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Is There an Epidemic of Autism?

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Is There an Epidemic of Autism?

ABBREVIATIONS. DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders, IV;* PDD, pervasive developmental disorder; PDD-NOS, pervasive developmental disorder-not otherwise specified.

The debate on the hypothesis of a secular increase in rates of autism would benefit from a clear recognition of the methodologic limitations of existing data. No psychiatric case register study has ever allowed for estimating and monitoring the incidence of autistic conditions over time.[1] Cross-sectional surveys hugely differ in their case definition and case identification methods that account for large variations in prevalence estimates both over time and across areas, precluding a meaningful analysis of time trends. That rates in recent surveys are substantially higher than 30 years ago merely reflects the adoption of a much broader concept of autism, a recognition of autism among normally intelligent subjects, changes in diagnostic criteria, and an improved identification of persons with autism attributable to better services.[1,2] The only epidemiologic study where case definition and identification could be held constant failed to detect an increase in rates of autism in successive birth cohorts from 1972 to 1985.[3]

Most of the claims about the 'epidemic' of autism are therefore based on referral statistics from various centers. The report of the Department of Developmental Services from California has been, and still is, widely quoted as evidence for an epidemic of autism.[4] The key data of this report (Table 1 and Fig 1) need a critical examination.

First, the figures apply to numbers rather than rates and fail to account for changes in the size and composition of the underlying population. Between 1987 and 1999, the population of California rose from 27 777 158 to 33 145 121 persons (+19.3%) and that of the 0- to 14-year-olds (the age group where most of the increase was reported) increased from 6 009 165 to 7 557 886 children (+25.8%). Positive migration fluxes to California both from within the United States and from abroad might also be differentially related to the presence of an autistic child in a family. None of these basic epidemiologic concerns were taken up in the report.

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TABLE 1. Autism and Other PDDs Registered in California (1987–1998)

	1987	1998	% Change
Autism (Full syndrome and residual state)	2778	10 360	272.9%
Other PDD	38	785	1965.8%
Autism suspected (Not diagnosed)	1086	1635	50.6%

Second, no attempt was made to control for changes in diagnostic concepts and definitions. The report refers to definitions in the *Diagnostic and Statistical Manual of the Mental Disorders, IV* (DSM-IV) but completely ignores that, in view of the wide age range of the sample and study period (1987–1998), multiple diagnostic systems were in fact used over the years producing heterogeneity in diagnoses in successive birth cohorts. In 1980, DSM-III introduced the terminology of pervasive developmental disorder (PDD) widening the previous concept of infantile autism. The change from DSM-III to DSM-III-R in 1987 was associated with an additional broadening of the concept of PDD at the expense of its specificity. In 1994, the diagnostic categories of Asperger syndrome, Rett syndrome and childhood disintegrative disorder were introduced for the first time in DSM-IV as subcategories of PDDs; moreover, the diagnostic boundaries of pervasive developmental disorders not otherwise specified (PDD-NOS) were inadvertently widely broadened because of editorial changes in the layout of the diagnostic criteria.[5] Not surprisingly, these 4 categories account for the largest increase in the California report (Table 1, Other PDD).

Third, in California and elsewhere, autistic children are now diagnosed at a much earlier age. A decreasing mean age at diagnosis will necessarily result in an increased number of reported cases, even assuming a stable prevalence or incidence. Thus, age-specific rates among older children are required to test time trends.

Fourth, the only comparison made in the report with an epidemiologic estimate was inaccurate. The report stated that the number (N = 1685) of new persons (of all ages) entering their database in 1998 exceeds that expected from one annual birth cohort; however, this comparison is nonsensical because it is confounded by age differences. More meaningful comparisons tell a very different story. Using a conservative estimate of 22.125/10 000 for all types of PDDs deriving from a recent review[1] and the January 1999 census estimates (http://www.census.gov) for California for the whole population (N = 33 145 121) and subjects aged 0 to 19 (N = 9 916 162), the expected numbers of subjects with a PDD in California in 1998 are 73 334 and 21 940 persons, respectively. Furthermore, as of July 2000, the total number of persons with autism registered to California Developmental Services was 13 054. Thus, as one would predict with routine administrative statistics, the California reports seriously underestimate the size of the problem (Table 1); and surely our calculations provide no basis for the claim of an epidemic based on the reports' figures.

Fifth, far from being specific to autism, upward trends were also reported for other disorders (such as cerebral palsy, epilepsy, or mental retardation) for which there is no epidemiologic evidence for a secular increase. This points towards a general methodologic and recording artifact at the source of the reported increases.

Yet, the most worrying aspect of the California report lies in the distortion of data graphically portrayed in Fig 1. The report states that Fig 1 derives from the ". . . 1991 population of persons (7915) with autism," therefore clearly indicating the cross-sectional nature of the sample. Instead of age, the report plots year of birth on the horizontal axis thereby artificially creating the impression of a prospective data collection. The note of caution in the text ('Data points in Fig 1 do not show how many persons enter the system in a given year, but how many already in the system were born in a given year') has been obviously overlooked by most commentators. This graphical display deliberately transforms what is an age effect into what seems a cohort effect, although the latter cannot be tested with such cross-sectional data. By analogy, any sample with a marked skewed age-distribution (for example, take a survey of Army personnel) could be misleadingly portrayed by replacing age by year of birth and giving the same impression of an upward trend over time than in Fig

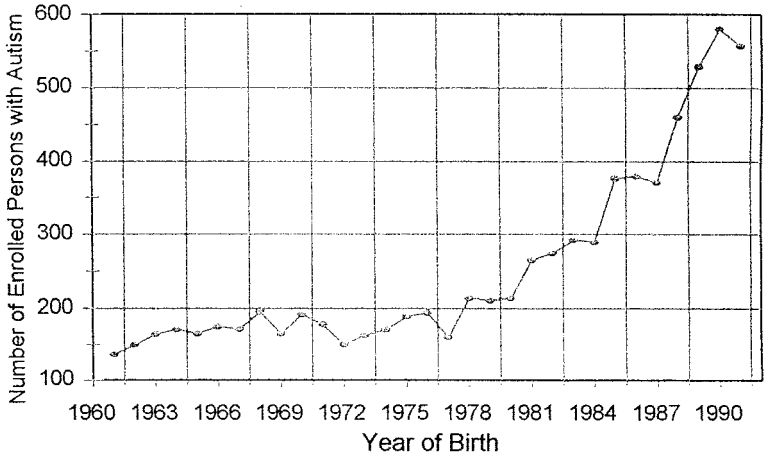

Fig 1. Distribution of birth dates of regional center eligible persons with autism (California).

1 (but nobody would interpret the transformed personnel Army data as indicative of rising numbers of militaries!). The point is that, in both examples, there was no passage of time allowing inferences to be made on trends over time.

The misuse of these data by some investigators[6] is another tribute to their poor research methodology. To date, the epidemiologic evidence for a secular increase in the incidence of PDDs is both meager and negative.[1] We simply lack good data to test hypotheses on secular changes in the incidence of autism. Because of specific methodologic limitations, the high prevalence rates reported in recent autism surveys cannot be used to derive conclusions on this issue.[1,2] Prevalence data nevertheless point to the magnitude of the problem, which had clearly been underestimated in the past. But there is no need to raise false alarms on putative epidemics nor to practice poor science to draw the attention to the unmet needs of large numbers of seriously impaired children and adults. More complex monitoring systems than those currently in place are needed to address the issue of secular changes in the incidence of PDDs. Maintaining case definition and identification constant, focusing on children in the upper range of school age years, controlling for changes in the population (ie, differential migration, etc. . .) and relying on adequate sample sizes are required for future epidemiologic efforts in this area.

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Postnatal Glucocorticoids in Very Preterm Infants: "The Good, the Bad, and the Ugly"?

ABBREVIATIONS. BPD, bronchopulmonary dysplasia; DXM, dexamethasone.

Premature births represent 7% to 10% of all births, but account for >85% of all perinatal complications and death. Survival of extremely premature newborns (<28 weeks' gestation) has increased because of the widespread use of surfactant treatment for respiratory distress syndrome, together with antenatal glucocorticoids and new ventilator strategies.[1] However, these infants are at high risk for long-term injury of both the lungs and the brain. Bronchopulmonary dysplasia (BPD) is one of the most frequent sequelae in extremely premature infants and results in increased health care costs, prolonged hospital stays with frequent rehospitalizations, and deleterious effects on subsequent growth and neurodevelopment.[2] Periventricular leukomalacia, the most severe form of white matter brain damage, is a frequent cause of cerebral palsy in children surviving preterm birth, with lifelong consequences.[3] Recent data suggest that a common treatment for one, dexamethasone for BPD, may have deleterious effects on both sequelae.

Northway et al[4] first described BPD as severe lung injury resulting from mechanical ventilation and oxygen exposure. With improved prenatal and postnatal care, preterm infants developing BPD now are generally very immature, and have antenatal and postnatal histories that differ from those of preterm infants in previous eras. The "new BPD," as described by Jobe,[5] is characterized by an arrest of lung development and interference with alveolarization. This more complex view of the pathogenesis of BPD includes prenatal lung inflammation in response to proinflammatory cytokine exposure in utero, together with postnatal exposure to proinflammatory stimuli, such as ventilation and oxygen. Jobe[5] postulates that these stimuli, together with glucocorticoid exposure and inadequate nutrition, can result in inhibition of alveolar and vascular development. Therein lies the irony: the postnatal dexamethasone (DXM) widely used for the treatment or prevention of BPD may suppress inflammation, but also may impair alveolarization and interfere with lung development.

Initial trials of DXM, a potent and long-acting glucocorticoid, in preterm infants with BPD showed short-term improvement in pulmonary function and weaning from the ventilator.[6,7] Over time, with increased survival of extremely premature infants, there has been a shift toward earlier use of DXM in newborns of lower and lower gestational ages.[8,9] The plethora of trials conducted over the past 2 decades have recently been evaluated in 3 meta-analyses according to the onset of treatment: 1) early postnatal (<96 hours of life),[10] 2) moderately early postnatal (7–14 days),[11] and 3) delayed (>3 weeks).[12] Although moderately early treatment decreased mortality and

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