



## Essential Minerals and Toxic Metals

Metals, both essential and toxic, are found in the human body and more than one quarter of the elements known in the periodic table are essential for human life.

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Toxic Metals and Essential Minerals in the Hair of Children with Autism and their Mothers

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### Introduction

While the cause of autism is unknown, there are suggestions that excessive mercury or other toxic metals, and/or a lack of essential minerals, may play a role. The amount of toxic metals and essential minerals can easily be assessed by blood, urine, and hair. Hair is especially useful for toxic metals, as they are much more concentrated in the hair. Since hair grows at a rate of 1-1.5 cm/month, a 2-3 cm sample from next to the scalp can provide an average over 2-3 months. It provides a measure of what is being transported in the body during that time, but will not be able to detect earlier exposures. There has been some recent well-publicized criticism of hair analysis studies [1], but the major criticism centered on differences in results between different labs, some of which were using inferior equipment and less rigorous preparation techniques. Those concerns can be addressed by using a single high-quality lab, with blinded testing of subjects vs. controls. In a classic review of over 250 reports, the EPA concluded that hair is "a meaningful and representative tissue" for measuring toxic metals and selected nutrients.[2]

There were several previous studies in the 1980's of the levels of toxic and essential minerals in the hair of children with autism [3] [4] [5] [6]. However, those studies suffered from several limitations, including small sample size, less accurate measurement techniques, no use of a non-contaminated shampoo, and use of siblings as controls.

In addition, there was a recent study by Holmes' et. al [7] of the level of mercury in the hair of infants (aged 12-24 months) who later were diagnosed with autism compared to controls (n=94 and 45, respectively). This study found that the autism group had 1/8 of the normal amount of mercury in their baby hair compared to controls, which suggests an inability to excrete mercury. They also found that the severity of autism had a strong inverse relationship with the level of mercury, with the most severe group having the lowest levels of mercury in their hair. This is consistent with the hypothesis that the group with the most inhibition of mercury excretion would be the most severely affected.

There has never before been an attempt to analyze the hair of the mothers of children with autism. Since the mothers are the major source of exposure to toxic metals, and also the source of essential minerals during gestation and breastfeeding, we felt that it would be important to also analyze the levels in their hair.

## **Participant Selection**

There were 51 children with ASD enrolled in the study, including 48 with autism, 2 with PDD/NOS, and one with Asperger's. There were 40 neurotypical children enrolled as controls in the study. There were 12 girls and 10 girls in the ASD and control groups, respectively, comprising 23.5% and 25% of their groups. There were two sets of twins in the ASD group, and one set of twins and one pair of siblings in the control group. Ages ranged from three to 15 years of age, with a mean age of 7.1 and 7.5 years for the children with ASD and the controls, respectively, with standard deviations of 3.0 years for each. Thus, there was overall a good match between the groups in terms of gender and age.

In the ASD group, children were also analyzed in terms of subgroups according to whether they had pica (16), regression (32), ear infections (26 had 8 or more ear infections), chronic constipation/diarrhea (32), sleep problems (31), or low muscle tone (15).

Mothers were asked to participate as well, but their participation was optional. Only mothers who had not dyed or permed their hair within two months of collecting samples were included in the data. (None of the children had had their hair permed or dyed). A total of 29 mothers of children with ASD and 25 mothers of typical children were enrolled in the study.

## **Hair Sampling**

All participants (children and mothers) were asked to wash their hair for two weeks with Johnson's and Johnson's "No Tears" Formula Baby Shampoo, without the use of any other hair care products (no conditioner, gel, hairspray, etc.). After two weeks, a sample of hair was cut using stainless steel scissors. The hair sample was taken from the nape of the neck, taking the one-inch closest to the neck. The samples were sent to Doctors Data Lab for analysis in a blinded fashion. Results are expressed as mcg / gm.

## **Summary of Statistically Significant Results**

### *Toxic Metals*

There was generally no difference between the children with ASD and the control children in terms of their heavy metals. The children with ASD had slightly lower levels of aluminum (16%,  $p=0.05$ ), and the difference was slightly more pronounced in the 3-6 year old group (24% lower,  $p=0.04$ ).

Overall, the pica subgroup had higher levels of aluminum, uranium, and barium, presumably due to increased consumption. However, their arsenic level was slightly lower, and the reason for this is unclear. It could be a random result, or perhaps arsenic is being less well excreted due to competition with higher levels of other toxic metals.

In terms of other subgroups, a test comparison of the subgroups did not reveal any statistically significant differences in any of the toxic metals for the regression, gastrointestinal, ear infection, or salivation subgroups. The Sleep disorder subgroup had slightly lower levels of arsenic than the non-sleep disorder ASD subgroup (0.08 vs. .11,  $p=0.02$ ), but the controls had an average level of 0.095, so this is likely to be a random result. Similarly, the Muscle Tone subgroup had lower levels of bismuth (0.10 vs. 0.35,  $p=0.05$ ), but the controls had an average level of 0.28, so again this may be a random result.

*Mothers:* In the mothers of children with ASD, there was no statistically significant difference in the level of heavy metals in their hair.

*Mercury:* Since mercury is of great interest as a possible cause of ASD, it is worthwhile to note that the mothers of children with ASD had 57% more mercury in their hair on average than the typical mothers, but this difference was not statistically significant ( $p=0.22$ ). When the subgroup of mothers of young children was considered, there was less difference. In terms of the validity of our testing, it should be pointed out that the median values we found for the typical mothers (0.18 mcg/g) are consistent with those of a recent large NHANES study of 702 women of age 16-49 years (0.2 mcg/g)[8]. Both of those median values for typical women are much lower than the median we found for the mothers of children with autism (0.40 mcg/g).

Also, the children with ASD had nearly normal levels of mercury in their hair, with the pica subgroup having 24% more than the controls, and the non-pica subgroup having 10% less. These results were not statistically significant. So, mercury levels did not appear abnormal in this group of children. However, it should be pointed out that this is long past their primary exposure to mercury (from thimerosal-containing vaccines, maternal seafood consumption, and maternal mercury dental fillings), so this hair measurement would not reflect such a long-previous exposure.

Our results are not necessarily inconsistent with the results of Holmes et al. , which found unusually low levels in baby hair, as the ages of their group (12-24 months) are quite different than ours (age 3-15 years). Actually, if both sets of data are valid, then they suggest a temporary loss of the ability to excrete mercury in young infants. This temporary loss could be explained by the excessive use of oral antibiotics in children with autism [9], as oral antibiotics have been shown to dramatically inhibit mercury excretion to 1/10 of normal in rats [10].

## **Essential Minerals**

### *Children*

*Iodine:* For the children with ASD, the mean level of iodine was much lower (45%) than for the control children, and the difference was highly statistically significant ( $p=0.005$ ). When the subgroup of age 3-6 years was considered, the magnitude of the difference was almost identical (47%), although the difference was not statistically significant due to the smaller number of children in the subgroup. This suggests that iodine could be an important factor in the early development of autism, presumably through its effect on thyroid function. Iodine deficiency was extremely common in parts of the US in the early 1900's, and caused many cases of goiters (enlarged thyroid) and cretinism (a form of mental retardation due to iodine deficiency). This prompted the federal government to mandate that iodine be added to salt (iodinized salt). However, based on our informal phone survey of several major snack food and fast food manufacturers, non-iodinized salt seems to be the form primarily used in french fries, potato chips, and other snack foods commonly eaten by young children. So, it is plausible that a small fraction of children in the US could still be marginally deficient in iodine, and that this could significantly affect their mental status. Also, it should be pointed out that according to the NHANES surveys I and III [11], average iodine levels in the US (measured in the urine) have declined more than 50% during the 20 year period from 1971-1974 to 1988-1994, so that an increasing fraction of the population has low levels of iodine that are likely to increase the risk for mental retardation. Thus, low iodine levels could be a cause or exacerbating factor for autism. However, it needs to be pointed out that hair measurements have not been validated for iodine as reflective of body status, so future studies of iodine levels in blood are warranted, as well as studies of thyroid function in autism.

Phosphorus was consistently slightly low, and strontium was consistently elevated, but the importance of those findings is unclear.

*Lithium:* In the subgroup of children ages 3-6, the children with ASD had a 30% lower level of lithium with a marginal statistical significance ( $p=0.04$ ).

Overall, the pica subgroup had low levels of sodium, chromium, and sulfur, with the low chromium level being the most statistically significant, and hence most likely to be a possible factor in the etiology of pica. The pica group also had elevated levels of strontium and copper, presumably due to increased consumption.

*Muscle Tone:* The children with low muscle tone had very low potassium (16 vs. 61,  $p=0.01$ , vs. controls =47), high copper (56 vs. 26,  $p=0.05$ , controls =33), high zinc (193 vs. 150,  $p=0.01$ , controls=147), and high barium (2.03 vs. 0.95,  $p=0.03$ , controls = 0.97). Potassium is needed for muscle contractions, so very low levels of it are likely to result in low muscle tone. The significance of the other results is unclear.

Overall, we think the most important results are the low level of iodine in the group as a whole, the low level of lithium in the younger children, and the low level of potassium in the children with low muscle tone. These findings suggest that deficiencies of these minerals could be part of the underlying cause of autism. Also, supplements of iodine and lithium could be beneficial to children with autism, and increased potassium could be useful to children with low muscle tone. For potassium, increased consumption of fruits and vegetables may be a safer source of potassium than supplements, due to the concern of potassium supplements on heart conditions.

*Lithium in Mothers:* In the mothers of children with ASD, the level of lithium was 40% lower than the mothers of typical children, and the result was marginally statistically significant ( $p=0.05$ ). Also, when the subgroup of mothers of children ages 3-8 was considered, the difference was more pronounced (56% lower) and more statistically significant ( $p=0.005$ ). Since low lithium was also observed in the younger children with ASD, this makes the result especially interesting. It should be pointed out that hair has been found to be a reliable method to assess lithium deficiency in goats, in agreement with measurements of blood, milk, and several other organs.[12] Lithium concentrations are highest in the brain,[13] and are highest during the first trimester, [14] so a deficiency of it during pregnancy could adversely affect fetal development, and especially brain development. Also, low levels of lithium in humans have been found to correlate with a wide range of behavioral problems, including aggression and decreased sociability. [15] [16] [17] One placebo-controlled treatment study found that low dose supplementation (400 mcg/day) was beneficial to drug addicts, resulting in increases in the subcategories of happiness, friendliness, and energy. [18] It should be noted that lithium is also used at dramatically higher doses (of the order of 1,000,000 mcg/ day) as a psychiatric medication for mood stabilization.

In addition, goats on a lithium-deficient diet were found to suffer from lowered immunological status and chronic inflammations, they had less lithium in their milk, and their infants were found to have reduced growth rates. We hypothesize that the low levels of lithium in the ASD mothers results in lower levels in their children, which may explain why the children suffer from a much higher level of ear infections in their first three years of life . In turn, that much higher level of ear infections results in much higher oral antibiotic use, which results in a temporary decrease in the ability to excrete mercury , and can also contribute to gastrointestinal problems by eliminating normal gastrointestinal flora. So, a low lithium level is plausible as an important factor in the etiology of autism.

There were no other statistically significant differences in the levels of toxic metals or essential minerals between the mothers of children with ASD and mothers of typical children. Only the lithium levels were abnormal in the mothers of children with ASD.

## Summary

We have evaluated the levels of 39 toxic metals and essential minerals in children with ASD, including the first evaluation of the hair of mothers of children with ASD. We believe that the most important results are:

1. Low iodine levels (-45%,  $p=0.005$ ) in the children with ASD, including in the young subgroup (-47%, not significant). Low iodine may result in significant impairment of thyroid function, and iodine deficiency is a known cause of cretinism, a type of severe mental retardation.
2. Low lithium levels in the young children ages 3-6 years (-30%,  $p=0.04$ ), in the mothers of children with ASD (-39%,  $p=0.05$ ) and especially in the mothers of young children ages 3-8 years (-56%,  $p=0.005$ ). The consistency of this result in the mothers and the children, and the high statistical significance in the young mothers, suggests that this is an important factor in ASD.

3. Phosphorus levels are consistently low (-11%,  $p=0.001$ ) in children with ASD, including young children. Although the magnitude of the effect is small, it is highly statistically significant. It is unclear if this small difference would have an effect on the symptoms of ASD, but it may be a clue to some other important mechanism. Also, the autistic children with fewer ear infections tend to have less phosphorus than those with many (175 vs. 200 mcg/g,  $p=0.004$ , controls = 213), but the meaning of this is also unclear.
4. Pica is strongly associated with a low level of chromium (-38%,  $p=0.002$ ), and moderately associated with low levels of sodium (-58%,  $p=0.05$ ). This suggests that nutritional supplements of chromium, and possibly sodium, could be beneficial in the treatment of pica. Pica is also (less strongly) associated with high levels of copper, strontium, uranium, and barium, presumably due to increased consumption.
5. Low muscle tone was associated with very low levels of potassium (-66%,  $p=0.01$ ), high zinc (31%,  $p=0.01$ ), high levels of barium (+109%,  $p=0.03$ ), and possibly high copper. This suggests that potassium levels in blood should be checked, and supplementation may be beneficial.
6. Mercury levels were not significantly different in the children with ASD, although it should be pointed out that this is long past their primary exposure to mercury (thimerosal in vaccines, maternal seafood consumption, maternal dental amalgams). Their mothers had a 57% higher level of mercury on average, but it was not statistically significant ( $p=0.22$ ).
7. Age-appropriate reference ranges are important for interpreting the results of hair analysis, as we found that the levels of many toxic metals and essential minerals were quite different for the control mothers than for the control children.

All of the results discussed above should be investigated in a larger study, to confirm the findings. These findings may be significant in terms of pointing to nutritional deficiencies (especially lithium, iodine, and potassium) as a contributing factor in the etiology of autism. Dietary supplementation with those minerals may help treat some of the symptoms of ASD in some children. Also, prenatal supplementation with lithium could possibly reduce the incidence of autism, and more investigation into maternal lithium levels in ASD is needed.

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