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Letter to Editor

Penicillamine - Preventing or "Curing" Autism Spectrum Disorders in the Neonatal Period?

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The important research article Marques: "Autism Spectrum Disorder: What Study We Need to Do?" [1] has encouraged us to write this letter. In this paper we focus on the urine (or rather on the 24-hour urine copper). There is indeed an increased incidence of Autism Spectrum Disorder (ASD) worldwide. "New Prevalence Numbers for 2014: 1 in 45 US Children have autism" [2], and it is most common among boys. Copper is implicated directly or indirectly in the pathogenesis of a large number of neurological diseases, including ASD [3], and we have found a direct evidence for the copper excess in the etiology of this disorder characterized by impairments in social interactions, communication, and emotional abilities, while sparing basic cognitive skills (Table 1).

http://dx.doi.org/10.1155/2011/385767
http://autism-genetic-risk-factor.blogspot.hu/2008/11/are-children-with-autism-heterozygous.html
http://autism-genetic-risk-factor.blogspot.hu/2008/11/if-genetic-risk-factor-for-autism-is.html
https://www.ncbi.nlm.nih.gov/pubmed/23823984/
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http://www.conem.org/2013/07/the-role-of-zinc-and-copper-in-autism-spectrum-disorders/
https://www.academia.edu/4079689/The_Role_of_Zinc_and_Copper_in_Autism_Spectrum_Disorders
http://www.autismweb.com/forum/viewtopic.php?p=196145
http://autism-genetic-risk-factor.blogspot.hu/2008/11/many-children-with-autism-have-high.html
https://www.naturalhealth365.com/copper_levels.html/

Table 1: *Elevated copper levels threaten human health and can cause ASD.*

In our recently published review article [4] we have expounded that excessive metal (copper) accumulation in the nervous system may be toxic, inducing oxidative/nitrosative stress (OS/NS), disrupting mitochondrial function, and impairing the activity of numerous enzymes. Damage caused by copper excess may result in permanent injuries, including severe neurological/neurodegenerative disorders (NDs). The immature and strikingly vulnerable neurons play an important role in the pathogenesis of bilirubin-induced neurologic dysfunction (BIND) as well. Our concept addresses the medical necessity of chelation therapy with D-Penicillamine (D-PA) in the neonatal period, as it is feasible that UCB molecule reviels particular affinity to copper stored in basal ganglia of the neonatal brain, where copper-bilirubin complex can be formed. Copper dyshomeostasis and oxidative stress have also been concerned in NDs such as ASD. Our recommandation: all newborns should be screened for ASD, particularly the premature babies and infants suffering from hyperbilirubinemia.

These conditions significantly increases the prevalence of NDs, including ASD. Although the 24-hour urine copper test is inconsistent in the neonatal period, and the normal value range may vary among different laboratories, the penicillamine challenge test has proved itself to be useful in the detection of high copper in the urine [5]. This test widely used in the diagnosis of Wilson's Disease which is a mitochondrial disorder that causes encephalopathy and depletes metallothionein. And "patients with Wilson's disease have relevant glutathione depression, with low levels of reduced glutathione and cysteine and high concentrations of oxidized glutathione [just like many children with autism]". [Table 1. - third link]. For those children who are voiding copper more than usually, high doses DPA therapy is necessary for 2 - 3 weeks.

Our concept was conceived because of long-term follow-up (3 - 40 years [6-8]) we found only 1 ASD in the children and adults who were treated with DPA in their neonatal period (N =5 50 patients so far). The 30 years old male patient was born as a premature infant and had a serious hyperbilirubinemia. He was treated with D-PA without success, because exchange transfusion was necessary.

Conflicts of Interest

The authors stated that there are no conflicts of interest regarding the publication of this paper.

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