

## **Chelation and Autism**

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### **Can chelation help autism?:**

Chelation is a legitimate medical therapy for disorders caused by an excess of certain metals. Copper, iron, mercury, arsenic and lead are all metals that can cause toxicity disorders that are successfully treated by chelation. Since about 1985, when the idea that autism might be caused by mercury poisoning first arose, many practitioners and groups have promoted chelation as a treatment for autism.

Clearly, the first question that must be settled is whether autism is caused by mercury (or other metal) toxicity – if it is not, then there is no point in treating it with chelation. Unfortunately, this question has become one of many “hot topics” in autism, with much heat and emotion obscuring the scientific data. The first step, then, is to look past the emotion and political maneuvering and examine the data.

When it was first proposed, the idea that autism might be due to mercury poisoning immediately showed a good deal of promise. After all, mercury is a well-known neurotoxin and, additionally, was used as a preservative (thimerosal) in the vaccines children received. With a degree of biological plausibility and a known exposure, the next step was to look for epidemiological data.

Unfortunately, well-designed studies take a while to complete and publish, which left an information vacuum that a number of people immediately began to fill with assertions that autism definitely was or certainly was not caused by the thimerosal in vaccines. This did not make any progress toward settling the question, but instead polarized the issue before the arrival of any real data.

Lurking in the background, undetected in the tumult, were data that could have pointed the way. At least two countries – Canada and Denmark – had removed thimerosal from their vaccines in the 1990's (Canada 1994, Denmark 1992) and yet had both experienced rises in autism prevalence similar to those in the US and UK. Additionally, while the childhood vaccines in the US included three (DTP, HiB, HepB) with thimerosal, in the UK only the DTP vaccine contained thimerosal. This meant that despite having a third the exposure, children in the UK experienced the same rise in autism prevalence.

In 2003, the first study<sup>1</sup>, from Denmark, showed that the prevalence of autism in that country had risen steeply even though thimerosal had been removed from vaccines in the early stages of that rise. This study was greeted by howls of outrage from some that advocated the connection between thimerosal/mercury and autism – the authors were

roundly disparaged and their integrity and objectivity were impugned. This did not change the fact that the autism prevalence in Denmark has continued to rise, following the same pattern as autism in the US and the UK.

In September 2004, a study out of the UK showed no association between thimerosal exposure and autism<sup>2</sup>. At the same time, a review of ten epidemiological studies of autism and thimerosal<sup>3</sup> found that the few studies that did find an association between thimerosal exposure and autism had serious methodological flaws. Chief among these flaws was using the Vaccine Adverse Event Reporting System (VAERS) as a source of data. The chief problem with the VAERS data is that reports can be entered by anyone and are not routinely verified.

To test this, a few years ago I entered a report that an influenza vaccine had turned me in The Hulk. The report was accepted and entered into the database. Because the reported adverse event was so... *unusual*, a representative of VAERS contacted me. After a discussion of the VAERS database and its limitations, they asked for my permission to delete the record, which I granted. If I had not agreed, the record would be there still, showing that any claim can become part of the database, no matter how outrageous or improbable.

Since at least 1998 (and possibly earlier), a number of autism advocacy groups have, with all the best intentions, encouraged people to report their autistic children – or autistic children of relatives and friends – to VAERS as being the result of a thimerosal-containing vaccine. This has irrevocably tainted the VAERS database with duplicate and spurious reports.

### **Testing for mercury:**

What then about the parents who have tested their children and found their mercury levels high? These children may have a legitimate problem with mercury poisoning...if the testing is valid. While laboratory accuracy – and cost – is an issue with many of the “mail-order” labs, a more serious problem is the manner in which the specimen is collected.

Many practitioners who advocate chelation are fond of using “provoked” or “stimulated” excretion studies. To do this, they administer a dose of a chelating agent (more about them later) and test the urine a few hours later. This practice will routinely and predictably elevate the urine mercury level to several times the “unprovoked” or “unstimulated” level<sup>4,5</sup>. Since the normal values listed on the laboratory report are for “unprovoked” specimens, the results can appear alarming.

The cost of many of the mail-order labs is also a significant concern. A brief survey of some of the bigger mail-order labs revealed that they charge between \$175 and \$300 for a “panel” of urine metal tests, including mercury. The local hospital lab charges \$35 for a urine mercury test. In most cases, the other metals included in the “panel” are of little or

no use – there is no research or clinical data that connects some of these other metals to any disorder whatsoever.

Another popular practice is the use of fecal mercury levels. Since mercury in the feces is a combination of ingested mercury that was not absorbed and the mercury excreted in the bile, there is no way to truly know how much mercury is being excreted. One thing that is certain, however, is that the fecal mercury level will be higher than the actual amount of excreted mercury, because there is mercury in the food we eat, the water we drink and the air we breathe.

This brings us (at long last) to chelation.

### **Chelation – what it is and how it works:**

Chelation works by using a compound that has a stronger attraction (affinity) for mercury than the tissues of the body. Since mercury has a very strong affinity for sulfur, all the effective mercury-chelating agents contain sulfur. This is not to say that any sulfur-containing molecule can act as a chelator, since body tissues also have sulfur-containing components, which are what the mercury binds to. An effective chelator needs to have a *higher* affinity than body tissues.

This simple fact is what eliminates some of the compounds that are being touted as chelating agents for mercury. Glutathione, for instance, which has a sulfur-containing amino acid, is not sufficiently greater in its affinity for mercury to be an effective chelator. Another widely used chelating agent, EDTA, not only has little affinity for mercury, but is also not absorbed when taken orally – it must be given intravenously.

The two agents that are most effective for chelating mercury are 2,3-dimercaptosuccinic acid (DMSA) and 2,3-dimercaptopropane-1-sulfonate (DMPS)<sup>6</sup>. DMSA has been widely used in the US – primarily for lead poisoning<sup>7</sup> – and has a good safety record<sup>8,9</sup>. DMPS has a long history of use in the Soviet Union, but has more toxicity problems<sup>10,11</sup>. DMPS is popular with some practitioners because it causes a very large rise in mercury excretion, primarily by prompt clearance of kidney mercury stores, making it very popular for “provoked” mercury testing.

DMPS is not approved by the USFDA for any purpose, primarily because it offers no medical advantages over DMSA and is more toxic. Both can be given by mouth, but only DMPS is available in an intravenous form. Given that there is little or no difference in their effectiveness, a practitioner who wants to use DMPS should be viewed with suspicion. I will focus on DMSA from this point on.

The sulfur-containing groups in DMSA (there are two) are *mercaptans*, relatives of the odorant that is put in natural gas to make it smell bad. In short, it stinks. This can be a problem not only for the child who has to take it, but also for the entire family, as urine that contains DMSA will also have a foul, sulfurous smell. While some manufacturers

claim to have overcome the smell “issue”, if the urine doesn’t smell foul, there is no DMSA being excreted.

One preparation that deserves comment is *transdermal* DMSA (or DMPS) – a cream or ointment that is rubbed onto the skin, presumably to chelate mercury. Both DMSA and DMPS are highly water-soluble and do not dissolve well in fat or oil, which means that they most likely won’t be absorbed through intact skin. It is interesting to note that none of the individuals or corporations selling this preparation has – to my knowledge – performed the simple test necessary to prove that it *is* absorbed. In the absence of this simple bit of data, it must be assumed that it *is not* absorbed.

Lipoic acid – a sulfur-containing fatty acid – has also been touted as a chelating agent, although its effectiveness has not been well studied. It has the advantage of being considered a “natural” substance, but the few studies that have examined it have found it less effective than DMSA<sup>12</sup>. It is fat-soluble and can *potentially* cross the skin, but this has not been tested. Its fat-solubility *may* (or may not) allow it to penetrate the brain tissue better, but this has also not been demonstrated.

A number of naturopathic remedies claim to remove mercury and heavy metals, but this claim is often based on the parent plant’s ability to remove mercury from the environment. As a result, these naturopathic remedies may themselves have a high degree of mercury contamination. At any rate, none of the naturopathic “chelating agents” have been tested to support their claims. In the final evaluation, only DMSA offers the combination of safety and effectiveness that would warrant its use. DMPS is a close second, limited only by higher toxicity.

### **Safety of chelation:**

Common, less serious side effects of DMSA include nausea, vomiting and diarrhea. Skin rashes have also been reported – these are often erroneously referred to as “mercury rashes” and attributed to the removal of mercury. Regrettably, the same rashes are seen in people who have no mercury toxicity and are merely due to a drug reaction. A rare and unpredictable reaction (and potentially lethal, if not treated promptly) is Stevens-Johnson Syndrome, a severe drug reaction that presents with lesions on the skin and in the mouth and gastrointestinal tract.

No significant adverse drug interactions have been reported with DMSA, but most of the children who have received DMSA have not been taking other medications. Increased zinc and copper excretion has been noticed in animal studies<sup>13</sup>, but this is apparently easily corrected by moderate zinc supplementation. Copper supplementation is generally not needed.

The more serious side effects of DMSA are primarily bone marrow suppression and liver injury<sup>14</sup>. In the thousands of children who received DMSA for lead poisoning, somewhere between 3% and 10% developed either elevated liver enzymes (a sign of liver cell injury), low white blood cell and/or platelet counts (a sign of bone marrow suppression)

or both. In all cases, these abnormalities resolved after DMSA was stopped. However, these children were being monitored with frequent blood tests and received treatment for less than three months.

There is a danger that long-term use of DMSA without close monitoring could lead to irreversible bone marrow or liver damage. This has not yet been reported, but is a compelling reason to limit the duration of DMSA therapy *and* to have blood tests done every one to three months. The safety of DMSA is well-established, but this safety has not been demonstrated over the long-term.

Finally, there are as many dosing schedules for DMSA as there are practitioners who make claims about it. As perhaps a ridiculous extreme, one practitioner has asserted that DMSA must be given every two to three hours *around the clock!* This person also insists that failure to follow this schedule will result in *more* mercury being deposited in the brain. Fortunately, this is absolutely wrong<sup>15,16!</sup> Doses as infrequent as once a week have been effective at removing mercury and lead, although at a much slower rate than the recommended dosing schedule of three times a day.

### **Summary:**

[1] Is autism due to mercury?

There is no convincing data supporting a link between mercury or thimerosal and autism. This is not to say that mercury and thimerosal *cannot* cause autism, just that there is no data to support the connection.

[2] Mercury testing.

Mercury testing, especially if done with a mail-order lab, can be both misleading and overly expensive. If you truly suspect mercury poisoning, spend \$35 for a urine mercury test at your local clinic or hospital – don't spend up to \$300 to get information of questionable accuracy and minimal utility.

[3] Chelating agents.

Many of the remedies promoted to remove mercury and other heavy metals are either not effective, not safe or both. Of the available chelating agents for mercury, DMSA offers the best safety *and* the best effectiveness.

[4] Safety.

Despite its impressive safety record, DMSA is not without side effects. Long-term treatment with DMSA has not been studied and may result in serious problems. Close medical monitoring is strongly recommended if you decide to use DMSA therapy on your child.

James R. Laidler, MD is a forty-something physician who is board-certified in Anesthesiology and Pain Medicine. He is currently engaged in a career change (a mid-life crisis without the red sportscar or the mistress) from academic clinical practice to research and has taken sanctuary in graduate school. His interest in autism developed after his older son was diagnosed with Pervasive Developmental Delay (PDD). Within two years, his younger son also developed classic signs of autism. Desperate to do something -- anything -- to help his children, he investigated innumerable therapies that were purported to cure or improve their condition. This desperation led to an extended foray into the field of "alternative" therapies. With this perspective on autism and its various controversies, Dr. Laidler has devoted considerable time and effort to providing parents and other interested people with the best information available on autism and its treatments.

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