977) of a higher incidence of residuae in the recipients of both drugs conjointly. Nevertheless, this discrepancy can easily be explained by the fact that Lindberg et al.'s (1977) subjects received ampicillin and chloramphenicol concommitantly for the duration of therapy, while the subjects of this study generally received both drugs until sensitivity of the hemophilus influenzae organism to ampicillin was proven. At that point, usually three days,

chloramphenicol was discontinued. Thus, the results of this study indicate that this is a valid regime which does not seem to result in a higher incidence of sequelae.

The fact that presence or absence of seizures during the illness bore no significant relationship to psychological outcome in the present investigation is contrary to the results reported by Bloor et al., (1950) which suggested that both the occurrence and amenability to treatment of seizures appeared to be factors affecting sequelae to meningitis. However, the treatment of seizures has since the 50's considerably improved and this may account for the disparity of the findings. Thus, at the Montreal Children's Hospital seizures present at onset of illness are reported to be under control within 24 hours (Pearson, Note 1). On the other hand, due to the small sample size these findings should be interpreted with caution.

The significant contribution of hospitalization length to the prediction of the probands performance on the Verbal, Perceptual-Performance, and General Cognitive indexes is unclear since no relationship of this variable to severity of the illness could be detected in the data. It could be that hospitalization length reflects individual differences in rate of recovery from this trauma, and that these same individual differences are related to level of intellectual development. It may also represent deprivation during hospitalization which varied from 8 to 60 days. On the other hand, it may be speculated that regardless of severity of illness parents of post-meningitic children with longer hospitalization lengths may have interpreted the episode as more severe and, subsequently tended to overprotect their children, expect less from them, etc. with the

result of hindering their development. It may be worth pursuing this hypothesis.

Finally, with respect to behavioral problems post-meningitic children were not found to differ significantly from their sibling controls. As a group boys were reported to exhibit more conduct and hyperactive behaviors than girls. This phenomenon is consistently reported in the literature (Peterson, 1961) and it could be related to girls in our society. The fact that post-meningitic children did not present a significantly higher incidence of behavioral problems is contrary to reported findings (Kresky et al., 1962; Sproles et al., 1969). However, it could be attributed to the fact that only "normal" survivors participated in this study, and it should be taken as reassuring. Another explanation could be that the behavioral measures used in this study failed to detect disorders in the younger children.

In conclusion, the results of this investigation generally suggest optimism with respect to the cognitive and behavioral functioning of post-meningitic children diagnosed as normal at one year following the meningeal episode. Overconcern by parents and educators is not warranted by these findings. Parents should avoid a protectionistic attitude and expect of their normal post-meningitic children as much as of their siblings. On the other hand, the results also indicate that the language development of these children may lag relative to other intellectual areas. Therefore, careful assessment and remediation of any observed deficits may lead to better achievement in the language areas. In addition, the development of spatial skills in children younger at onset of illness should be specifically followed one year post-illness.

Research is needed to test the hypothesis put forth in this study that as in the case of aphasic children the language deficiencies of post-meningitic children may be due to central auditory processing disturbances for rapid auditory information. In exploring this hypothesis a paradigm similar to Tallal's (1976) could be used.

Finally, it is suggested that future research on the sequelae of hemophilus influenzae meningitis takes into account the variable of age at illness in an attempt to shed more light on the relationship of this variable to outcome of the disease.

Reference Note

[1]Pearson, L. Personal communication, May 19, 1979.

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Appendix A

Developmental and Medical Status Data Forms and Report Letters to Parents and Physicians

Child Development and Birth History Data Form

Patient Name: _____ _____
Last First

Father's Name: _____ _____
Last First

Hospital Unit No.: _____

Sex: Male_____ Female_____

Birthdate: _____
Day Month Year

Age: _____

Address: _____

School's Name: _____

School's Address: _____

Language at Home: _____ At School: _____

Telephone no. at Home: _____ At Work: _____

Parents Status: Married_____ Divorced or Separated_____

Widowed_____ Single_____

No. of Siblings: _____

Sex of Siblings: _____

Age of Siblings: _____

Name of Siblings: _____

Siblings Developmental History if unusual: _____

_____

_____

_____

Pregnancy and Delivery of Patient: Normal _____

Complications _____

_____

Premature: Yes_____ No_____ Gestational Age_____

Milestones prior to illness: Normal_____ Delayed_____

Sat alone:_____ Walked_____ First Words_____

Date Hemophilus Influenzae Meningitis Diagnosed:_____
Day Month Year

Age at Time of Illness:_____

Time elapsed since illness:_____

Severity of Illness:_____

How was the causative organism identified?: CSF_____ Blood_____

Had the patient seizures?: Yes_____ No_____

When did the patient have seizures?: At the time of hospitalization only_____

After the third hospitalization day_____

Treatment Administered: Penicillin_____ Ampicillin_____

Chloramphenicol_____ Combination of_____

_____

Response to Therapy: Good_____ Poor _____

Hospitalization Length:_____

Diagnosis at Discharge from Hospital: Normal_____ Minor Neurological Sequelae_____

Major Neurological Sequelae_____

EEG at Last Check-Up Visit: Normal_____ Abnormal_____

Date of Last Check-Up and Diagnosis:_____
Day Month Year

Physical Examination at Last Check-Up Visit:Normal_____ Abnormal___

Audiogram Date:_____ Diagnosis:_____
Day Month Year

Development since Illness: Normal_____ Abnormal_____

What Areas are not Developing Normally?:_____

_____

Behavioral Changes since Illness: Yes___ No___If Yes specify_____

_____

Psychological Tests Results if available:_____

_____

Father's Age:_____ Mother's Age:_____

Father's Occupation:_____Mother's Occupation:_____

Father's Education:_____Mother's Education:_____

Father's Religion:_____Mother's Religion:_____

Unusual Illnesses in Parents' Families:_____

_____

Any cases of retardation in the parents' families:_____

_____

SES:_____

Letter to Treating Physicians

Dear Dr.

We are kindly requesting you to complete the enclosed form with medical data from your follow-up examination of the child Your collaboration will be extremely helpful for the purposes of the study here described.

The departments of Infectious Diseases and Psychology at the Montreal Children's Hospital are studying the sequelae of children who have had Haemophilus influenzae meningitis in the last six years. The children involved will include those who have appeared normal at discharge and one year post-illness. They will be assessed with respect to cognitive and behavioral functioning in relation to sibling controls.

With the decline of mortality, the question of whether or not the survivors suffer from psychological sequelae became of paramount importance. Sell et al. (1972), in two separate studies, found: (a) the mean global IQ of the probands to be significantly lower than their non-meningitic siblings, and (b) lower psycholinguistic scores in a population of children with meningitis of various etiological agents.

Feigin and Dodge (1976) found low intellectual achievement in 28% of children following discharge, and severe defects persisting in 8%. Many minor neurological and also audiometric deficiencies disappeared with time. Lindberg et al. (1977) found 26.8% neurological and psychological residua both with auditory impairment being the most common type of sequelae.

None of the studies provide information on the differential effects of age at illness and length of follow-up period. The present study will assess the "normal" survivors of H-flu meningitis as compared to non-meningitic siblings in specific areas of functioning: memory, verbal, quantitative, perceptual-performance, and general intellectual functioning. Outcome will be analyzed in relation to age of the children at the time of illness, time elapsed since illness, presence or absence of seizures during illness, and treatment.

Each child is being seen at the Montreal Children's Hospital for testing. Thank you very much for any help you are able to give us.

Yours sincerely,

Medical Data Request Form

Name of child: _____
(please print)

Date of last visit: _____

School progress: Normal _____ Other _____

Social situation: _____

Current medication: _____

Subsequent medical problems: _____

_____

CNS Examination: _____

Linguistic ability: Adequate _____ Delayed _____

Audiometric Evaluation: Date conducted _____

Diagnosis _____

Developmental level: Adequate _____ Delayed _____

If delayed, in which areas? _____

_____

Letter to Parents

Dear Parents,

As you well know, the department of Infectious Diseases at the Montreal Children's Hospital follows children that suffered from Haemophilus influenzae meningitis, in an attempt to diagnose, as early as possible, any abnormalities in the child due to the illness, so that adequate treatment to remediate them, if present, can be provided.

We are writing to ask your child to participate in a follow-up project.

Modern medical treatment has resulted in many children who suffered this illness appearing perfectly healthy to the pediatricians at discharge. We are also interested in ensuring that these children function well in the areas of development important for school performance, e.g. attention, memory. Information in these areas is of great importance in planning adequate educational programs for these children. We also wish to help them at a stage of development when improvement of any deficits is most likely to occur.

The department of Infectious Diseases at this hospital in collaboration with Concordia University are undertaking a study that, hopefully, will shed light on the mentioned issues.

We would like to come to the Montreal Children's Hospital for a 1-1/2 hour interview, at a time convenient for you. During the interview the child will play some games and work with materials interesting to a child their age. We would like one parent

to accompany the child to fill in a brief questionnaire, and they may attend the interview if they wish. In some families we will also ask if a brother or sister close in age could come.

We will be telephoning you in a week or two to answer any questions you might have and to ask for your participation. We think your collaboration in this study will be interesting and beneficial to your child. It is also of great importance in future planning for children like your child who suffered from Haemophilus influenzae meningitis.

Many thanks in advance. In the hope of speaking to you soon, we remain:

Sincerely yours,

Appendix B

Characteristics of Probands and Sibling Controls

Description of the Sample of Post-Meningitic Children

	Post-Meningitic	Post-Meningitic with Sibling Control
Mean age at illness (months)	17.6 (14.3)[a]	17.5 (14.5)[a]
Mean follow-up (months)	49.6 (21.7)[a]	44.6 (19.9)[a]
Mean length of hospitalization	14.6 (8.0)[a]	15.6 (10.6)[a]
Number of children having seizures	6 (13.9)[b]	3 (14.2)[b]
Number of children treated only with ampicillin	25 (58.1)[b]	11 (52.3)[b]
Number of children treated with combined therapy (ampicillin and chloramphenicol)	18 (41.8)[b]	10 (47.6)[b]
Total N per group	43	21

Note: [a]Numbers in parentheses indicate standard deviations

[b]Numbers in parentheses indicate percentages.

Characteristics of the Sample of Probands

and Sibling Controls

	Probands	Probands[a]	Siblings
Mean age at testing (months)	69.6 (21.1)[b]	62.1 (22.2)[b]	74.8 (18.8)[b]
Mean age at testing of children tested in English	68.2 (18.7)[b]	63.0 (18.5)[b]	76.0 (22.7)[b]
Mean age at testing of children tested in French	65.7 (25.0)[b]	60.6 (27.3)[b]	72.3 (13.6)[b]
Mean Hollingshead SES rating	41.7 (18.6)[b]	39.0 (17.9)[b]	39.0 (17.9)[b]
Number of males	28 (62.8)[c]	11 (52.3)[c]	12 (57.1)[c]
Number of Negro children	2 (4.6)[c]	1 (4.7)[c]	1 (4.7)[c]
Number of English speaking children	20 (46.5)[c]	13 (61.9)[c]	13 (61.9)[c]
Number of French speaking children	14 (32.6)[c]	8 (38.1)[c]	8 (38.1)[c]
Number of children whose mother tongue was other than English or French	9 (20.9)[c]	0.0	0.0
Number of children tested in English	26 (60.5)[c]	13 (61.9)[c]	13 (61.9)[c]
Number of children tested in English that were males	11 (25.5)[c]	5 (38.4)[c]	5 (38.4)[c]
Number of children tested in French that were males	17 (83.3)[c]	6 (75)[c]	7 (87)[c]
Total N per group	43	21	21

Note: [a]Probands who had a sibling participating in the study

[b]Numbers in parentheses indicate standard deviations

[c]Numbers in parentheses indicate percentages.

Summary of Comparisons between Post-Meningitic

Children and Sibling Controls

Group	N	Mean Age at Testing[a]	SD	t-test
Post Meningitic	21	62.1	22.2	-1.77
Sibling Controls	21	74.8	18.8	
Post Meningitic Children Tested In English	13	63.0	18.5	-1.63
Sibling Controls	13	76.0	22.7	
Post Meningitic Children Tested In French	8	60.6	27.3	-.83
Sibling Controls	8	72.3	13.6	

[a]Age in months

Appendix C

Assessment Instruments

French Version of Peabody Picture Vocabulary Test

Form A

EXAMPLES

A. lit
B. poisson
C. papillon

ADDITIONAL

A. cuiller
B. chaise
C. crayon

A. mamma
B. papa
C. pomme

1. (4) auto
2. (3) vache
3. (1) bebe
4. (2) fille
5. (1) ballon
6. (3) bloc
7. (2) clown
8. (1) clef
9. (2) tarte
10. (2) poulet
11. (4) souffler
12. (4) lavabo
13. (1) creuser
14. (1) jupe
15. (4) attraper
16. ( ) tambour
17. (3) feuille
18. (4) attacher
19. (1) cloture
20. (2) baton
21. (4) abeille
22. (3) buisson
23. (1) verser
24. (1) coudre
25. (3) pamplemousse
26. (2) maitresse
27. (3) construire
28. (3) fleche
29. (2) kangourou
30. (3) accident
31. (3) nid
32. (3) char d'assaut
33. (1) enveloppe
34. (2) cueillir
35. (1) insigne
36. (3) lunettes
37. (2) paon
38. (3) reine
39. (4) carrosse
40. (1) fouet
41. (4) filet
42. (4) taches de rousseur
43. (3) aigle
44. (2) torsion
45. (4) cirer
46. (2) cadran
47. (2) baillir
48. (2) debouler
49. (1) signal
50. (1) capsule
51. (4) sous-marin
52. (4) thermos
53. (3) projecteur
54. (4) groupe
55. (3) plaquer
56. (1) transport
57. (1) comptoir
58. (2) ceremonie
59. (3) gousse
60. (2) orignial
61. (3) diriger
62. (4) entonnoir
63. (2) delice
64. (3) couferencier
65. (2) communication
66. (4) archer
67. (1) stade
68. (1) excaver
69. (4) assaillir
70. (1) acrobate
71. (1) meringue
72. (3) appareil
73. (4) chimiste
74. (3) arctique
75. (4) destruction

French Version of Peabody Picture Vocabulary Test

Form A

(Cont'd)

76. (3) porteur
77. (2) côte
78. (4) hisser
79. (1) lamentation
80. (2) ressort
81. (3) kayak
82. (2) sentinelle
83. (4) sillon
84. (1) poutre
85. (3) fragment
86. (2) planer
87. (3) deuil
88. (4) escarpment
89. (2) crise
90. (1) submerger
91. (3) descendre
92. (2) pouf
93. (1) canine
94. (1) sonder
95. (3) alpinisme
96. (3) evaluer
97. (4) confiner
98. (4) précipitation
99. (1) pignon
100. (1) amphibie

French Version of Peabody Picture Vocabulary Test

Form B

1.	(2)	table	26.	(3)	conducteur	51.	(1)	locomotive
2.	(4)	autobus	27.	(2)	nouer	52.	(2)	ruche
3.	(2)	cheval	28.	(1)	cerf-volant	53.	(4)	moulinet
4.	(3)	chien	29.	(1)	rat	54.	(1)	insecte
5.	(4)	soulier	30.	(1)	l'heure	55.	(1)	ronger
6.	(4)	doigt	31.	(4)	(une) voile	56.	(2)	arme
7.	(3)	bateau	32.	(2)	ambulance	57.	(3)	rampe
8.	(2)	enfants	33.	(2)	coffre	58.	(1)	idole
9.	(1)	cloche	34.	(4)	ski	59.	(1)	globe
10.	(4)	tortue	35.	(2)	hamcon	60.	(3)	morse
11.	(2)	grimper	36.	(1)	des pinces	61.	(1)	classer
12.	(1)	lampe	37.	(3)	guepe	62.	(3)	cisailles
13.	(3)	assis	38.	(2)	barbier	63.	(1)	horreur
14.	(2)	veston	39.	(3)	parachute	64.	(4)	chef-cuisinier
15.	(1)	tirer	40.	(4)	selle	65.	(4)	recolter
16.	(2)	bague	41.	(3)	temperature	66.	(3)	construction
17.	(1)	clou	42.	(1)	capitaine	67.	(4)	observatoire
18.	(2)	frapper	43.	(2)	baleine	68.	(4)	aide
19.	(3)	pneu	44.	(4)	monnaie	69.	(2)	eriger
20.	(3)	échelle	45.	(1)	equilibre	70.	(3)	pur-sang
21.	(1)	serpent	46.	(3)	toile d'araignee	71.	(4)	épi
22.	(1)	rivière	47.	(3)	serment	72.	(4)	parure
23.	(4)	sonner	48.	(1)	querelle	73.	(3)	cordonnier
24.	(4)	cuire	49.	(3)	borne-fontaine	74.	(2)	automne
25.	(2)	cornet	50.	(4)	jumelles	75.	(3)	mecontentement

French Version of Peabody Picture Vocabulary Test

Form B

(Cont'd)

76. (4) erudit
77. (1) oasis
78. (3) souder
79. (3) etonnement
80. (1) flanc
81. (2) chaume
82. (1) jurisprudence
83. (2) arbrisseau
84. (3) portail
85. (4) demeure
86. (1) lubrifier
87. (2) pieton
88. (3) vallon
89. (3) jubilant
90. (2) charge
91. (2) poursuite
92. (4) gobelet
93. (2) rongeur
94. (3) confidences
95. (4) allonge
96. (1) fouiller
97. (2) douves
98. (3) salutation
99. (2) barrière
100. (3) poulain

Peterson Problem Checklist

Name of child_____ Case No._____

Name of rater_____ Relationship to child_____

Please indicate which of the following constitute problems, as far as this child is concerned. If an item does not constitute a problem, encircle the zero, thus, 0; if an item constitutes a mild problem, encircle the one, 1 ; if an item constitutes a severe problem, encircle the two, 2 . Please complete every item.

0 1 2	1.	Thumb-sucking
0 1 2	2.	Restlessness, inability to sit still
0 1 2	3.	Attention-seeking, "show-off" behavior
0 1 2	4.	Skin allergy
0 1 2	5.	Doesn't know how to have fun; behaves like a little adult
0 1 2	6.	Self-consciousness; easily embarrassed
0 1 2	7.	Headaches
0 1 2	8.	Disruptiveness; tendency to annoy and bother others
0 1 2	9.	Feelings of inferiority
0 1 2	*.	Dizziness, vertigo
0 1 2	10.	Boisterousness, rowdiness
0 1 2	11.	Crying over minor annoyances and hurts
0 1 2	12.	Preoccupation; "in a world of his own"
0 1 2	13.	Shyness, bashfulness
0 1 2	14.	Social withdrawal, preference for solitary activities
0 1 2	15.	Dislike for school
0 1 2	16.	Jealousy over attention paid other children
0 1 2	*	Difficulty in bowel control, soiling
0 1 2	17.	Prefers to play with younger children
0 1 2	18.	Short attention span
0 1 2	19.	Lack of self-confidence
0 1 2	20.	Inattentiveness to what others say
0 1 2	21.	Easily flustered and confused
0 1 2	22.	Lack of interest in environment, generally "bored" attitude
0 1 2	23.	Fighting
0 1 2	24.	Nausea, vomiting
0 1 2	25.	Temper tantrums
0 1 2	26.	Reticence, secretiveness
0 1 2	27.	Truancy from school
0 1 2	28.	Hypersensitivity; feelings easily hurt
0 1 2	29.	Laziness in school and in performance of other tasks
0 1 2	30.	Anxiety, chronic general fearfulness
0 1 2	31.	Irresponsibility, undependability
0 1 2	32.	Excessive daydreaming
0 1 2	33.	Masturbation
0 1 2	34.	Hay fever and/or asthma
0 1 2	35.	Tension, inability to relax

Peterson Problem Checklist

(Cont'd)

0 1 2	36. Disobedience, difficulty in disciplinary control
0 1 2	37. Depression, chronic sadness
0 1 2	38. Uncooperativeness in group situations
0 1 2	39. Aloofness, social reserve
0 1 2	40. Passivity, suggestibility; easily led by others
0 1 2	41. Clumsiness, awkwardness, poor muscular coordination
0 1 2	42. Stuttering
0 1 2	43. Hyperactivity; "always on the go"
0 1 2	44. Distractibility
0 1 2	45. Destructiveness in regard to his own and/or others' property
0 1 2	46. Negativism, tendency to do the opposite of what is requested
0 1 2	47. Impertinence, sauciness
0 1 2	48. Sluggishness, lethargy
0 1 2	49. Drowsiness
0 1 2	50. Profane Language, swearing, cursing
0 1 2	51. Prefers to play with older children
0 1 2	52. Nervousness, jitteriness, jumpiness; easily startled
0 1 2	53. Irritability; hot-tempered, easily aroused to anger
0 1 2	* Enuresis, bed-wetting
0 1 2	54. Stomach aches, abdominal pain
0 1 2	55. Specific fears, e.g., of dogs, of the dark

Please note here any problems not mentioned above.

_____

_____

_____

*Numbers have been omitted for items which were rated but not analyzed. Remaining numbers thus correspond to those in subsequent tables.

Liste Controle des Problemes de Peterson

Nom de l'enfant:_____

Nom de l'evaluateur:_____

Degre de parente avec

l'enfant:_____

Parmi les signes et malaises ci-dessous, veuillez indiquer lequel (ou lesquels) s'applique(nt) a l'enfant. S'il n'y a aucun probleme, encerclez le chiffre "0"; si le signe ou malaise n'est pas trop grave, encerclez le chiffre "1"; si le probleme est serieux, encerclez le chiffre "2". Veuillez, s'il vous plait, considerer tous les postes.

0 1 2	1.	Sucer son pouce
0 1 2	2.	Instable, incapable de rester assis
0 1 2	3.	Veut attirer l'attention, comportement de vantardise
0 1 2	4.	Signes d'allergie sur la peau
0 1 2	5.	Ne sait comment s'amuser, se comporte comme un petit adulte
0 1 2	6.	Conscience de soi; facilement embarrasse
0 1 2	7.	Maux de tete
0 1 2	8.	Conduite erratique, tendance a ennuyer et a importuner les autres
0 1 2	9.	Sentiments d'inferiorite
0 1 2	*	Etourdissements, vertiges
0 1 2	10.	Combativite, brutalite
0 1 2	11.	Pleure pour des riens et petits malaises
0 1 2	12.	Preoccupe; "dans un monde a lui"
0 1 2	13.	Timidite, gene
0 1 2	14.	Insociable, prefere des activites en solitaire
0 1 2	15.	N'aime pas l'ecole
0 1 2	16.	Jaloux de l'attention portee aux autres enfants
0 1 2	*	Manque de controle des selles, salit son linge
0 1 2	17.	Prefere jouer avec des plus jeunes
0 1 2	18.	"Crises de nerfs" si on ne s'interesse pas a lui tout de suite
0 1 2	19.	Manque de confiance en soi
0 1 2	20.	N'ecoute pas ce que disent les autres
0 1 2	21.	Facilement deroute et confus
0 1 2	22.	Absence d'interet pour ce qui l'entoure, attitude generale d'ennui
0 1 2	23.	Aime se battre
0 1 2	24.	Nausees, vomissements
0 1 2	25.	Sautes d'humeur
0 1 2	26.	Reticence, aime a garder ses secrets
0 1 2	27.	Delits a l'ecole
0 1 2	28.	Hyper-sensible, vite choque
0 1 2	29.	Paresse a l'etude et dans la realisation d'autres taches
0 1 2	30.	Angoisses, frayeurs generales frequentes
0 1 2	31.	Irresponsable, pas fiable

Liste Controle des Problemes de Peterson

(Cont'd)

0 1 2	32.	Reveries excessives dans ses actes
0 1 2	33.	Fievre des foins (rhumes) et/ou asthme
0 1 2	35.	Tension, incapacite de relaxer
0 1 2	36.	Desobeissance, difficile a s'adapter a une discipline de comportement
0 1 2	37.	Depression, cafard ou tristesse chroniques
0 1 2	38.	Non-cooperant(e) dans des situations de groupe
0 1 2	39.	Retracte; reserve
0 1 2	40.	Passivite, influencable, se laisse facilement mener par les autres
0 1 2	41.	Maladroit(e), gauche, mouvements mal coordonnes
0 1 2	42.	Begaie
0 1 2	43.	Hyper-activite, toujours pret a bouger
0 1 2	44.	Facilement distrait(e)
0 1 2	45.	Porte(e) a detruire ce qui lui appartient, soit a lui ou aux autres
0 1 2	46.	Negativisme, tendance a faire le contraire de ce qui est demande
0 1 2	47.	Impertinence, obstination
0 1 2	48.	Laisser-aller; lethargie
0 1 2	49.	Endormi(e)
0 1 2	50.	Gros mots, jurons (sacres)
0 1 2	51.	Prefere jouer avec les plus ages
0 1 2	52.	Nervosite, facilement emu(e); se saisit facilement
0 1 2	53.	Irritabilite; coleres; se faches facilement
0 1 2	*	Incontinence d'urine
0 1 2	54.	Brulements et maux d'estomacs
0 1 2	55.	Peurs, exemples: des chiens, de l'obscurite

Veuillez indiquer ici tout autre signe ou malaise non mentionne ci-haut: _____

_____

_____

*Enumeration non effectuee pour des signes et malaises evalues mais non analyses. Les numeros restants correspondent ainsi aux tableaux subsequents.

Conners' Short Form Rating Scale

Child's Name_____

Parent's Observations:

Information obtained_____
Month Day Year

By_____
Name of Parent

Please indicate which of the following constitute problems, as far as this child is concerned. If an item does not constitute a problem, check "Not at all"; if an item constitutes a mild problem, check "Just a little"; if an item constitutes a severe problem, check "Pretty much"; if an item constitutes a very severe problem, check "Very much". Please complete every item.

Observation	Not at all	Just a little	Pretty much	Very much
1. Restless or overactive				
2. Excitable, impulsive				
3. Disturbs other children				
4. Fails to finish things he starts - short attention span				
5. Constantly fidgeting				
6. Inattentive, easily distracted				
7. Demands must be met immediately-easily frustrated				
8. Cries often and easily				
9. Mood changes quickly and drastically				
10. Temper outbursts, explosive and unpredictable behavior				

Comments:

Formulaire en condense de l'echelle d'evaluation de Conners

Nom de l'enfant: _____

Observation des parents:

Information obtenue: _____
mois jour annee

Par: _____
nom du pere ou de la mère

Parmi les signes et malaises ci-dessous, veuillez indiquer lequel (ou lesquels) s'applique(nt) a l'enfant. S'il n'y a aucun probleme, crochez "pas du tout". Si le signe ou malaise n'est pas trop grave, crochez "Tres peu". Si le probleme est serieux, crochez "Assex prononce". Si le probleme est tres serieux, crochez "Beaucoup". Veuillez, s'il vous plait, considerer tous les postes.

Observation	Pas du tout	Tres peu	Assez prononce	Beaucoup
1. Turbulent, hyper-actif				
2. Emotif, impulsif				
3. Importune les autres enfants				
4. Ne finit pas ce qu'il a commence - il faut s'en occuper tout de suite				
5. Constamment nerveux				
6. Inattentif - facilement distrait				
7. Doit être satisfait sur le champ-facilement frustre				
8. Pleure souvent et facilement				
9. Sautes d'humeur prononcees				
10. Coleres, reactions violentes inattendues				

Commentaires:

Appendix D

Consent Forms in English and in French

CONSENT FORM

I agree/do not agree to have my child/children _____ and _____ participate in the study of the cognitive and behavioral functioning of children subsequent to *Haemophilus influenzae* meningitis directed by Dr. A.B. Doyle of Concordia University. I understand that all individual results will be kept confidential in reports of this study.

NAME: _____

DATE: _____

SIGNATURE: _____

ADDRESS: _____

TELEPHONE #: _____

FORMULE DE CONSENTMENT

Je suit d'accord/je ne suis pas d/accord pour que mon enfant/enfants _____ et _____ participe à l'étude du developpement et du comportement des enfants qu'ont souffert de la meningite a Haemophilus influenzae dirigee par A.B. Doyle de l'Universite Concordia. Je suis au courant que tous les resultats individuels seront gardes confidentiellement dans les rapports sur cette etude.

NOM: _____

DATE: _____

SIGNATURE: _____

ADRESSE: _____

TELEPHONE: _____

Appendix E

Intercorrelations among Variables for

Post-Meningitic Children (N=43)

	Age at illness	Follow-up	Seizures	Treatment	Sex	Age at Testing	SES	Language at Testing	Language at Home	No. of Siblings	Birth Order	Hospitalization Length	Verbal	Perceptual	Quantitative	Cognitive Index	Memory	Peabody	Conners'	Peterson Conduct
Follow-up	-.33																			
Seizures	.25	.00																		
Treatment	.18	-.83	-.05																	
Sex	-.05	.06	-.31	-.09																
Age at Test	.31	.78	.17	-.71	.02															
SES	-.06	-.06	.08	.19	-.12	-.10														
Language at Testing	.01	-.02	.22	.06	-.22	-.02	.21													
Language at Home	-.04	.05	.01	-.11	-.24	.01	.09	.32												
Number of Siblings	-.18	.44	.05	-.31	-.00	.33	.23	.20	-.00											
Birthorther	-.18	.33	-.05	-.21	.04	.21	.27	.25	.02	.94										
Hospitalization	-.11	.21	-.28	-.08	.28	.14	-.20	-.17	-.20	-.01	.04									
Verbal	.19	-.15	.02	.05	.27	-.02	-.26	-.36	-.43	-.08	-.11	-.19								
Perceptual	.22	.23	.06	-.32	.29	.39	-.11	.17	-.00	.09	.11	-.19	.43							
Quantitative	.19	.00	.00	-.08	.21	.13	.05	-.28	-.21	-.06	-.04	-.20	.65	.57						
Cognitive index	.25	-.02	.02	-.12	.31	.15	-.20	-.21	-.26	-.07	-.06	-.23	.86	.75	.85					
Memory	.22	-.03	.01	-.02	.28	.11	-.15	-.33	-.33	-.04	-.07	-.15	.80	.58	.83	.88				
Peabody	.28	.23	.32	-.25	.02	.42	-.04	.41	-.25	.30	.30	-.12	.23	.49	.22	.36	.19			
Conners'	.01	.01	.12	.06	-.24	.02	.14	.34	.24	-.15	-.20	-.12	-.33	-.16	-.25	-.30	-.31	-.01		
Peterson Conduct	-.04	.07	.16	-.03	-.10	.03	.20	.33	.06	-.01	-.06	-.03	-.11	-.07	-.13	-.12	-.15	.17	.70	
Peterson Personality	-.02	.18	.14	-.11	.02	.16	.23	.27	.04	.08	-.01	.02	-.14	-.04	-.14	-.13	-.09	.13	.56	.85

For $p < .05$ (two-tailed) critical r (41) = .30

Appendix F

Summary Tables of Multivariate Analyses of Covariance

Summary Table for Multivariate Analyses of Covariance of Cognitive Measures for Children Tested in English (N=13)

Variables	Mean SQ	Univariate F	df
Verbal Subtest	297.84	3.05	1/11
Perceptual-Performance Subtest	4.65	.04	1/11
Quantitative Subtest	4.65	.05	1/11
Memory Subtest	9.84	.08	1/11
Peabody Picture Vocabulary Test	924.03	7.26*	1/11

* $p < .05$

Summary Table for Multivariate Analyses of Covariance of Behavioral Measures for Children Tested in English (N=13)

Variables	Mean SQ	Univariate F	df
Conners' Hyperactivity Score	2.46	0.19	1/11
Peterson Conduct Problem Score	12.46	0.90	1/11
Peterson Personality Problem Score	0.03	0.01	1/11

Summary Table for Multivariate Analyses of

Covariance of Cognitive Mesures for

Children Tested in French (N=8)

Variables	Mean SQ	Univariate F	df
Verbal Subtest	.87	.02	1/6
Perceptual-Performance Subtest	81.42	.39	1/6
Quantitative Subtest	122.46	2.94	1/6
Memory Subtest	8.37	.08	1/6
Peabody Picture Vocabulary Test Score	100.89	.25	1/6

Summary Table for Multivariate Analyses of

Covariance of Behavioral Measures

for Children Tested in French (N=8)

Variables	Mean SQ	Univariate F	df
Conners' Hyperactivity Score	.18	.01	1/6
Peterson Problem Conduct Score	.11	.006	1/6
Peterson Personality Problem Score	6.52	.45	1/6