

Review

Thimerosal and autism: a renewed issue

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Abstract

Autism was and still is an unresolved tragedy in the fields of pediatrics and psychiatry, with an apparent increased incidence and prevalence rates—reaching what is called an “autism epidemic”. Etiologically, genetics is the field of extensive investigation with clear evidence of multiple susceptibility genes on different chromosomes. But, epidemics can not be explained by genetics, so environmental factors are considered a more logical explanation. Such factors include childhood vaccines, especially the measles component of measles-mumps-rubella vaccine, and vaccine preservatives, namely thimerosal because of its mercury content. In this review, different views are presented about the issue of Thimerosal and autism.

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1. Introduction

Autism spectrum disorder is a neurodevelopmental syndrome with onset prior to age 36 months. Diagnostic criteria consist of impairments in social relatedness and communication, repetitive behaviors and stereotypic abnormal movements [1].

2. Prevalence

Previous epidemiologic surveys conducted in Europe, Asia, and North America estimated the prevalence of autism to be between 2 and 21 per 10000 in the general population [2].

Autism prevalence rates from studies published before 1985 are 4-5 per 10000 children. Since 1985, non-US studies have reported higher rates of autism ranging from 10-25 per 10000 [3].

Even higher rate of 62.6 per 10000 was reported from a study conducted in the United Kingdom [4], which was replicated in the same area by the same researchers but on a later birth cohort with a rate of 60.6 per 10000 [5].

While the rates were 2 per 1000 in Japan, 1 per 1000 in Nova Scotia, Canada, 1-4 per 1000 in Southern Sweden [6], and 1.1 per 1000 in China [7].

In 1998 a prevalence rate of 67 per 10000 was reported in Brick Township, New Jersey [8], while it was 34 per 10000 in metropolitan Atlanta, Georgia [3].

One of the most recent published studies, found 64.9 per 10000 rate in Montreal, Quebec, Canada [9], which is nearly 6.5 times the rate reported in 1988 study in Canada [10].

An increase in prevalence estimates has been observed over time [11], reviews and surveys conducted in the last 5 years have consistently reported prevalence rates of about 6 per 1000 for the whole pervasive developmental disorders spectrum. This roughly threefold increase in PDD prevalence overtime, com-

pared with 2 per 1000 rate reported in 1979 [12], has generated concerns about a possible autism epidemic [13].

This epidemic has been identified by Yazbak 2003, who prompted health authorities to conduct independent and unbiased clinical studies in order to determine all causes of autism epidemic [14].

3. Etiology

Determining the cause of autism is critical to permit appropriate diagnostic, treatment, and preventive measures to be enacted [15].

The major categories proposed as causing autism are genetic influence and prenatal or postnatal environmental factors [6].

4. Genetics of Autism

Overwhelming evidence exists for a large genetic component in autism [16-20].

Twin studies show a 60-90% concordance rate for autism in monozygotic twins, contrary to concordance rate between 0% and 20% in dizygotic twins [17,21,22]. The rate of autism among siblings of affected probands is 2% to 3% [23].

This pattern of sharply increasing risk for first-degree relatives and monozygotic twins relative to the population prevalence 1.1 per 1000 [24], does not fit a simple dominant or recessive pattern, but rather indicates the involvement of multiple genes interacting with one another to lead to disease susceptibility.

5. Objective

To review the studies, research reports, and publications about thimerosal and autism.

6. Search Strategy

I conducted a thorough search of *MEDLINE*, *MEDSCAPE*, and *PubMed* and personally contacted many researchers and authors to collect studies. Any available reference lists of relevant articles were searched and authors were contacted when feasible to obtain reprints of prominent papers.

7. Vaccines and Autism

Vaccines, particularly measles, mumps, and rubella (MMR) vaccine (25-29), and thimerosal-containing vaccines [30,31], have been postulated as a cause for the epidemic increase of autism spectrum disorder.

8. Thimerosal and Autism

Exposure to mercury has previously been shown to cause immune, sensory, neurological, motor and behavioral dysfunctions similar to traits defining or associated with autistic disorders, and with similarities in neuroanatomy, neurotransmitters and biochemistry [30-33].

Geier and Geier 2003 study comparing Diphtheria-Tetanus – acellular Pertussis (DTaP) vaccine with and without thimerosal have shown a statistically and clinically significant increase in neurodevelopmental disorders (NDs) in those vaccinated with thimerosal- containing vaccines [34]. This study has been critiqued by Mann JR 2003, who stated that; in the meantime, it seems prudent for clinicians to use thimerosal-free vaccines when possible [35]. And mentioned passively by Clements CJ 2006, who concluded that the problem of thimerosal and autism may solve itself as more and more vaccines are being delivered as mono-dose polyvalent presentations that do not require a preservative [36]. i.e., the critics took the same position of Geier and Geier in diplomatic words.

But the hard criticism of Geier and Geier work was in a report from the American Academy of Pediatrics, which warned against use of data from the Vaccine Adverse Event Reporting System (VAERS) inappropriately in the study [37], and referred to the negation of thimerosal/autism correlation in Nelson and Bauman article [38].

Nelson and Bauman were more conservative in their conclusion; if thimerosal was an important cause of autism, the incidence of autism might soon begin to decline. This is exactly what was noted as significant decreasing trends in newly diagnosed neurodevelopmental disorders observed from mid-2002 through 2005 following removal of most thimerosal-containing vaccines [39,40], while the same authors found significant increase in the incidence rate of neurodevelopmental disorders after thimerosal-containing DTaP vaccines, which potentially may be explained by the toxic buildup of mercury from successive doses of vaccines [41].

One of the latest reviews of publications on thimerosal and autism was that of Clements and McIntyre [42], who identified 12 publications [34,41,43-52], then tabulated their findings and made analysis of the results. The reviewers acknowledged the 6 studies that negate association between thimerosal and autism [47-52], and criticized the 6 studies by Geier and Geier [41,43-46], who insisted on proved association. Clements CJ 2006

wrote; it is worth noting that the 6 of Geier papers clearly fly in the face of the weight of scientific evidence [36], throughout this review this was not the situation.

9. Conclusion

There is no agreement what was the real reason of autism epidemic, but the environmental factors are more logic as we can identify and remove, so that we can avoid a severe and disabling disorder like autism. Thimerosal use in some wealthy countries is decreasing, but the issue still relates to newly introduced vaccines and in the poor countries where the multi-dose thimerosal-containing vials remain in use [42].

Based on the current hypothesis that removal of thimerosal from childhood vaccines would reduce the number of neurodevelopmental disorders, we are looking for world wide replication of Geier and Geier study to verify this idea.

On the other hand, exposure of infants to mercury from the environment, like breast milk, should be evaluated according to dietary habits and food sources (53).

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