# Etiologic yield of subspecialists' evaluation of young children with global developmental delay

*Michael I. Shevell, MD, CM, FRCPC, Annette Majnemer, PhD, Peter Rosenbaum, MD, CM, FRCPC, and Michal Abrahamowicz, PhD*

**Objective:** To determine the etiologic yield of subspecialists' evaluation of young children with global developmental delay. In addition, variables that may predict finding an underlying etiology were also identified.

**Methods:** All children <5 years of age, referred over an 18-month period to subspecialty services for initial evaluation of a suspected developmental delay, were prospectively enrolled. Diagnostic yield was ascertained after the completion of clinical assessments and laboratory investigations requested by the evaluating physician.

**Results:** Ninety-nine children (71 boys) were found to have global developmental delay; 96% had a mild or moderate delay documented. An etiologic diagnosis was determined in 44. Four diagnoses (cerebral dysgenesis, hypoxic-ischemic encephalopathy, toxin exposure, chromosomal abnormalities) accounted for 34 of 44 (77%) of the diagnoses made. The presence of co-existing autistic traits was associated with significantly decreased diagnostic yield (0/19 vs 44/80, $P < .0001$), whereas specific historical features (eg, family history, toxin exposure, and perinatal difficulty; 23/32 vs 21/67, $P = .0002$) and findings on physical examination (eg, dysmorphology, microcephaly, and focal motor findings; 35/48 vs 9/51, $P < .0001$) were significantly associated with identifying a diagnosis. Multiple logistic regression analysis identified antenatal toxin exposure, microcephaly, focal motor findings, and the absence of autistic traits as significant predictor variables for the identification of an etiology.

**Conclusion:** An etiologic diagnosis is often possible in the young child with global developmental delay, particularly in the absence of autistic features. Etiologic yield is augmented by presence of specific findings on history or physical examination on initial assessment. (J Pediatr 2000;136:593-8)

*From the Departments of Neurology/Neurosurgery, Pediatrics, and Epidemiology and Biostatistics and School of Physical & Occupational Therapy, McGill University, Montreal, Quebec, Canada; and the Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada.*

Supported by a grant from the Hospital for Sick Children Foundation. Dr Shevell is a Chercheur Boursier Clinicien (Clinical Research Scholar) of the Fonds de recherche en santé de Québec. Dr Rosenbaum is a National Health Scientist of the National Health Research & Development Program (Canada). Dr Abrahamowicz is a Distinguished Scientist of the Medical Research Council (Canada).

Submitted for publication Aug 26, 1999; revision received Nov 8, 1999; accepted Dec 1, 1999.

Reprint requests: Michael Shevell, MD, CM, FRCPC, Room A-514, Montreal Children's Hospital, 2300 Tupper St, Montreal, Quebec, H3H 1P3 Canada.



0022-3476/2000/$12.00 + 0 **9/21/104817**

doi:10.1067/mpd.2000.104817

Among other priorities, expeditious determination of a possible underlying etiology is essential to the evaluation of the young child with developmental delay.[1] Accurate determination of such an etiology has specific implications regarding estimation of recurrence risk, treatment, management of possible associated conditions, prognosis, and the design of prevention programs.[1-3] Some interventions could potentially modify individual outcomes. Furthermore, determination of an underlying etiology serves to limit additional unnecessary testing and empowers the family by providing a better understanding of the child's problem and the reason(s) for it.[4]

**See editorial, p. 569.**

| | |
|---|---|
| CT | Computed tomography |
| HIE | Hypoxic-ischemic encephalopathy |
| MCH | Montreal Children's Hospital |
| MRI | Magnetic resonance imaging |

Variability in reported etiologic yield in children with developmental delay reflects ongoing improvement in diagnostic technology, the extent of investigations undertaken, the presence or absence of an evaluation by a subspecialist, and the characteristics of the sample population.[5] Such variability has led to uncertainty about the appropriate extent of laboratory investigations for this population.[3,6-8] Agreement does exist that an all-inclusive, unfocused approach is not warranted from medical, personal (ie, excessive interventions), or economic perspectives. Empiric evidence is lacking to justify the need for specific testing in young

children with global developmental delay.

This prospective study was designed to determine the etiologic yield and spectrum in a cohort of young children with global developmental delay seen by subspecialist physicians in an ambulatory care setting at a children's hospital in a university health center. Features evident at initial assessment were recorded at that time to ascertain whether they were predictive of a successful determination of etiology.

## SUBJECTS AND METHODS

### *Inclusion Criteria*

All children referred to either the ambulatory pediatric neurology clinics and offices or the developmental pediatric clinics of the Montreal Children's Hospital of the McGill University Health Center between June 1, 1996, and November 30, 1997 (18 months inclusive) were identified prospectively. Eligibility requirements were age <5 years and referral for the initial evaluation of a suspected developmental delay. Informed consent was obtained for study participation, and the study protocol was approved by the hospital's institutional review board.

### *Exclusion Criteria*

Children were excluded if the suspected developmental delay was not confirmed or if they failed to attend all the diagnostic investigations requested by the evaluating physician. Recruitment from specialty clinics at the MCH targeting high-risk groups (eg, Neurogenetics or Neonatal Follow-up) was excluded.

### *Definitions*

*Global developmental delay* was defined as a significant delay in 2 or more developmental domains (gross/fine motor, cognition, speech/language, personal/social, or activities of daily living).[1] *Significant* was defined as performance 2 or more SDs below the mean on norm-referenced developmental screening or assessment tests. *Etiology* was defined according to the standard of Schaefer and Bodensteiner[6] as "a specific diagnosis that can be translated into useful clinical information for the family, including providing information about prognosis, recurrence risks and preferred modes of available therapy." A causal linkage was assumed between the identified diagnosis and the child's developmental delay.

A total of 6 subspecialty physicians (4 pediatric neurologists and 2 developmental pediatricians) practicing in the MCH setting participated in this study.

### *Procedures*

At initial assessment, an information sheet, completed on each subject by the study's research assistant, included name, sex, reason for referral, name of referring physician, specialty of referring physician, age at which parents suspected the developmental delay, and age at initial subspecialty assessment. Physicians performed specific laboratory testing at their own discretion on a case-by-case basis. An assessment strategy or mandatory testing protocol of subjects was not put into place or suggested by the study's investigators. However, the rationale for the physician's selection of a particular test (ie, screening purposes or specific indication) was ascertained at initial assessment. The testing selected for a particular patient was documented by each physician, as were the salient features of the history and physical examination. This information was collected through standardized questionnaires completed by the evaluating physician on each subject at the time of the patient's initial evaluation.

At least 6 months after initial assessment, the medical records of all subjects were systematically reviewed by one investigator (M.I.S.), and the following were ascertained: pertinent clinical features (eg, family history, antenatal drug or alcohol exposure, perinatal difficulties, microcephaly, and focal findings), compliance with recommended testing, results of recommended testing, etiologic determination (if any), type of etiology determined, and impact (if any). To determine the type and severity of childhood developmental disability, reports of evaluations in occupational therapy, speech therapy, physiotherapy, and psychology were obtained and reviewed in addition to the initial subspecialists' evaluations. On the basis of these reports, subjects were assigned to a category of childhood developmental disability (ie, global developmental delay, motor delay, cerebral palsy, developmental language disorder, or pervasive developmental disorder). Severity or extent of delay was assigned by comparing overall functional age equivalent determined by a variety of standardized measures with chronologic age. Mild delay was defined as a functional age of <33% below the chronologic age, moderate delay as functional age 34% to 66% of chronologic age, and severe delay as functional age <66% of the actual chronologic age.[1] For example, a 36-month-old child would be considered to be mildly delayed if functioning at 24 months, moderately delayed if functioning at 18 months, or severely delayed if functioning at 12 months.

From the data obtained, descriptive statistics on the population of interest were generated. Association between presence of features at initial intake and etiology was analyzed by 2-tailed Fisher exact test. A multiple logistic regression model was undertaken with etiology determination (yes/no) as the dependent variable. To identify predictive variables for association with successful determination of etiology, forward selection with $P < .05$ was used as the entry criterion. Two levels of multiple logistic analysis were carried out with the common strategy of restricting the subset of independent variables evaluated to those that were significant in the simpler "within group" analysis.

# RESULTS

## *Sample Characteristics*

Over the 18 months of study enrollment, 224 children met inclusion criteria, had no exclusion criteria, and completed the laboratory investigations requested by the evaluating physician. Referrals came from community pediatricians for 146 children (65.2%), hospital-based pediatricians for 22 (9.8%), general/family practice physicians for 20 (8.9%), and pediatric subspecialists for 16 (7.1%). Twenty children (8.9%) were referred by allied health services or were self-referred by parents. Of the 224 children, 99 were documented to have a global developmental delay and are the focus of this article. Of the remaining children, 16 had a pure motor delay, 6 had cerebral palsy, 72 had developmental language disorder (isolated speech and language delay), and 31 had pervasive developmental disorder (autism spectrum). Of the 99 children with global developmental delay, 71 were male. Their mean age at time of assessment was 37.6 months (SD ± 15.2 months). The initial age at which parents suspected a developmental delay for this group was recorded as 23.7 months (SD ± 13.0 months). Sixty-four children were evaluated by pediatric neurologists and 35 by developmental pediatricians; 47 had a mild delay, 48 a moderate delay, and 4 a severe delay.

Diagnostic investigations were selective: 58 had FMR-1 (fragile X mutation) molecular genotyping performed, 63 had a karyotype (cytogenetics) study, 60 had electroencephalography, 58 had computed tomography, and 17 had magnetic resonance imaging performed (7 of these children had undergone CT as well). In total, 26 children underwent specific metabolic investigations (eg, capillary blood gas, lactate, ammonia, serum amino acids, urine organic acids, very long chain fatty acids); 70 underwent some form of genetic analysis (cytogenetic or FMR-1); and 68 had a neuro-imaging study.

*Table I.* Clinical features and etiologic determination (bivariate analysis)

| Clinical features (N) | Etiology determined (%) Yes | No | *P* value (Fisher exact test) |
|---|---|---|---|
| Sex | | | |
| Male (71) | 41 | 59 | .27 or NS |
| Female (28) | 54 | 46 | |
| Autistic features | | | |
| Present (19) | 0 | 100 | <.0001 |
| Absent (80) | 55 | 45 | |
| Historical factors | | | |
| Positive (32) | 72 | 28 | .0002 |
| Negative (67) | 31 | 69 | |
| Physical findings | | | |
| Positive (48) | 73 | 27 | <.0001 |
| Negative (51) | 18 | 82 | |

*NS,* Not significant.

## *Etiologic Determination*

On completion of the history, physical examination, and selected laboratory investigations in the 99 subjects with global developmental delay, an etiologic diagnosis was made in 44 (44%). Etiologic diagnoses fell into the following categories: cerebral dysgenesis in 10, hypoxic-ischemic encephalopathy in 9, exposure to toxins (eg, intrauterine alcohol or cocaine exposure) in 9, chromosomal anomalies in 6 (fragile X syndrome and Prader-Willi syndrome), profound psychosocial neglect in 3, neuromuscular disorder in 2, genetic syndrome (Johansson-Blizzard syndrome and Möbius syndrome) in 2, sequelae of infection (congenital) in 1, leukodystrophy in 1, and multiple sensory impairments in 1. HIE was diagnosed by means of a combination of intrapartum historical/laboratory findings and subsequent neonatal encephalopathy and compatible imaging study. Toxin exposure was diagnosed on the basis of objective historical data and consistent physical findings (eg, fetal alcohol syndrome). When stratified according to severity of delay, 25 of 47 (53.2%) with a mild delay had an etiology determined, as did 15 of 48 (31.3%) of those with moderate delay and all 4 (100%) of those with severe delay. No difference in the frequency of laboratory investigations was evident between groups stratified according to severity of delay.

Evaluation of associations between features evident from initial history and physical examination and determination of etiologic diagnosis are shown in Table I. Sex was not predictive of etiologic determination. The presence of autistic features (eg, repetitive behaviors, avoidance of eye contact, desire for sameness, social isolation, and lack of imaginative play) was a strong negative predictor of diagnostic yield: no etiology was determined in all 19 children who had both global developmental delay and autistic features; in contrast, etiology was determined in 44 of 80 children (55%) who had global developmental delay alone. Sex, age, and developmental profile of those with autistic features did not differ significantly from those without autistic features. The presence of any feature in the history (eg, family history, consanguinity, intrapartum or neonatal complications, developmental regression, or toxin exposure) was predictive of etiologic determination. Physical findings (ie, macrocephaly, microcephaly [nonfamilial], dysmorphism, and focal abnormalities) were also predictive of an eventual etiologic determination.

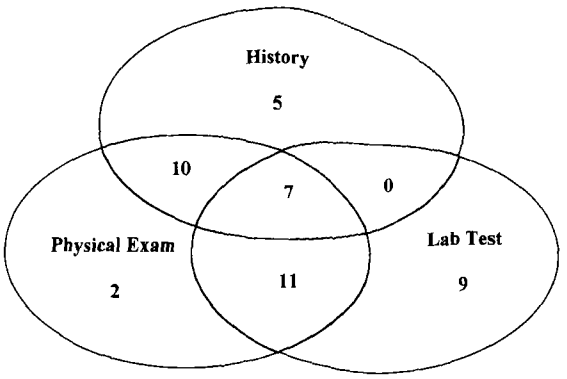


*Fig 1.* Venn diagram showing relative contributions of history, physical examination, and laboratory investigations to determination of etiologic diagnosis. Numerical values represent actual number of cases ($n = 44$).

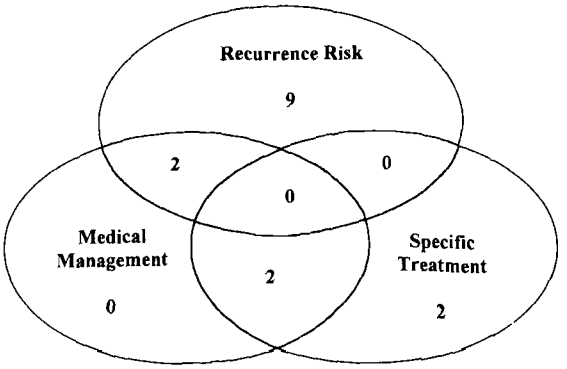


*Fig 2.* Venn diagram showing number of cases in which determination of an etiologic diagnosis had an impact on estimation of risk of recurrence, medical management, or specific treatment.

*Table II.* Clinical features significantly associated with determination of an etiology (multivariate analysis)

| Clinical features | Odds ratio (95% CI) | P value (multiple logistic regression) |
|---|---|---|
| Historical features | 4.54 (1.64-12.53) | .0035 |
| Autistic features | ∝ | <.0001 |
| Toxin exposure | 1.00 | .0300 |
| Microcephaly | 31.65 (3.93-255.16) | .0010 |
| Focal motor findings | 7.91 (1.53-41.05) | .0014 |

Multiple logistic regression analysis carried out on groups of candidate variables revealed statistical significance for the following: (1) historical features, (2) autistic features, (3) toxin exposure, (4) microcephaly, and (5) focal motor findings (Table II). It should be noted that an infinity odds ratio was obtained for autistic features because all those with this finding (n = 19) had no etiology determined. Similarly, an odds ratio of 1.00, with no 95% CI range, was obtained for toxin exposure because all those with this historical observation (n = 9) had an etiology determined.

Multiple logistic regression analysis including all identified significant variables revealed the following variables to remain significant: (1) autistic features (odds ratio = ∝, $P = .001$), (2) microcephaly (odds ratio = 13.63, 95% CI 1.64-113.47, $P = .016$), and (3) historical features (odds ratio = 3.85, 95% CI 1.32-11.24, $P = .014$).

Determination of etiology did not appear to be influenced by whether cytogenetic testing was done on a screening basis or for a specific indication (eg, family history, dysmorphology, or suspicion of a specific syndrome). Three of 32 (9.4%) cytogenetic studies done for a specific indication had a diagnostic yield versus 2 of 38 (6.3%) done on a screening basis (Fisher exact test, $P = .65$). The diagnostic yield for neuro-imaging studies was significantly associated with performance for a specific indication (eg, microcephaly or focal motor findings), as opposed to performance on a screening basis. Fourteen of 34 (41.2%) neuro-imaging studies done for a specific indication had a diagnostic yield versus 5 of 36 (13.9%) done on a screening basis (Fisher exact test, $P = .015$).

The relative contributions of the history, physical examination, and laboratory investigation etiologic determination were ascertained and are summarized (Fig 1). In 27 of 44 (61.4%) cases in which an etiology was determined, laboratory investigations contributed to the diagnosis, and in 9 of 44 (20.5%), laboratory tests were the sole means of etiologic determination. Conversely, 17 of 44 (38.6%) cases had an etiology determined on the basis of the history and/or physical examination done by the subspecialist physician.

Impact of determining etiology is summarized in Fig 2. In 15 of 44 (34.1%) cases in which an etiology was determined, an impact was apparent beyond understanding of specific pathogenesis. Such an impact modified the clinical estimate of risk for recurrence, mandated an alteration in medical follow-up, or resulted in a specific therapeutic intervention.

## DISCUSSION

In this prospective study, a presumed etiology was determined in 55% of

young children who had global developmental delay without any autistic features. It is not surprising that this is substantially greater than oft-cited studies from the 1980s, given the substantial technological advances in both cytogenetics and imaging modalities.[9-12] It is consistent with more recent community-based surveys.[13,14] However, it is also more than twice the diagnostic yield found in a recently published cross-sectional survey of 10-year-old mentally retarded children born between 1975 and 1977 in metropolitan Atlanta.[2] In that study identification of etiology was limited to a retrospective review of medical records in which the occurrence and nature of any evaluations by subspecialists or laboratory investigations carried out in an affected child were not identified. Thus compared with that study, our higher diagnostic yield likely reflects the benefits of both improved technology and evaluation by a pediatric neurologist or developmental pediatrician. Furthermore, our subjects were identified at a medical, rather than an educational, point of entry. Our diagnostic yield closely approximates the figure of 63% obtained in a retrospective study carried out in the same institution (MCH) in a sample of children who had global developmental delay without autistic features derived from a single neurologist's practice.[1] This validates the estimate of that original study. A standardized investigative protocol was not put into place for this study. The results may suggest a standardized protocol for future prospective evaluation.

We believe that the patients in this cohort represent a reasonable cross-section (approximation) of the spectrum of global developmental delay present in the ambulatory practice setting. An increasing tendency of primary care providers to refer children with suspected developmental delay to developmental specialists has been documented.[15,16] In addition, in a survey of physicians in our local referral network, 72% stated that they referred all or most of their patients with developmental delay to hospital-based neurology or developmental pediatric clinics for evaluation.[1] Full medical care coverage of the entire population resident in Quebec also removes any economic barriers to subspecialty evaluation that may be present in other jurisdictions. Furthermore, 96% of our sample had a mild or moderate delay, reflecting the ambulatory, community orientation of the sample. We excluded subspecialty neurology clinics (eg, Neurogenetics, Neonatal Follow-up) at the MCH as sites for recruitment for this study because this would favor detection of an etiologic factor.

As in our original retrospective study, 4 diagnostic categories (cerebral dysgenesis, HIE, toxin exposure, and chromosomal anomalies) account for the preponderant etiologic diagnoses made (3/4 in this study vs 2/3 in the original).[1] Missing from our etiologic spectrum are entities identified by the newborn screening that is mandatory in Quebec (eg, aminoacidopathy) or through early characteristic dysmorphology evident before developmental delay (eg, Down syndrome). Entities such as human immunodeficiency virus encephalopathy and lead intoxication are likely absent because of local sociodemographic factors. The socioeconomic status of our population was predominantly middle class; 70% of fathers had some education beyond high school, just over 10% of families were receiving social assistance, and just under 10% of children were either adopted or in foster care.

Classification of presumed etiologies reveals 64% to be prenatal (cerebral dysgenesis, toxin exposure, chromosomal anomalies, genetic syndrome, congenital infection), 21% perinatal (HIE) with a supposed prenatal disposition,[17] and 16% postnatal in onset (neglect, neuromuscular syndrome, leukodystrophy, and sensory impairment). Of these 7 "postnatal" causes, 4 were in fact genetically determined at conception, consistent with previously published studies.[2,9,10] Furthermore, almost one half (21/44) have etiologies that are potentially preventable (HIE, toxins, neglect), suggesting strategies and targets for future prevention programs.

The prospective nature of this study permitted the identification of features evident on initial history and physical examination that could predict successful etiologic determination. These included the following: (1) the absence of co-existing autistic features, (2) antenatal toxin exposure, (3) microcephaly, and (4) focal motor findings. It is interesting that the presence of dysmorphic features, often believed to be a prerequisite for undertaking cytogenetic studies,[3] was not predictive of etiologic yield.

Imaging studies performed for a specific indication (eg, microcephaly) were more than 3 times as likely to result in an etiologic yield than when done on a screening basis. The local (MCH) tendency to use CT in preference to MRI, for reasons of cost and accessibility, likely results in an underestimation of etiologies that could be identified through the technically superior MRI modality. Diagnostic MRI findings in the face of a normal CT scan in this clinical setting have been reported in small case series.[18] No significant difference in diagnostic yield was found for cytogenetic studies carried out with or without specific clinical indication. However, the value of these 2 tests done on a screening basis should not be downplayed because they contributed to 18% of the diagnoses made. The value of laboratory investigations in this clinical setting is additionally supported by the observation that laboratory testing contributed to an etiologic diagnosis in 61% of cases. Furthermore, in 21% of cases, a laboratory test was the sole means of establishing a diagnosis that was not apparent from history or physical examination. Metabolic testing conducted in 26 subjects did not contribute to an etiologic diagnosis in a single patient in our cohort. Rarely (<10% of instances) was such testing undertaken

on an indicated basis as opposed to a screening basis. The low yield of such testing, especially on a routine basis, has been noted in other studies.[19,20] It appears that metabolic testing in the setting of developmental delay should be reserved for those situations (eg, positive family history, parental consanguinity, or developmental regression) that heighten the likelihood of these diagnoses.

Although these observations support the value of laboratory investigations such as karyotyping and neuro-imaging in this clinical setting, the data also highlight the value of the subspecialist's evaluation itself. In 17 of 44 cases in which etiology was determined, findings on history or physical examination, alone or in combination, were sufficient for diagnosis.

Beyond the establishment of causality, determination of an etiology had further clinical importance in 15% of the total cohort, or in approximately one third of those in whom an etiologic diagnosis was made. Estimation of risk of recurrence was most often affected, but in 6 of 15 cases it led to a modification of medical management or specific treatment with the potential to affect eventual outcome for the child. Such an impact must be factored into any potential cost-benefit analysis of evaluations, although quantification of such benefits can be difficult to ascertain in an accurate, tangible way.[5] The desire of the family to obtain a causal diagnosis is evidenced by our observation that only 14 of 258 (5.4%) children referred for evaluation of developmental delay failed to complete requested investigations.

Determination of an underlying etiology is an essential part of the triad of clinical service delivery to this population, which also includes early identification[21] and prompt provision of rehabilitation services.[22] This should occur within a framework of care in which communication between the primary care service provider and the subspecialist exists and support to the families involved is emphasized. By demonstrating etiologic yield in 55% of evaluations of children with global developmental delay without co-existing autistic features, this prospective study highlights that this descriptive diagnosis is not an end point but a "prompt" to consider the identification of underlying causal mechanisms, which can often be identified through a detailed history and physical examination by a subspecialist and the judicious use of laboratory investigations. Screening tests should include karyotyping and neuro-imaging studies.

*We wish to recognize the collaboration of the evaluating physicians: Ron Barr, Charles Larson, Bernard Rosenblatt, Kenneth Silver, and Gordon Watters. We thank Victoria Stubec, Joseph Falworth, and Betty Cindric for their research assistance in data collection and coordination of the project. We also thank Alba Rinaldi for secretarial assistance.*

## REFERENCES

1. Majnemer A, Shevell MI. Diagnostic yield of the neurologic assessment of the developmentally delayed child. J Pediatr 1995;127:193-9.
2. Yeargin-Allsopp M, Murphy CC, Cordero JF, Decoufle P, Hollowell JG. Reported biomedical causes and associated medical conditions for mental retardation among 10 year old children, metropolitan Atlanta, 1985 to 1987. Dev Med Child Neurol 1997;39:142-9.
3. Curry CJ, Stevenson RE, Aughton D, Byrne J, Carey JC, Cassidy S, et al. Evaluation of mental retardation: recommendations of a consensus conference. Am J Med Genet 1997;72:468-77.
4. Rosenbaum PL. Prevention of psychosocial problems in children with chronic illness. Can Med Assoc J 1988;139:293-5.
5. Shevell MI. The evaluation of the child with a global developmental delay. Semin Pediatr Neurol 1998;5:21-6.
6. Schaefer GB, Bodensteiner JB. Evaluation of the child with idiopathic mental retardation. Pediatr Clin North Am 1992;39:929-43.
7. Levy SE, Hyman SL. Pediatric assessment of the child with developmental delay. Pediatr Clin North Am 1993;40:465-77.
8. First LR, Palfrey JS. The infant or young child with developmental delay. N Engl J Med 1994;330:478-83.
9. Akesson IIO. The biologic origin of mild mental retardation. Acta Psychiatr Scand 1986;74:3-7.
10. McLaren J, Bryson SE. Review of recent epidemiological studies of mental retardation: prevalence, associated disorders, and etiology. Am J Ment Retard 1987;92:243-54.
11. Moeschler JB, Bennett FC, Cromwell LD. Use of the CT scan in the medical evaluation of the mentally retarded child. J Pediatr 1981;98:63-5.
12. Lingam S, Read S, Holland IM, Wilson J, Brett EM, Hoare RD. Value of computerized tomography in children with non-specific mental subnormality. Arch Dis Child 1982;57:381-3.
13. Wellesley D, Hockey A, Stanley F. The etiology of intellectual disability in Western Australia: a community based study. Dev Med Child Neurol 1991;33:963-73.
14. Curry CJ, Sandhu A, Fritos L, Wells R. Diagnostic yield of genetic evaluations in developmental delay/mental retardation [abstract]. Clin Res 1996;44:130A.
15. Dobos AEJ, Dworkin PH, Bernstein BA. Pediatricians' approaches to developmental problems: Has the gap been narrowed? Dev Behav Pediatr 1994;15:34-8.
16. Wallerstein R, Seshadri K. Are referrals to developmental pediatricians appropriate? Clin Pediatr 1994;33:564-8.
17. Freeman JM, Nelson KB. Intrapartum asphyxia and cerebral palsy. Pediatrics 1988;82:240-9.
18. Van Bogaert P, Baleriaux D, Christophe C, Szliwowski HB. MRI of patients with cerebral palsy and normal CT scan. Neuroradiology 1992;34:52-6.
19. Carson NAJ, Neill DW. Metabolic abnormalities detected in a survey of mentally backward individuals in Northern Ireland. Arch Dis Child 1962;37:505-13.
20. Allen WP, Taylor H. Mental retardation in South Carolina VII. Inborn errors of metabolism. Proc Greenwood Genet Ctr 1996;15:76-9.
21. Squires J, Nickel RE, Eisert D. Early detection of developmental problems: strategies for monitoring young children in the practice setting. Dev Behav Pediatr 1996;17:420-7.
22. Majnemer A. Benefits of early intervention for children with developmental disabilities. Semin Pediatr Neurol 1998;5:62-9.