Autism: An Emerging Public Health Problem

CRAIG J. NEWSCHAFFER, PHD[a]
LAURA KRESCH CURRAN, BA[a]

Over the past decade, autism has emerged as a major public health concern in the United States. Although known for more than fifty years as one of the most severe childhood neuropsychiatric disorders, it was thought to be quite rare. Now, however, it is recognized that autism includes a much broader spectrum of affected individuals, beyond those with classic features. Recently, there has been much speculation that the underlying risk of the condition, in all its forms, may be increasing with time. Undoubtedly, more and more individuals have been seeking educational, medical, and social services to help confront the formidable challenges of autism. All this comes at a time when, despite a decade-long intensive search for autism genes, there is continued bafflement over the condition's etiology. In this article, we review the factors responsible for the emergence of autism as a public health problem and briefly discuss the public health response to date and the prospects for the future.

DEFINING AUTISM

Diagnosis of autism is purely behaviorally based. Individuals with autism have impairments in social interaction and communication and exhibit some rote or repetitive, often self-stimulatory, behaviors.[1] In each of these dimensions, the impairment can range from mild to profound. A low-functioning individual with autism might be completely non-verbal, cognitively impaired, self-injurious, and virtually unable to connect with even the closest of family members. A very high-functioning individual with autism could be verbal, of above-average cognitive ability, have idiosyncratic areas of interest with a tendency to gear social interaction around these, and may have formed strong bonds with family, teachers, and some peers. Recognizing this spectrum, many refer to the broad range of autistic-like conditions as Autism Spectrum Disorders (ASDs). Clinically, they are often still referred to as pervasive developmental disorders (PDDs). Classic autism, the form with behavioral features closest to those described by Kanner,[2] is called *autistic disorder* or *nuclear autism*. Once thought to be the predominant form, it may well account for less than half of the ASDs.[3] Over time, the diagnostic criteria for autistic disorder have been modified, new

[a]Department of Epidemiology, Center for Autism and Developmental Disabilities Epidemiology, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Address correspondence to: Craig J. Newschaffer, PhD, Dept.of Epidemiology, Johns Hopkins Univ., Bloomberg School of Public Health, 615 North Wolfe St., Rm. E6142, Baltimore, MD 21205; tel. 410-955-1268; fax 410-502-6652; e-mail <cnewscha@jhsph.edu>.

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criteria have been added for other ASDs (pervasive developmental disorders not otherwised specified [PDD NOS], and Asperger Syndrome), and the way these criteria have been applied in practice has changed.[4]

WHAT IS THE PUBLIC HEALTH BURDEN OF AUTISM?

Prevalence

Most of the epidemiologic data on autism prevalence come from studies of autistic disorder, not the full spectrum of ASDs. Through the 1990s, the most commonly accepted estimates of the overall population prevalence of autistic disorder fell in the range of 5–10 per 10,000 with, for still unknown reasons, prevalence in males appearing to be three to four times that of females,[3] with the gender disparity being more pronounced among those without cognitive impairment and those without any dysmorphic features.[3–5] More recent studies have yielded prevalence estimates for autistic disorder many times the upper limit of this range, although these studies tend to be smaller in scale and subject to more random variability.[6–8] However, most of these smaller investigations have used more intensive case identification procedures. Although this pattern implies an increase with time, inferences about trends in the prevalence of autistic disorder must be made with caution because studies differed in design, populations, and methods and criteria for identifying cases.

Administrative data, the routine information collected by service delivery programs, have probably fueled most of the recent speculation about rising autism prevalence. Autism became a recognized federal category for special education classification in 1990, and the number of children classified with autism by state education departments across the country has since increased approximately 25% per year.[9] It is noteworthy, however, that the special education category of "other health impairments," which includes children with attention deficit hyperactivity disorder, has experienced increases of similar magnitude.[9] In 1999, the Californa Division of Developmental Disabilities (DDS) published a widely cited report on the number of individuals with autism registered with that agency, documenting large annual increases in the numbers of individuals with an autism classification.[10] However, when population denominators were applied to these autism case counts, prevalence in the most recent years was still below what would be expected based on the epidemiologic studies.[11] Two investigations following up on these data—one an ecologic analysis and one a small survey—have examined whether the apparent increase in the number of individuals classified with autism in California could be a byproduct of changes in the way people with developmental disabilities are categorized by the state.[12,13] The findings, however, were not in agreement and the question remains open. California DDS recently published an update to their 1999 report that shows counts of individuals with autism classifications still on the rise.[14]

Currently, there is no consensus on the population prevalence of ASDs. A plausible range for autistic disorder is probably somewhere between 10 and 20 per 10,000, with the prevalence of all ASDs to be two to three times that. The Centers for Disease Control and Prevention (CDC) reported a 1996 ASD prevalence of 34 per 10,000 in Metropolitan Atlanta,[6] and a 1998 survey of one British county found an ASD prevalence of 63 per 10,000.[6,15] Virtually all agree that the number of children with ASD diagnoses has increased markedly over the last decade, as has the demand for services. However, the extent to which the increase can be attributed to a combination of shifting diagnostic tendencies and increased ASD awareness or to changes in true risk is unclear. This situation is troubling, as service providers are uncertain whether the recent increases are likely to continue, communities wonder about "clusters" that might warrant a special public health response, and researchers speculate about what underlying mechanisms might be consistent with a short-term change in prevalence.

Severity

The level of impairment and consequent service needs of individuals with ASD, while variable, is quite high for even the least severe cases. Impairment is life-long, and considerable support is required to navigate routine educational and social situations. A large segment of autism cases (estimates range from less than 10% to 30%) have other medical conditions such as Fragile X, tuberous sclerosis, or neurofibromatosis.[16–18] Approximately 70% of people with autistic disorder are cognitively impaired, 40% severely.[3] The proportion of those with cognitive deficits among all individuals with ASDs is likely lower, but no good estimate is yet available. Cognitive status appears to be the single strongest predictor of functional outcome.[19,20] However, it has been demonstrated that behaviorally-based interventions started early in life can curtail problematic behavior and foster communication and social skill growth.[21,22] Certain pharmacological treatments have also been shown to reduce problematic behaviors in particular case subgroups.[23,24] Numerous other interventions have also been proposed over the years, but remain unproven. More than 30% of the parents

of a recent consecutive case series of 250 children with autism reported ever trying some form of complementary or alternative medicine. (Personal communication, David. S. Mandell, Sc.D, University of Pennsylvania Center for Autism and Developmental Disabilities Research and Epidemiology, November 2002.) Follow-up studies have estimated that from 5% to 17% of adults with autism have near-normal or normal social lives with acceptable functioning at work.[4] Those studies, however, tended to over-represent individuals with autistic disorder as opposed to other ASDs, and were done on cohorts less likely to receive early behavioral-intervention than today's children.

Cost

Much of the cost of autism, such as the emotional strain and altered lifestyles of affected families, is of course impossible to quantify. There are also substantial challenges to estimating the economic costs of the disorder. Aside from uncertainty over prevalence, reliable data on a number of relevant cost categories are lacking. The one recently published autism cost study was conducted in the United Kingdom and estimated the lifetime costs to society for a person with autism there to be an amount equivalent to nearly $4 million (1998 U.S. dollars).[25] Similar analyses using the limited cost data available in the United States have been completed, but have not been published in the peer-reviewed literature.[26,27] Nonetheless, these do concur in general terms with the UK study in that, assuming a middle-range estimate for population prevalence, the annual cost of autism in this country would be counted in terms of billions of dollars, exclusive of the substantive economic costs associated with other ASDs. The financial burden for certain expensive direct services, particularly intensive behaviorally-based intervention, is often shouldered completely by the families of those affected.

EARLY DETECTION

Because functional improvements are typically seen with early behavioral intervention,[21,22] screening tools based on existing diagnostic approaches have been

Richard Brown, the artist who painted this "Winter Scene," has autism; he showed no artistic talent until age 22. Since then, his paintings have been exhibited throughout the country, and he has earned thousands of dollars for autism organizations through the sale of his greeting cards and calendars.

developed. The American Academy of Neurology currently recommends that children failing routine developmental exams be screened with one of two such tools—the Modified Checklist for Autism in Toddlers (M-CHAT) or the Autism Screening Questionnaire (now referred to as the Social Communication Questionnaire).[28] However, existing tools vary in the manner in which they are administered and the extent to which they have been validated. To develop better approaches, researchers are now closely following cohorts of infant siblings of autistic children as well as doing studies that compare pre-diagnostic videotapes of autism case and control subjects. The latter approach has led to a finding that deviations from normal patterns of movement may be useful in diagnosing ASD as early as 4–6 months of age.[29]

Given the inherent uncertainties of behaviorally-based screening, interest in potential autism biomarkers has been intense. One promising study found that levels of certain neuropeptides and neurotrophins measured in archived newborn heel stick blood cards discriminated between children later diagnosed with autism and those free of developmental problems.[30] However, levels in children with autism were not appreciably different from those in children with idiopathic mental retardation, suggesting that these are non-specific indicators of general developmental problems rather than an autism-specific marker.

Can autism be prevented?

Unfortunately, the uncertainty over the etiology of autism has hindered primary prevention efforts. For a number of years, researchers mistakenly emphasized parent behavior as contributing to autism causation. Then, after reports in the late 1970s and early 1980s documented high rates of co-occurrence of nuclear autism in monozygous twin pairs,[31–34] the focus shifted to genetics. Today, while a substantive heritable component to ASD is undeniable, aside from some consistent findings pointing to an area on chromosome 7q,[35–38] the gene-finding studies are far from congruent and no single genetic model has yet met the challenge of consistently explaining autism's gender disparity and variable phenotype across available family datasets.[39] Investigations of particular candidate genes have also been inconclusive; however, WNT2,[40] reelin,[41,42] and HOX[43] genes may still prove important. This lack of conclusive genetic findings suggests that the model of inheritance underlying autism is quite complex. Inheritance is likely non-Mendelian, perhaps involving a polygenic mechanism with a large number of distinct genes,[37] or genomic imprinting, where maternally and paternally inherited alleles of a gene are differentially expressed.[44] Also possible is a scenario where the maternal genotype itself affects risk (e.g., maternal genes that influence the in-utero environment).[45] Finally, the genes that increase the risk of autism (either the mother's or the affected proband's) may do so only in the presence of exposures to certain nonheritable factors.[46]

However, to date, few nonheritable factors have been implicated in autism etiology, and even fewer are believed to play a causal role. Available anatomical evidence has been interpreted as supporting origins for autism during prenatal brain development,[47,48] although no single anatomical or pathophysiological theory is considered definitive.[49] There are some children with autism who develop normally through 18 to 30 months of age and then abruptly lose language and social skills. The proportion of all ASD cases with this regressive autistic phenotype is unknown, although some speculate it could be as high as 30%.[50] Although the mere existence of this group is sometimes interpreted as supporting the existence of a nonheritable early life risk factor for autism, it is entirely possible that regressive autism results from pathologic processes fully established at birth.

Possible nonheritable autism risk factors that have received the most attention are pre- and perinatal maternal infections, birth complications, chemical exposure, and, most recently, childhood vaccinations. Associations of autism with maternal infection and birth complications have been reported with some consistency,[51–54] but have not received much emphasis because of concerns over study design (e.g., small sample sizes, recall biases), reverse causation (i.e., pathology linked to autism causes birth complications, rather than the complications causing autism), and minimal attributable risk impact. A link between thalidomide exposure in pregnancy and autism has been established;[55,56] however, epidemiologic studies of other medications used in pregnancy have not been consistent in their findings,[52,53] and the few studies of other chemical exposures in pregnancy offer little support for any association.[57]

In the last five years, a great deal of attention has been focused on the possible role of childhood vaccination in autism. Public anxiety was stimulated by the spread of anecdotal reports of developmental regression coincident with vaccination and the publication of a study documenting intestinal abnormalities in a small number of children with autism,[58] most of whose parents reported autistic symptoms beginning just after measles, mumps, and rubella (MMR) vaccination. Concurrently, others pointed to the ubiquitous presence of the potentially neurotoxic ethylmercury-containing vaccine preservative, thimerosal, in childhood vaccines.[59]

Three expert reviews[60,61] released in 2000–2001[60–62] unanimously concluded that the data then available did not support an association between MMR vaccination and autism. The first large-scale, individual-level epidemiologic study of this subject, published in late 2002, also has reported no association between MMR vaccine and autism.[63] While fewer data are available at this point, similar conclusions have been reached by expert review panels with regard to thimerosal exposure.[60,64] Epidemiologic studies are underway but, in accordance with a 1999 recommendation by the Food and Drug Administration, the U.S. Public Health Service (PHS), and the American Academy of Pediatrics (AAP), all U.S.-licensed vaccines on the recommended immunization schedule for children younger than 6 years of age are now available in thimerosal-free forms. However, in developing countries where single dose vials are impractical, thimerosal is still used.[64]

At this time, it is difficult to formulate preventive strategies for autism. The AAP currently recommends that parents of children with ASD be counseled about the increased risk in subsequent children, estimated to be from 3% to 9%.[65,66] Other more involved counseling protocols have also been proposed.[67] Should a putative autism gene be identified, a considerable amount of additional research would still be needed before any kind of genetic testing was implemented.[68] We also lack clear direction on exposure avoidance strategies that might be effective in the prevention of autism. That we have yet to identify susceptibility genes is likely also the single most important barrier to discovering etiologically significant and potentially modifiable exposures.

The public health response

Since 1995, the Department of Health and Human Services has sharpened its focus on ASDs. From 1995 to 2001, research funding for autism has quintupled from $11 to $56 million.[68,69] At the same time, both the CDC and the National Institutes of Health (NIH) have developed new initiatives, building a federal foundation for the public health response to autism. Catalyzed by the Children's Health Act of 2000,[71] the CDC is supporting the development of population-based ASD surveillance projects in eight states and has funded five centers of excellence in autism and developmental disabilities epidemiology to conduct surveillance and to begin a large, multi-centered autism case-control study. These CDC projects should provide more accurate ASD prevalence estimates and, it is hoped, lead to the discovery of modifiable risk factors. The Children's Health Act also charged the NIH to fund at least five centers of excellence in clinical and basic science research on autism, and to form an Autism Coordinating Committee where representatives from five NIH institutes, the CDC, the FDA, and the U.S. Department of Education could regularly exchange ideas.[71]

Through a federal mandate under the Individuals with Disabilities Education Act, states can secure funding to provide developmental screening and early intervention to infants and toddlers.[71] These programs, while not exclusively focused on autism, have been an important means of raising early warnings that can lead to diagnoses of ASDs and have been available in all states since 1994. In New Jersey, a Governor's Council on Autism Research was formed that, in addition to funding research, also supports the development of a state autism registry and an educational initiative on early detection targeting parents and physicians. There has been much publicity in California surrounding the $34 million state funding of a new autism research and treatment center, the Medical Investigation of Neurodevelopmental Disorders (MIND) Institute. The MIND Institute is involved in a study of environmental chemical exposures and autism risk, funded by the National Institute of Environmental Health Sciences and the Environmental Protection Agency. It is also working to develop new diagnosis and early detection tools, and is providing training and consultation to community physicians about detection and diagnosis.

Clearly, energy and resources are now being directed toward a re-assessment of autism from a population perspective. This seems entirely appropriate, given the gaps in knowledge on the burden, causes, and most effective intervention strategies for ASDs. We hope that this will lead to the knowledge base needed to support a more informed and comprehensive public health response to autism in the future.

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REFERENCES

1. Lord C, Risi S. Frameworks and methods in diagnosing autism spectrum disorder. Ment Retard Dev Disabil Res Rev 1998;4:90-6.
2. Kanner L. Autistic disturbances of affective contact. Nerv Child 1943;2:217-50.
3. Fombonne E. The epidemiology of autism: a review. Psychol Med 1999;29:769-86.
4. Gillberg C, Wing L. Autism: not an extremely rare disorder. Acta Psychiatr Scand 1999;99:399-406.
5. Miles JH, Hillman RE. Value of a clinical morphology examination in autism. Am J Med Genet 2000;91:245-53.

6. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children. JAMA 2001;285:3093-9.
7. Baird G, Charman T, Baron-Cohen S, Cox A, Swettenham J, Wheelwright S, Drew A. A screening instrument for autism at 18 months of age: a 6-year follow up study. J Am Acad Child Adolesc Psychiatry 2000;39:694-702.
8. Bertrand J, Mars A, Boyle C, Bovef, Yeargin-Allsopp M, Decoufle P. Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. Pediatrics 2001;108:1155-61.
9. Department of Education (US). Twenty-second annual report to Congress on the implementation of the Individuals with Disabilities Education Act. Jessup (MD): US Department of Education; 2000.
10. California Health and Human Services Agency. Changes in the population of persons with autism and pervasive developmental disorders in California's Developmental Services System: 1987 through 1998. A report to the legislature. Sacramento: CHHS, Department of Developmental Services; 1999.
11. Fombonne E. Is there an epidemic of autism? Pediatrics 2001;107:411-2.
12. Croen LA, Grether JK, Hoogstrate J, Selvin S. The changing prevalence of autism in California. J Autism Dev Disord 2002;32:207-15.
13. Byrd RS. Report to the legislature on the principal findings from the epidemiology of autism in California: a comprehensive pilot study. Davis (CA): M.I.N.D. Institute, University of California, Davis; 2002.
14. California Department of Developmental Services. Autism spectrum disorders—changes in the California caseload. An update: 1999 through 2002. Sacramento: CDDS; 2003.
15. Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. Prevalence of autism in a US metropolitan area. JAMA 2003;289:49-55.
16. Fombonne E, Du Mazaubrun C, Cans C, Grandjean H. Autism and associated medical disorders in a French epidemiological survey. J Am Acad Child Adolesc Psychiatry 1997;36:1561-9.
17. Gillberg C, Coleman M. Autism and medical disorders: a review of the literature. Dev Med Child Neurol 1996; 38:191-202.
18. Barton M, Volkmar F. How commonly are known medical conditions associated with autism? J Autism Dev Disord 1998;27:273-8.
19. Rutter M. Autistic children: infancy to adulthood. Semin Psychiatry 1970;2:435-50.
20. Gillberg C, Steffenburg S. Outcome and prognostic factors in infantile autism and similar conditions: a population-based study of 46 cases followed through puberty. J Autism Dev Disord 1987;17:273-87.
21. National Research Council, Committee on Educational Interventions for Children with Autism. Educating children with autism. Washington: National Academy Press; 2001.
22. Rogers SJ. Brief report: early intervention in autism. J Autism Dev Disord 1996;26:243-6.
23. Buitelaar JK, Willemsen-Swinkels SH. Medication treatment in subjects with autistic spectrum disorders. Eur Child Adolesc Psychiatry 2000;9 Suppl 1:I85-I97.
24. Lewis MH. Brief report: psychopharmacology of autism spectrum disorders. J Autism Dev Disord 1996;26:231-5.
25. Jarbrink K, Knapp M. The economic impact of autism in Britain. Autism 2001;5:7-22.
26. Greschwind SA. The economic burden of autism. Los Angeles: The Cure Autism Now Foundation; 2000.
27. Honeycutt A, Dunlap L, Chen H, al Homsai G. The cost of developmental disabilities. Task Order No. 0621-09. Revised final report. Research Triangle Park (NC): Research Triangle Institute; 2000.
28. Filipek PA, Accardo PJ, Ashwal S, Baranek GT, Cook EH Jr, Dawson G, et al. Practice parameter: screening and diagnosis of autism. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society. Neurology. 2000;55: 468-79.
29. Teitelbaum P, Teitelbaum O, Nye J, Fryman J, Maurer RG. Movement analysis in infancy may be useful for early diagnosis of autism. Proc Natl Acad Sci USA 1998; 95:13982-7.
30. Nelson KB, Grether JK, Croen LA, Dambrosia JM, Dickens BF, Jelliffe LL, et al. Neuropeptides and neurotrophins in neonatal blood of children with autism or mental retardation. Ann Neurol 2001;49:597-606.
31. Steffenburg S, Gillberg C, Hellgren L, Andersson L, Gillberg IC, Jakobsson G, Bohman M. A twin study of autism in Denmark, Finland, Iceland, Norway and Sweden. J Child Psychol Psychiatry 1989;30:405-16.
32. Folstein S, Rutter M. Infantile autism: a genetic study of 21 twin pairs. J Child Psychol Psychiatry 1977;18:297-321.
33. Bailey A, Le Couteur A, Gottesman I, Bolton P, Simonoff E, Yuzda E, Rutter M. Autism as a strongly genetic disorder: evidence from a British twin study. Psychol Med 1995;25:63-77.
34. Ritvo ER, Freeman BJ, Mason-Brothers A, Mo A, Ritvo AM. Concordance for the syndrome of autism in 40 pairs of afflicted twins. Am J Psychiatry 1985;142:74-7.
35. Philippe A, Martinez M, Guilloud-Bataille M, Gillberg C, Rastam M, Sponheim E, et al. Genome-wide scan for autism susceptibility genes. Paris Autism Research International Sibpair Study. Hum Mol Genet 1999;8:805-12.
36. A genomewide screen for autism: strong evidence for linkage to chromosomes 2q, 7q, and 16p. International Molecular Genetic Study of Autism Consortium. Am J Hum Genet 2001;69:570-81.
37. Risch N, Spiker D, Lotspeich L, Nouri N, Hinds D, Hallmayer J, et al. A genomic screen of autism: evidence for a multilocus etiology. Am J Hum Genet 1999;65:493-507.
38. Further characterization of the autism susceptibility locus AUTS1 on chromosome 7q. Hum Mol Genet 2001; 10:973-82.
39. Folstein SE, Rosen-Sheidley B. Genetics of autism: com-

plex aetiology for a heterogenous disorder. Nat Rev Genet 2001;2:943-55.
40. Stokstad E. New hints into the biological basis of autism. Science 2001;294:34-7.
41. Andres C. Molecular genetics and animal models in autistic disorder. Brain Res Bull 2002;57:109-19.
42. Persico AM, D'Agruma L, Maiorano N, Totaro A, Militerni R, Bravaccio C, et al. Reelin gene alleles and haplotypes as a factor predisposing to autistic disorder. Mol Psychiatry 2001;6:150-9.
43. Ingram JL, Stodgell CJ, Hyman SL, Figlewica DA, Weitkamp LR, Rodier PM. Discovery of allelic variants of HOXA1 and HOXB1: genetic susceptibility to autism spectrum disorders. Teratology 2000;62:393-405.
44. Skuse DH. Imprinting, the X-chromosome, and the male brain: explaining sex differences in the liability to autism. Pediatr Res 2000;47:9-16.
45. Johnson WG. DNA polymorphism-diet-cofactor-development hypothesis and the gene-teratogen model for schizophrenia and other developmental disorders. Am J Med Genet 1999;88:311-23.
46. London EA. The environment as an etiologic factor in autism: a new direction for research. Environ Health Perspect 2000;108 Suppl 3:401-4.
47. Kemper TL, Bauman M. Neuropathology of infantile autism. J Neuropathol Exp Neurol 1998;57:645-52.
48. Rodier PM, Ingram JL, Tisdale B, Nelson S, Romano J. Embryological origin for autism: developmental anomalies of the cranial nerve motor nuclei. J Comp Neurol 1996;370:247-61.
49. Rapin I. Autism. N Engl J Med 1997;337:97-104.
50. Zimmerman AW, Gordon B. Neural mechanisms in autism. In: Accardo PJ, Magnusen C, Capute AJ, editors. Autism: clinical and research issues. Baltimore: York Press; 2000.
51. Eaton WW, Mortensen PB, Thomsen PH, Frydenberg M. Obstetric complications and risk for severe psychopathology in childhood. J Autism Dev Disord 2001;31:279-85.
52. Deykin EY, MacMahon B. Viral exposure and autism. Am J Epidemiol 1979;109:628-38.
53. Piven J, Simon J, Chase GA, Wzorek M, Landa R, Gayle J, Folstein S. The etiology of autism: pre-, peri-, and neonatal factors. J Am Acad Child Adolesc Psychiatry 1993;32:1256-63.
54. Rodier PM, Hyman SL. Early environmental factors in autism. Ment Retard Dev Disabil Res Rev 1998;4:121-8.
55. Ingram JL, Peckham SM, Tisdale B, Rodier PM. Prenatal exposure of rats to valproic acid reproduces the cerebellar anomalies associated with autism. Neurotoxicol Teratol 2000;22:319-24.
56. Rodier PM. The early origins of autism. Sci Am 2000; 282:56-63.
57. Agency for Toxic Substances and Disease Registry (US), Division of Toxicology, Emergency Response and Scientific Assessment Branch. Chemical specific consultation: hazardous substance exposures and autism. Atlanta: ATSDR; 1999.
58. Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Lancet 1998;351:637-41.
59. Bernard S, Enayati A, Redwood L, Roger H, Binstock T. Autism: a novel form of mercury poisoning. Med Hypotheses 2001;56:462-71.
60. Medical Research Council. MRC review of autism research: epidemiology and causes. London (UK): Medical Research Council; 2001.
61. Yeates-Frederikx MH, Nijman H, Logher E, Merckelbach HL. Birth patterns in mentally retarded autistic patients. J Autism Dev Disord 2000;30:257-62.
62. Institute of Medicine, Board on Health Promotion and Disease Prevention, Immunization Safety Review Committee. Stratton K, Gable A, Shetty P, McCormick M, editors. Immunization safety review: measles-mumps-rubella vaccine and autism. Washington: National Academy Press; 2001.
63. Madsen K, Hviid A, Vestergaard M, Schendel D, Wohlfahrt J, Thorsen P, et al. A population-based study of measles, mumps, and rubella vaccination and autism. N Engl J Med 2002;347:1477-82.
64. Institute of Medicine, Board on Health Promotion and Disease Prevention, Immunization Safety Review Committee. Stratton K, Gable A, McCormick MC, editors. Immunization safety review: thimerosal-containing vaccines and neurodevelopmental disorders. Washington: National Academy Press; 2001.
65. Ritvo ER, Freeman BJ, Pingree C, Mason-Brothers A, Jorde L, Jenson WL, et al. The UCLA-University of Utah epidemiologic survey of autism: prevalence. Am J Psychiatry 1989;146:194-9.
66. Smalley SL, Asarnow RF, Spence MA. Autism and genetics. A decade of research. Arch Gen Psychiatry 1988; 45:953-61.
67. Simonoff E. Genetic counseling in autism and pervasive developmental disorders. J Autism Dev Disord 1998;28: 447-56.
68. Khoury MJ, Thrasher JF, Burke W, Gettig EA, Fridinger F, Jackson R. Challenges in communicating genetics: a public health approach. Genet Med 2000;2:198-202.
69. Department of Health and Human Services (US). HHS fact sheet: HHS on the forefront of autism research [cited 2001 Nov 16]. Available from: URL: http://www.hhs.gov/news/press/2001pres/01fsautism.html
70. National Institute of Mental Health (US). Report to Congress on autism. Bethesda (MD): National Institutes of Health; 2002.
71. Children's Health Act of 2000, Pub. L. No. 106-310, 114 Stat. 1101 (Oct. 17, 2000) (cited 2002 Mar 19). Available from: URL: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=106_cong_public_laws&docid=f:publ310.106.pdf
72. Individuals with Disabilities Education Act of 1997, Pub. L. No. 105-17, 111 Stat. 37 (June 4, 1997) (cited 2002 Mar 19). Available from: URL: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=105_cong_public_laws&docid=f:publ17.105.pdf