# Probable Causes of Autism And Related Disorders
by Mark Force, DC

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Background

In General

Autism is a neurological developmental disorder that exhibits a wide range of severity ranging from severe functional disability to mild, even barely perceptible, cognitive abnormalities. The recent trend has been to refer to autism and related neurological developmental disorders as Autism Spectrum Disorder (ASD). The other designation Persistent Developmental Disorder is still used, but is less favored by researchers.

There are strong genetic links to autism with a range of chromosomal markers indicating that there is no single causative genetic fault. The presence of ASD is the result of an interaction of genetic predisposition and environmental factors that affect neurological development at critical points of fetal, infant, and child maturation. I refer to this phenomenon of critical points of development being adversely impacted as a Genetic-Environmental Developmental Event (GEDE).¹

Environmental factors appear to have marked impact on expression of the genetic predisposition both through controlling development of the nervous system at critical points of development and modifying gene expression afterward. Environmental factors primarily concern exposure to toxic agents, sufficiency of critically important nutrients, and the cognitive, behavioral, and sensory environment.

Because ASD is so strongly influenced by genetics and developmental events, the disorder has no cure. This does not mean that dramatic and lasting improvements in function can't be had for people with ASD; it does mean that the impact and results genetic influences and developmental events will be forever present. For the person with ASD, their environmental factors will have to be controlled for the rest of their lives to minimize the effects of GEDEs. This underscores the vital importance of early intervention upon any suspicion of the disorder to minimize or prevent further GEDEs that impair neurological development. This also leads to strong recommendation that prevention of ASD is begun preconception for any couple that is at risk for having ASD offspring!

Common behaviors found with ASD² are:

- Need for predictability; resistance to any change in routine
- Poorly developed verbal skills; tends to uses pointing, grunting, etc.

¹ Underlying this phenomenon is the concept of developmental susceptibility as promoted by the Center for Environmental Health and Susceptibility at the University of North Carolina at Chapel Hill, NC.

² For more complete info on the signs and symptoms of ASD go to the National Institutes of Health website, specifically http://www.nimh.nih.gov/publicat/autism.cfm#symptoms.
• Unresponsive or under-responsive to sounds despite normal hearing
• Repetitive movements and/or speech; ritualized behaviors
• Responses inappropriate to external environment
• Prefers being alone; disdain for touch and interaction
• Inpatient, intolerant, and tends to tantrums
• Little or no eye contact
• Obsessive attachment to objects
• Over-sensitivity or under-sensitivity to pain
• Physical over-activity or extreme under-activity
• Poor motor skills and lack of sensory integration

This article will, hopefully, provide information and resources that will help those who want to understand and address the disorder in a grounded and useful manner. Some of the issues brought up in this overview article will be covered in more detail in future articles.

History
Classic autism was first described in 1943 in a paper written by child psychiatrist Leo Kanner at Johns Hopkins University. He is considered an authority in pediatric psychology and literally wrote the book, Child Psychiatry (1934). He stayed active in pediatric psychiatry theory until his death, in 1981, at 87. Before Kanner’s observations such children would typically be classified as emotionally disturbed or mentally retarded.

Incidence
The incidence according to the National Institutes of Health (NIH) is around 1 in 1,000 children. This figure varies depending on sources used and the variability is probably accounted for by inclusion criteria used when determining frequency of the disorder in the population.

A study by the CDC of autism cases in metropolitan Atlanta since 1996, found approximately 3.4 in 1,000 children. These figures are in with a CDC investigation from New Jersey and studies from the United Kingdom and Canada.\(^3\)

These same epidemiological studies from Atlanta concluded there is no difference in the incidence between white and black populations and that ASD is roughly 4 times more frequent in boys than in girls.

Some researchers attribute the increased incidence to more awareness of the problem and better diagnostics.

The NIH, from a study published in the Archives of General Psychiatry, has recently confirmed the experience that many parents have had of their seemingly normally developing children developing the characteristic behaviors of autism between their first and second birthdays. This phenomenon, called autistic regression, is estimated to account for 25% of ASD. No differences were found at ages 3 and 4 between children with a history of regression versus those with early-developing forms of autism.\(^4\)

**The Amish Effect**

An interesting development in the epidemiology of ASD is recent reports of the incidence of autism in the Amish of Pennsylvania, which is very low when compared to the general US population.\(^5\) The Amish as a group have much lower vaccination rates than the general population and this has been proposed as a possible epidemiological relationship to the low rate of ASD in this group.

It is interesting to note that there is a much higher incidence of some genetic disorders because of multi-generational marrying within Amish society. Also, the Amish diet is not particularly high in unrefined foods as, surprisingly, the use of white flour and sugar and other processed foods tends to be quite high in this group.

**Physiology**

**Overview**

As with most illnesses, there are specific patterns of physiology that are associated with them. Studying and understanding the physiology, hopefully, gives insight to the underlying process and genetic and environmental factors that lead to a disorder.

This section will focus on the physiology associated with ASD, though connections to genetic and environmental factors will be made. The genetic and environmental aspects of ASD will be covered in more detail in later sections.

**Overview Of Changes In Physiology**

One model indicates that there is a widespread imbalance in the ratio of excitatory to inhibitory synapses in the neurons of the brain.\(^6\)

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Digestion

Children with ASD have markedly higher incidence of digestive dysfunction when compared to control groups.\(^7\)

Karoly Horvath, at the University of Maryland School of Medicine performed gastrointestinal evaluation on 36 and found incidence of chronic inflammation throughout the intestinal tract that was markedly more common than in the general population. Horvath suggested that the intestinal inflammation was likely linked to the irritability, aggression, and nighttime awakenings commonly found in autistics.\(^8\)

Liver Function

One recent study found that in one group of 18 autistic children, 16 had blood levels of toxic chemicals exceeding adult maximum tolerance. The high levels of chemicals are probably caused by inadequate breakdown rather than excessive exposure. The result is higher free radical activity and a tendency toward autoimmune responses and allergies. The central nervous system (brain and spinal cord) is more prone to damage from these problems since the nervous system is still developing and the blood brain barrier is not yet fully functioning in children.

Autistic children may have problems metabolizing and detoxifying environmental chemicals and metabolic wastes due to impaired sulfation in the liver. This may underlie the multiple chemical sensitivities often seen in those with autism. It may also account for the increase of behavioral problems after children eat foods containing phenol, tyramine, and phenyl compounds, which are normally neutralized through the sulfation process.\(^9\)

Chronic Inflammatory Bowel Disease & The Immune System

There is a very strong correlation between chronic intestinal inflammation and autism. The severity of autism correlates with the severity of the inflammation in the bowel.\(^10\) There is typically a very strong history of impaired appetite, colic, multiple courses of antibiotics, diarrhea, constipation, abdominal distress, and other signs and symptoms of dysfunction of the digestive tract in kids with ASD.\(^11\)

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Pediatric specialists in Rome found 43% of autistic children had increased intestinal permeability (leaky gut syndrome), whereas all of the controls had normal permeability. Increased permeability is most commonly a result of chronic inflammation of the intestinal tract.

Increased intestinal permeability is widely believed to lead autoimmune dysfunction, food allergies, digestive problems, bacterial and fungal overgrowth in the intestinal tract, and nutritional deficiencies. All of these health challenges are extremely common in people with ASD and immune dysregulation has recently been found to be more common in autistic when compared to general populations. Immune dysfunction has been proposed as a cause of neurodevelopmental and neurodegenerative disorders.

Oxidative Stress and Inflammation

Most autistic subjects show a moderate increase in lipid peroxidation, a marker of oxidative stress, with a subgroup showing marked elevations.

Researchers have suggested that inflammatory reactions in early life may be part of the etiology of autism.

Allergies

Allergies are an extremely common finding in autistic children when compared to controls.

A study of 36 autistic patients reported marked improvement in behavior after 8 weeks of an elimination diet designed to reduce exposure to food allergens, primarily wheat (gluten) and milk (casein). Increased antibody responses, both immediate (IgE) and delayed (IgG), were found in the autistic children compared to a healthy control group.

Imbalances of the Autonomic Nervous System

My personal clinical experience has been that most kids with autism are sympathetic dominant (fight-or-flight state). Their nervous systems are over-stimulated. This is shown in their general state of agitation (disengagement is often an adaptation to this state). The balance of this

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14 Sperner-Unterweger B; Immunological Aetiology of Major Psychiatric Disorders: Evidence And Therapeutic Implications; Drugs, Volume 65, Number 11, 2005, pp. 1493-1520(28)


18 ibid
system can be measured objectively through heart rate variability. The overstimulation of the nervous system (sympathetic dominance of the autonomic nervous system (ANS)) has a wide range of effects on neurotransmitter levels and functions, digestion, inflammation, blood sugar regulation, control of immune response, and

Why is this important? Over-stimulation of the autonomic nervous system leads to excessively high cortisol levels, depletion of neurotransmitters, dysregulation of the pituitary and pineal glands and hypothalamus of the brain, and excessive oxidation of sugars leading to blood sugar handling stress (hypoglycemias).

The autonomic nervous system (ANS) is made up of two parts – the sympathetic nervous system (fight-or-flight response) and the parasympathetic nervous system (relaxation response). The parasympathetic (PNS) branch controls digestion – production of digestive enzymes and the mucous that lines the gut, peristalsis (muscular action) in the intestines, and absorption. It also regulates the immune response in the gut wall. Recent research indicates that imbalance of the parasympathetic nervous due to low acetylcholine levels (the neurotransmitter that runs the PNS) is an underlying cause of inflammation in the gut.

The sympathetic nervous system was evaluated in 11 primary autistic patients and their families. The plasma levels of norepinephrine (NE), the neurotransmitter of the sympathetic nervous system, was higher in both the autistic subjects and their relatives when compared to the control subjects. These findings indicate a chronically overstimulated state of the sympathetic nervous system in those with autism and their families.

**Imbalances of Neurotransmitters**

Neurotransmitters are the “brain chemicals”, actually found throughout the body, which run your nervous system.

Imbalances of neurotransmitter levels, distribution, and metabolism are found more commonly than in the general population.

Amino acids are essential precursors for manufacturing neurotransmitters in the body. The levels of amino acids in the plasma of autistic and Asperger syndrome patients, along with those of their siblings and parents, were found to be abnormal when compared to controls. Increased glutamic acid, phenylalanine, asparagine, tyrosine, alanine, and lysine and decreased glutamine were found with the other amino acids within normal ranges. These results show that children

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19 Evaluation of the autonomic nervous system through heart rate patterns (http://www.nervexpress.com/).


with autistic spectrum disorders come from a family background of dysregulated amino acid metabolism.  

**Melatonin**

Evidence suggests that autistic children are much more prone to circadian rhythm (sleep-wakefulness cycle) dysfunction and disrupted sleep patterns than their healthy peers.  

Clinical research has linked abnormal levels of tryptophan and serotonin, which the body uses as source material for producing melatonin, to autistic behavioral symptoms in adults. Methylation of serotonin into melatonin, supported by the action of trimethylglycine and dimethylglycine, takes place in the pineal body.  

Nightly melatonin supplementation in children with autism and other neurological and developmental disorders appears to improve sleep patterns in up to 80% of these children. Utilizing melatonin to improve the sleep habits of autistic children also reduced the amount of emotional and behavior problems in the children.  

Indeed, an abnormal circadian secretion pattern of melatonin has even been called a "biological parameter" of the condition.

This study of 14 autistic children evaluated the whole 24-hour circadian rhythm by collecting blood samples at 4-hour intervals. Results were compared to 20 age-matched controls. None of the autistic children showed normal circadian rhythm of melatonin. Levels of melatonin were considerably lower than the control with the lowest values during the dark phase of the 24 hour.

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23 Plasma Amino Acid Levels in Children with Autism and Their Families
Authors: Aldred S.1; Moore K.M.2; Fitzgerald M.2; Waring R.H.3
Source: Journal of Autism and Developmental Disorders, Volume 33, Number 1, February 2003, pp. 93-97(5)


Serotonin

Serotonin regulates sleep, mood, circadian rhythm (day-night cycle) of hormone, basal metabolism (metabolic rates and body temperature, appetite, and inflammation. It also affects sensory perceptions and generally relaxes the nervous system.

Autistic kids have impaired metabolism and production of serotonin. Blood levels of serotonin are abnormally high in those with ASD. Yet, key parts of the brain are low in serotonin in ASD groups, especially areas of the brain (dentatothalamocortical pathway) that process sensory information and speech. Between the ages of 3 to 8 years of age, it is normal for serotonin to be three times higher than levels found in adults. In kids with ASD, serotonin levels are the same levels as adults.32

Twenty autistic adults, not taking SSRI antidepressants, were put on a low tryptohan diet to induce depletion of serotonin. Significant increases in behaviors such as pacing, rocking, self-hitting, as well as more anxiety and less happiness were observed. In general, the autistic patients with highest baseline plasma levels of tryptophan showed the most severe responses after a tryptophan depletion was induced.33

A study by Belgian researchers found that plasma concentrations of tryptophan were significantly lower in a group of autistic teenagers than in age-matched controls.34

Research at Johns Hopkins University School of Medicine has indicated that high plasma platelet serotonin levels could be used as screening test for the genetic predisposition for developing autism.35

GABA (Gamma Amino Butyric Acid)

Gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the adult brain, has been implicated in the etiology of autism.


Research suggests that in addition to glutamate decarboxylation, formation of free GABA also occurs from the action of carnosinase on homocarnosine. Homocarnosine in the CSF have been suggested as a method of measuring brain GABA concentration.

L-Carnosine affects the gamma-aminobutyric acid (GABA)-homocarnosine interaction resulting in enhancement of GABA levels. Thirty-one children with autistic spectrum disorders in an 8-week, double-blinded study to determine if 800 mg L-carnosine daily would result in observable behavioral changes versus placebo. After 8 weeks on L-carnosine, children showed statistically significant improvements on the Gilliam Autism Rating Scale.

A study of an 11 year old autistic child of the chromosome 4q deletion subtype showed abnormalities in glutamate and glycine receptors. Glutamate receptors, in particular, maintain structural and functional plasticity of synapses and regulate GABA activity. Amino acid imbalances, indicating abnormal glutamate and glycine metabolism have been found. Studies have shown small neuronal size and increased cell packing density in limbic system structures including the hippocampus, consistent with curtailing of normal development. GABA receptors have been found to be abnormally low in density in these areas of the brain.

Genetically determined abnormalities in the GABA receptors GABRA4 and GABRB1 have been implicated in the etiology of autism.

Studies have shown that autistics have abnormal function of glutamate receptors (glutamate regulates GABA synthesis). Drugs that limit the action of glutamate can induce autistic-like behaviors in healthy subjects.

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Investigation of glutamic acid decarboxylase, which is responsible for normal conversion of glutamate to gamma amino butyric acid in the brain, were shown to be approximately 50% lower in parietal and cerebellar areas of autistic brains versus controls.\textsuperscript{44}

Marked improvement in speech, eye contact, and attention in autistic children after administration of secretin has been observed.\textsuperscript{45} The proposed mechanism has been secretin’s affect on glutamate metabolism in congruence with autism being hypothesized by some researchers to be a hypoglutamatergic disorder. The effects of secretin were investigated in the rat brain and considerable increases in microdialysate glutamate and gamma-aminobutyric acid (GABA) levels were observed.\textsuperscript{46} Secretin has been proposed as a modulator of GABA activity as well as GABA levels.\textsuperscript{47}

**Catecholamines (Dopamine, Norepinephrine, and Epinephrine)**

Serum dopamine beta-hydroxylase (DbetaH) helps convert dopamine to norepinephrine. Genetically determined low maternal serum DbetaH activity has been proposed to result in a suboptimal uterine environment, which, in conjunction with genetic susceptibility of the fetus, results in autism spectrum disorder in some families.\textsuperscript{48}

Phenylethanolamine-n-methyltranferase (PNMT) catalyzes the methylation (aided by dimethylglycine and trimethylglycine) of norepinephrine to epinephrine in the adrenal medulla. PNMT and adrenergic receptors are also found in the CNS.\textsuperscript{49}

**Acetylcholine**

Levels of cholinergic enzyme and receptor activity were measured in the frontal and parietal cerebral cortex of deceased autistic adults. M1 acetylcholine receptor binding in parietal cortex was up to 30% lower than normal in the autistic subjects. In both the parietal and frontal cortices, nicotinic receptors were 65%–73% lower in the autistic group than in the normal subjects. In the basal forebrain, the level of brain-derived neurotrophic factor in the autistic group was three times as high as the level of the normal group.\textsuperscript{50}

\textsuperscript{44} Fatemi SH, Halt AR; Glutamic acid decarboxylase 65 and 67 kDa proteins are reduced in autistic parietal and cerebellar cortices; Biol Psychiatry. 2002 Oct 15; 52(8):805-10.

\textsuperscript{45} Horvath K, Stefanatos G; Improved social and language skills after secretin administration in patients with autistic spectrum disorders.; J Assoc Acad Minor Phys 1998;9(1):9-15


\textsuperscript{49} Harper’s Biochemistry, 24th Ed., p561

\textsuperscript{50} Elaine K. Perry, B.Sc., Ph.D., Mandy L.W. Lee, B.Sc., et al; Cholinergic Activity in Autism: Abnormalities in the Cerebral Cortex and Basal Forebrain; Am J Psychiatry 158:1058-1066, July 2001
The cholinergic system has been implicated in the development of autism on the basis of neuronal nicotinic acetylcholine receptor (nAChR) losses in cerebral and cerebellar cortex. Findings indicate acetylcholine receptor abnormalities that occur in the thalamus in autism that may contribute to the sensory or attentional deficits found with the disorder.\textsuperscript{51}

**Histidine**

Histidine is a stimulating neurotransmitter that has been found to be up to seven times higher than the upper normal values) has been found in some autistics.\textsuperscript{52} Histadelia (high histamine levels) is found in a subgroup of schizophrenics that are characterized by having phobias, obsessive-compulsive behaviors, addictive predispositions, and depression.\textsuperscript{53} Since folic acid levels have been found to be low in other research on autistics and folic acid aggravates histadelia, the observation of high histamine in some some autistics probably represent an autistic subgroup.

**Vitamin Imbalances**

**Folic Acid**

Low CSF levels of 5-methyltetrahydrofolate, the biologically active form of folic acid, have been found in this observational study of an autistic girl. Treatment with folinic acid corrected both the low CSF 5-methyltetrahydrofolate and improved motor skills.\textsuperscript{54}

**Dimethylglycine (DMG) & Trimethylglycine (TMG)**

Dr. Rimland, from the Autism Research Institute of San Diego, has written a paper on using DMG for autistics and cites the primary changes in autistic behaviors while using DMG are improvements in speech and increased frustration tolerance with less outbursts.\textsuperscript{55}

In his paper, Dr. Rimland cites the results of Lee Dae Kun, Director of the Pusan (Korea) Research Center on Child Problems, who supplemented 39 autistic children, ages three to seven with DMG, for three months, with behavioral improvement in 80%.\textsuperscript{56}

**B6 Deficiency**

A study has observed high levels of excitatory neurotransmitter amino acids, such as glutamic acid and aspartic acid in younger children with autism. B6 deficiency has been proposed to be


\textsuperscript{52} Kotsopoulos S, Kutty KM.; Histidinemia and infantile autism.; Autism Dev Disord. 1979 Mar;9(1):55-60.

\textsuperscript{53} Mental and Elemental Nutrients; Carl Pfeiffer, MD; Keats Pub (January, 1976)

\textsuperscript{54} P. Moretti, MD, T. Sahoo, et al; Cerebral folate deficiency with developmental delay, autism, and response to folinic acid.; Neurology 2005;64:1088-1090


\textsuperscript{56} ibid
an underlying cause of these findings, since B6 regulates glutamic acid, aspartic acid, and GABA. This study also reported higher levels of the inhibitory amino acid taurine in the autistic children, which may occur as their bodies try to "compensate" for excess levels of the excitatory neurotransmitters.  

Numerous studies have established that vitamin B-6/magnesium treatment can significantly help somewhere around half of all autistic children and adults with no major side effects.  

Research has shown that combined B6 and magnesium therapy must be used to significantly and measurably improve brain functions of autistic children. The behavioral improvement observed with the combination vitamin B6-magnesium was associated with significantly decreased urinary homovanillic acid (HVA) excretion and normalized evoked potential (EP) amplitude and pattern, whereas none of these changes in this study were observed when either vitamin B6 or magnesium was administered alone.

Mineral Imbalances

Dr. Lynn Wecker and his colleagues at Louisiana State Medical Centre observe that trace elements imbalances in the human body can disrupt neurotransmitter function and produce marked changes in behavior—many of which are consistent with symptoms of autism. For this reason, Dr. Wecker and his team evaluated trace element concentrations in the hair of autistic children. They found clear deficiencies of calcium, copper, zinc, and chromium that were so striking that they allowed them to discriminate between autistic children and healthy controls with a high degree of accuracy, using just test results.

Calcium

One of the important actions of GABA seems to be it’s ability increase free calcium within nerve cells and Ca channel signaling abnormalities in the central nervous system has been implicated in autism.

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Magnesium

Magnesium also blocks the excito-toxic effects of glutamate, which is found to be high in autistic individuals. Magnesium also plays an important role in the metabolic regulation of taurine which can substitute for magnesium in the presence of magnesium deficiencies.63

Magnesium deficiencies are often associated with attention-deficit disorder and hyperactivity, indicating that it has an important role in neuro-regulation.64

Zinc

Zinc has a critical role in optimal gene expression, especially of the nervous system, is required for the production antioxidant enzymes, and production of dopamine, GABA, and serotonin (indirectly melatonin) requires zinc. Zinc is a critical constituent and cofactor in more than twenty metalloenzymes that regulate metabolism and transport of minerals, particularly metallothionein.

Excess copper, cadmium, sugar and alcohol intake, and estrogen inhibit zinc activity and deplete the mineral. Additionally, high estrogen levels tend to cause increased absorption of copper and cadmium.

Zinc deficiency adversely affects nucleic acid synthesis and prolongs the mitotic interval, resulting in inaccurate transcription and cell division. The result of zinc deficiency on cell division is most evident during fetal stage development. Zinc deficiency has been shown to directly result in gross abnormalities of the brain, spinal cord, eye, and olfactory tract.65 Even transitory deficiency of zinc in pregnant animals can lead to birth defects and behavioral problems in the offspring.66

Zinc deficiency has also been associated with reduced learning capacity, impaired immune response, and allergies.67

Copper

Excessive copper levels are a extremely common finding in those with ASD.

High copper levels are often found to be associated with fatigue, depression, nervousness, irritability, muscle and joint pain, tiredness, behavioral problems, learning disabilities, and mental

63 Richard Smayda, D.O.; Contemporary Review Of Therapeutic Benefits Of The Amino Acid Taurine; Magnesium Online Library (http://www.mgwater.com/taurine.shtml)

64 Kozielec T, Starobrat-Hermelin B. Assessment of magnesium levels in children with attention deficit hyperactivity disorder (ADHD). Magnes Res;1997 Jun;10(2):143-8

65 Hurley, L, Shrader, R; Congenital Malformations of the Nervous System in Zinc Deficient Rats; Neurobiology of the Trace Minerals Zinc and Copper, Intl Rev Neurobio, 1972

66 Food and Nutrition Board (NRC); Zinc in Human Nutrition; Nat Acad Sciences, 1970

diseases. Often ceruloplasmin and serum copper is found to be normal and 24-hour urinary copper excretions has to be measured to determine the copper excess.68

The antioxidant enzymes superoxide dismutase and antioxidant proteins ceruloplasmin (copper-binding) and transferrin (iron-binding) are found to be deficient in autistic children when compared to their non-autistic, developmentally normal siblings. Lack of these metal-binding and antioxidant proteins appears to lead to increased oxidative stress as measured by lipid peroxidation. A “striking” correlation was found between deficient ceruloplasmin and transferrin and the regressive form of autism.69

Zinc/Copper Ratio and Metallothionein

It has been postulated that women having abnormally low zinc/copper ratio (high copper and low zinc levels) will be unable to support optimal neurological development of her fetus and that this process may lead to the abnormal neurological morphology and function found with autism.70

Copper and zinc have been shown to modulate GABA receptor activity.71

Metallothionein (MT), a cysteine-based protein, transports metals such as copper, zinc, mercury, and cadmium in the body. MT modulates release of gaseous cell mediators (hydroxyl radicals, nitric oxide), regulation of cell proliferation and death (apoptosis), and binding, transport, and exchange of heavy metals (zinc, cadmium, copper).72

Metallothionein (MT) is found in almost all mammalian tissues. Isoforms of MT-1 and may be involved in developmental processes occurring at various stages of gestation and deficiency at key stages of gestation may affect normal development of the fetus. MT regulates toxicokinetics and biochemistry of cadmium, zinc, mercury and copper various organs and tissues, primarily the liver, kidney, and CNS. , are often related to metallothionein.73

Metallothionein Functions in Body Processes74

- Regulates zinc and copper transport
- Detoxification of mercury, cadmium, and other toxic metals

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68 Richard Passwater, Elmer Cranton; Trace Elements, Hair Analysis, and Nutrition; Keats (1983)
69 Tórsdóttir Gudlaug; Hreidarsson Stefán, et al; Ceruloplasmin, Superoxide Dismutase and Copper in Autistic Patients; Basic & Clinical Pharmacology & Toxicology, Volume 96, Number 2, February 2005, pp. 146-148
70 Johnson S.; Micronutrient accumulation and depletion in schizophrenia, epilepsy, autism and Parkinson's disease?; Med Hypotheses. 2001 May;56(5):641-5.
72 Simpkins CO; Metallothionein in human disease; Cell Mol Biol (Noisy-le-grand) 2000 Mar;46(2):465-88
74 Metallothionein and Autism; Pfeiffer Treatment Center, Naperville, Illinois; Second Edition 2002
- Development and regulation of immune system
- Development and normal pruning of brain neurons
- Prevents yeast overgrowth in the intestines
- Production of enzymes that break down gluten and casein
- Controls intestinal inflammation
- Production of stomach acids
- Regulates sense of taste and texture of tongue epithelia
- Regulates hippocampal function, behavior, emotional memory, and socialization

A study by the Pfeiffer Treatment Center found that 99% of ASD subjects displayed biochemical imbalances consistent with MT dysregulation and 85% showed severely elevated Copper/Zinc ratios in blood.\textsuperscript{75}

**Lithium**
Lithium may be required as a modulator of prostaglandin synthesis from essential fatty acids.\textsuperscript{76}
Lithium plays a role in regulating serotonin activity in the central nervous system.\textsuperscript{77}
Autistic children and their mothers consistently test deficient in lithium and researchers have recommended lithium supplementation of mothers prenatally.\textsuperscript{78}

**Iodine**
Most children with autism have low levels of iodine. Iodine deficiency is the most common worldwide cause of mental retardation. Researchers have recommended prenatal supplementation of iodine.\textsuperscript{79}

**Essential Fatty Acids**
Essential fatty acids are critical nutrients for the brain function deficiency may be a causative factor in neurological developmental disorders like autism.

Polyunsaturated fatty acids (PUFAs) make up 20% of the brain's dry weight and influence the function of neurotransmitters, including serotonin.

One preliminary study found that average, total levels of omega-3 (n-3 PUFAs) in the autistic children were about 20% lower than in mentally retarded children used as controls. Levels of one important n-3 fat, docosahexaenoic acid (DHA), were 23% lower. These deficiencies resulted in a significantly higher ratio of n-6 to n-3 PUFAs in the autistic children. Similar patterns have been found in other neurodevelopmental disorders characterized by major

\textsuperscript{75} ibid

\textsuperscript{76} Horrobin, D; Lithium Research Review Series Vol. 1; Human Sciences Press (New York)

\textsuperscript{77} Science, 1981; 213:1529

\textsuperscript{78} J.B. Adams; C.E. Holloway; F. George; D. Quig; Hair Analysis of Children with Autism and their Mothers; Hair Analysis July 14, 2003

\textsuperscript{79} ibid
neurological communication dysfunction such as schizophrenia, attention-deficit disorder, and Rett's syndrome. Some researchers have theorized a "phospholipid spectrum of disorders" that result in ADHD, dyslexia, and autism. This could explain why these conditions often overlap, cluster in families, and often share similar clinical features. Researchers have recommended RBC fatty acid testing in patients with autism spectrum and related disorders.

DHA

Docosahexaenoic acid (DHA) is a major component of neuronal membranes, is critical for neurological development, protects neurons from oxidative damage, and regulates neurotransmitter functions.

A study of the results of DHA supplementation of pregnant rats significantly changed the fatty acid composition and increased the levels of serotonin, dopamine, and somatostatin in the rat offspring hippocampus. DHA has also been found to enhance acetylcholine metabolism and modulate glutamate transport, as well.

Research demonstrated that rats exposed from conception to a diet deficient in DHA content exhibit alterations in adult behavior indicative of altered dopaminergic function along with altered morphology in the cortical and limbic areas of the brain. Some of these behavioral alterations were reversed by DHA supplementation initiated at weaning.

DHA protects neurons against the cytotoxicity of glutamate and increases the activities of the antioxidant enzymes glutathione peroxidase and glutathione reductase.

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85 Levant B, Radel JD, Carlson SE.; Decreased brain docosahexaenoic acid during development alters dopamine-related behaviors in adult rats that are differentially affected by dietary remediation.; Behav Brain Res. 2004 Jun 4;152(1):49-57.

Genetic Factors

Strong evidence supporting the genetic foundation predisposing for the development of autism is that monzygotic (identical) twins exhibit over 90% concurrent rate for autism, though the degree of autism may vary widely.

Many geneticist believe ASD is caused by interplay between genes and environmental factors in children who have an underlying genetic susceptibility to the disorder.

A study published in JAMA reported that children with severe development disorder involving both autism and psychosis may have excessive levels of phenylalanine, a condition known as phenylketonuria (PKU), which can lead to brain damage and seizures.87

UCLA geneticist Rita Cantor recently pinpointed the location of an autism gene on chromosome 17, called 17q21.88

Immunologist Judy Van de Water of the University of California at Davis discovered that the protective cells of autistic youngsters display impaired defense to bacterial compounds when compared normal children. She proposes that genetic predisposition, when combined with certain environmental factors, probably accounts for the development of retrograde autism and is working on a lab test to evaluate newborns for the risk of developing autism.89

Brain-derived neurotrophic factor (BDNF) regulates a wide variety of processes in the nervous system, including neural development, function and survival. Evidence suggests that excess BDNF is involved in the pathogenesis of epilepsy, mania and autism.90

Abnormalities of the chromosome region 15q11q13 are known to lead to altered behaviour, developmental delay/mental retardation, and seizures/epilepsy. Researchers have suggested evaluation for this genetic fault in any infant or child with early central hypotonia, minor dysmorphic features, developmental delay, autism or autistic-like behaviour, and who subsequently develops hard to control seizures/epilepsy.91

Research at Duke’s Center for Human Genetics examined 14 genes that affect function of GABA receptors in the central nervous system.


89 Joan Arehart-Treichel; Roots of Autism May Be Embedded In Immune System; Psychiatric News June 3, 2005, Volume 40 Number 11.

90 Tsai SJ.; TrkB Partial Agonists: Potential Treatment Strategy For Epilepsy, Mania, And Autism.; Med Hypotheses. 2005 Jul 12

Subjects were from 470 Caucasian families with at least one autistic member (266 families had more than one member with autism).

A gene called GABRA4 was found to be associated with autism risk and interaction of this gene with another gene, GABRB1, was found to compound autism risk. GABA activity filters information coming into the nervous system to prevent overstimulation. It has long been felt by researchers that compromised GABA filtering results in the “sensory overwhelm” behavior that is commonly seen in people with ASD.\(^92\)

**Environmental Factors**

The CDC has found most American carry in their bodies numerous pesticides and other toxic chemicals that are harmful to health. Some of these were found in higher concentration in children than adults including pyrethroids (household pesticides) and phthalates (cosmetics, soft plastics).

A CDC study looked for 148 toxic compounds in the urine and blood of close to 2,400 people age 6 and older in 2000 and 2001. Lead levels were found to be less than in previous studies, but 1 in 18 women of childbearing age had mercury that exceeded EPA standards.

In a CDC study of 698 Danish children with autism born after 1972 and diagnosed before 2000, the following factors were found to be associated with an increased risk of ASD: breech presentation at birth, delivery before 35 weeks, a parent who had a diagnosis of schizophrenia-like psychosis before the date that autism was diagnosed in the child, and low birth weight at delivery.\(^93\)

Some scientists suspect that maternal viral infections are one of the principal noninherited causes of ASD. Epidemiological studies indicate an increased risk of ASD in the children of mothers exposed to German measles (rubella) early in pregnancy.\(^94\)

Scientists have found diminished size and concentration of Purkinje cells in the brains of mice whose mothers were exposed to rubella while pregnant. It has been conjectured that the effect is related to the immune response of the mother to the infection and may be a phenomenon that is triggered by other infectious agents in addition to rubella.\(^95\) These would be supported by the observation that autoimmune diseases, such as rheumatoid arthritis, are common in families of people with ASD.

\(^92\) Pericak-Vance, M.; American Journal of Human Genetics, September 2005; vol 77, online edition


\(^94\) Chess, Stella; Autism in Children with Congenital Rubella; Journal of Autism and Childhood Schizophrenia, 1, 1, 33-47, Jan-Mar 71

Autopsies of people with ASD have revealed 50% reduction in Purkinje cell size when compared to normal subjects. Recent studies have shown abnormal GABA activity in Purkinje cells along with a 40% reduction in activity of a key enzyme for Purkinje cell function. Purkinje cells are found in the cerebellar area of the brain and control coordination of body movement and awareness.

**Toxic Metals**

Research shows that exposure to heavy metals such as lead and mercury can impair brain development at very early ages—even at low doses previously deemed "harmless." A study of 40 boys with ASD compared to 40 boy controls, revealed statistically significant elevations of lead, mercury, and uranium in the boys with ASD.

**Mercury**

In a study comparing the mercury excretion of 221 children with autism vs. 18 non-autistic children, the children with autism excreted 4x as much mercury after receiving DMSA (a chelating agent) for 3 days.

A recent study showed that genetically susceptible strains of young mice have impaired neurological development with exposure to mercury when genetically unsusceptible strains will develop normally at the same level of mercury exposure.

Methylation is a chemical process that functions in elimination of toxic metals, such as mercury, and the gene expression required for normal development. Exposing neuronal cells to thimerosol, the form of mercury found in vaccines, dropped methylation activity significantly. Richard Deth, a neuropharmacologist, believes that thimerosal interferes with the conversion of dietary forms of B12 into the active form and so impedes DNA methylation and disrupts normal gene expression.

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96 SH Fatemi, AR Halt, et al; Purkinje Cell Size is Reduced in Cerebellum of Patients With Autism; Cellular and Molecular Neurobiology; Volume 22, Number 2, April, 2002, 171-175.


99 Fido, Abdullahi; Al-Saad, Samira; oxic Trace Elements in the Hair of Children with Autism; Autism The International Journal of Research and Practice, v9 n3 p290-298 Aug 2005


101 M Hornig, D Chian and WI Lipkin; Neurotoxic effects of postnatal thimerosal are mouse strain dependent; Molecular Psychiatry (2004), 1–13

Vaccinations

It is interesting to note, both statistically and epidemiologically, that the incidence of autism in the United States has correlated very closely with the increased use of thimerosal containing vaccines and the body burden of mercury these vaccines cause.\(^{103}\) It has been suggested that the mercury dose of individual vaccinations are not toxic, but that accumulated exposure may be.\(^{104}\)

Thimerosal, a mercury-based preservative, has become a public health issue as more and more vaccines have been added to the mandatory schedule of vaccines and the cumulative dose of this dose-dependent neurotoxin has increased. Polio, DPT, and MMR were the only vaccines on the mandatory schedule before 1989.

By 1999, twenty-two vaccines were on the schedule and the cumulative exposure to mercury stood around 180 times the EPA limit. Interestingly, the dramatic increase in autism rates has paralleled the increase in immunization schedules since 1989.

Thimerosal was removed from most childhood vaccines as a "precautionary" measure in 1999 and upon the recommendation of the American Academy of Pediatrics and U.S. Public Health Service. Thimerosal is still present in many tetanus and flu vaccines.

It is also interesting to note that autism incidence has decreased since the remanufacture of most vaccines without thimerosal.\(^{105}\)

A recent report from the Journal of American Physicians and Surgeons indicates that since mercury was removed from childhood vaccines, the rates of autism and other neurological disorders (NDs) in children has dropped by as much as 35%.

Independent researchers evaluated the CDC’s Vaccine Adverse Event Reporting System (VAERS) and the California Department of Developmental Services (CDDS) databases for the incidence of reported childhood NDs.

Reported autism rates in California hit a high of 800 in May 2003. The researchers found that the numbers went down to 620 in 2005. This number represents an actual decrease of 22% and a decrease of 35% from projections.

The outcome of this analysis contradicts recommendations of the Institute of Medicine, which examined vaccine safety data from the National Immunization Program (NIP) of the CDC. Concerning this outcome, the authors state, "The IOM stated that the evidence favored rejection of a causal relationship between thimerosal and autism, that such a relationship was not

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\(^{103}\) Mark R. Geier, M.D., Ph.D.; Thimerosal in Childhood Vaccines, Neurodevelopment Disorders, and Heart Disease in the United States; Journal of American Physicians and Surgeons Volume 8 Number 1 Spring 2003

\(^{104}\) Leslie K. Ball, MD, Robert Ball, MD, and R. Douglas Pratt, MD; An Assessment of Thimerosal Use in Childhood Vaccines; PEDIATRICS; Vol. 107 No. 5 May 2001, p 1147-1154

\(^{105}\) David A. Geier, B.A., Mark R. Geier, M.D., Ph.D.; Early Downward Trends in Neurodevelopmental Disorders Following Removal of Thimerosal-Containing Vaccines; JAAPS, Vol 11, No 1, Spring 2006
biologically plausible, and that no further studies should be conducted to evaluate it."

**Dental Fillings**
The mercury in dental fillings is an amalgam, or blend, of copper, silver, and mercury. It has been used in fillings for around 150 years. Amalgam fillings contain small amounts of inorganic mercury, which according to the American Dental Association (ADA) is not biologically active in the body.

However, Austria, Canada, Denmark, Germany, and Sweden have banned or limited mercury fillings, especially in children and pregnant women.

**Comparing Autism & Mercury Poisoning**

Note: This table is from the Safe Minds website and has been reformatted from the original in layout for clarity. The content has not been changed. The Safe Minds website is highly recommended!!

<table>
<thead>
<tr>
<th>Dysfunction</th>
<th>Mercury Poisoning</th>
<th>Autism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychiatric Disturbances</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social deficits, shyness, social withdrawal</td>
<td>Social deficits, social withdrawal, shyness</td>
<td></td>
</tr>
<tr>
<td>Depression, mood swings; mask face</td>
<td>Depressive traits, mood swings; flat affect</td>
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<tr>
<td>Anxiety</td>
<td>Anxiety</td>
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<tr>
<td>Schizoid tendencies, OCD traits</td>
<td>Schizophrenic &amp; OCD traits; repetitiveness</td>
<td></td>
</tr>
<tr>
<td>Lacks eye contact, hesitant to engage others</td>
<td>Lack of eye contact, avoids conversation</td>
<td></td>
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<tr>
<td>Irrational fears</td>
<td>Irrational fears</td>
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<tr>
<td>Irritability, aggression, temper tantrums</td>
<td>Irritability, aggression, temper tantrums</td>
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<tr>
<td>Impaired face recognition</td>
<td>Impaired face recognition</td>
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<tr>
<td><strong>Speech, Language &amp; Hearing Deficits</strong></td>
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<tr>
<td>Loss of speech, failure to develop speech</td>
<td>Delayed language, failure to develop speech</td>
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<tr>
<td>Dysarthria; articulation problems</td>
<td>Dysarthria; articulation problems</td>
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<tr>
<td>Speech comprehension deficits</td>
<td>Speech comprehension deficits</td>
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<tr>
<td>Verbalizing &amp; word retrieval problems</td>
<td>Echolalia; word use &amp; pragmatic errors</td>
<td></td>
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<tr>
<td>Sound sensitivity</td>
<td>Sound sensitivity</td>
<td></td>
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<tr>
<td>Hearing loss; deafness in very high doses</td>
<td>Mild to profound hearing loss</td>
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<tr>
<td>Poor performance on language IQ tests</td>
<td>Poor performance on verbal IQ tests</td>
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<tr>
<td><strong>Sensory Abnormalities</strong></td>
<td></td>
<td></td>
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<tr>
<td>Abnormal sensation in mouth &amp; extremities</td>
<td>Abnormal sensation in mouth &amp; extremities</td>
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<tr>
<td>Sound sensitivity</td>
<td>Sound sensitivity</td>
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<tr>
<td>Abnormal touch sensations; touch aversion</td>
<td>Abnormal touch sensations; touch aversion</td>
<td></td>
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<tr>
<td>Vestibular abnormalities</td>
<td>Vestibular abnormalities</td>
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<tr>
<td>Dysfunction</td>
<td>Mercury Poisoning</td>
<td>Autism</td>
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<tr>
<td>Motor Disorders</td>
<td>Involuntary jerking movements – arm flapping, ankle jerks, myoclonal jerks, choreiform movements, circling, rocking</td>
<td>Stereotyped movements – arm flapping, jumping, circling, spinning, rocking; myoclonal jerks; choreiform movements</td>
</tr>
<tr>
<td></td>
<td>Deficits in eye-hand coordination; limb apraxia; intention tremors</td>
<td>Poor eye-hand coordination; limb apraxia; problems with intentional movements</td>
</tr>
<tr>
<td></td>
<td>Gait impairment; ataxia – from incoordination &amp; clumsiness to inability to walk, stand, or sit; loss of motor control</td>
<td>Abnormal gait and posture, clumsiness and incoordination; difficulties sitting, lying, crawling, and walking</td>
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<td></td>
<td>Difficulty in chewing or swallowing</td>
<td>Difficulty chewing or swallowing</td>
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<td></td>
<td>Unusual postures</td>
<td>Unusual postures</td>
</tr>
<tr>
<td>Cognitive Impairments</td>
<td>Borderline intelligence, mental retardation – some cases reversible</td>
<td>Borderline intelligence, mental retardation – sometimes “recovered”</td>
</tr>
<tr>
<td></td>
<td>Poor concentration, attention, response inhibition</td>
<td>Poor concentration, attention, shifting attention</td>
</tr>
<tr>
<td></td>
<td>Uneven performance on IQ subtests</td>
<td>Uneven performance on IQ subtests</td>
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<tr>
<td></td>
<td>Verbal IQ higher than performance IQ</td>
<td>Verbal IQ higher than performance IQ</td>
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<tr>
<td></td>
<td>Poor short term, verbal, &amp; auditory memory</td>
<td>Poor short term, auditory &amp; verbal memory</td>
</tr>
<tr>
<td></td>
<td>Poor visual and perceptual motor skills, impairment in simple reaction time</td>
<td>Poor visual and perceptual motor skills, lower performance on timed tests</td>
</tr>
<tr>
<td></td>
<td>Difficulty carrying out complex commands</td>
<td>Difficulty carrying out multiple commands</td>
</tr>
<tr>
<td></td>
<td>Alexia (inability to comprehend the meaning of written words)</td>
<td>Hyperlexia (ability to decode words while lacking word comprehension)</td>
</tr>
<tr>
<td></td>
<td>Deficits in understanding abstract ideas &amp; symbolism; degeneration of higher mental powers</td>
<td>Deficits in abstract thinking &amp; symbolism, understanding other’s mental states, sequencing, planning &amp; organizing</td>
</tr>
<tr>
<td>Unusual Behaviors</td>
<td>Stereotyped sniffing (rats)</td>
<td>Stereotyped, repetitive behaviors</td>
</tr>
<tr>
<td></td>
<td>ADHD traits</td>
<td>ADHD traits</td>
</tr>
<tr>
<td></td>
<td>Agitation, unprovoked crying, grimacing, staring spells</td>
<td>Agitation, unprovoked crying, grimacing, staring spells</td>
</tr>
<tr>
<td></td>
<td>Sleep difficulties</td>
<td>Sleep difficulties</td>
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<tr>
<td></td>
<td>Eating disorders, feeding problems</td>
<td>Eating disorders, feeding problems</td>
</tr>
<tr>
<td>Self injurious behavior, e.g. head banging</td>
<td>Self injurious behavior, e.g. head banging</td>
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<table>
<thead>
<tr>
<th>Dysfunction</th>
<th>Mercury Poisoning</th>
<th>Autism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Impairments</td>
<td>Poor eye contact, impaired visual fixation</td>
<td>Poor eye contact, problems in joint attention</td>
</tr>
<tr>
<td>“Visual impairments,” blindness, near-sightedness, decreased visual acuity</td>
<td>“Visual impairments”; inaccurate/ slow saccades; decreased rod functioning</td>
<td></td>
</tr>
<tr>
<td>Light sensitivity, photophobia</td>
<td>Over-sensitivity to light</td>
<td></td>
</tr>
<tr>
<td>Blurred or hazy vision</td>
<td>Blurred vision</td>
<td></td>
</tr>
<tr>
<td>Constricted visual fields</td>
<td>Not described</td>
<td></td>
</tr>
</tbody>
</table>

| Physical Disturbances | Increase in cerebral palsy; hyper- or hypo-tonia; abnormal reflexes; decreased muscle strength, especially upper body; incontinence; problems chewing, swallowing, salivating | Increase in cerebral palsy; hyper- or hyptonia; decreased muscle strength, especially upper body; incontinence; problems chewing and swallowing |
| Rashes, dermatitis/dry skin, itching; burning | Rashes, dermatitis, eczema, itching |
| Autonomic disturbance: excessive sweating, poor circulation, elevated heart rate | Autonomic disturbance: unusual sweating, poor circulation, elevated heart rate |

| Gastro-intestinal Disturbances | Gastroenteritis, diarrhea; abdominal pain, constipation, “colitis” | Diarrhea, constipation, gaseousness, abdominal discomfort, colitis |
| Anorexia, weight loss, nausea, poor appetite | Anorexia; feeding problems/vomiting |
| Lesions of ileum & colon; increases gut permeability | Leaky gut syndrome |
| Inhibits dipeptidyl peptidase IV, which cleaves casomorphin | Inadequate endopeptidase enzymes needed for breakdown of casein & gluten |

<p>| Abnormal Biochemistry | Ties up –SH groups; blocks sulfate transporter in intestines, kidneys | Low sulfate levels |
| Has special affinity for purines &amp; pyrimidines | Purine &amp; pyrimidine metabolism errors lead to autistic features |
| Reduces availability of glutathione, needed in cells &amp; liver to detoxify heavy metals | Low levels of glutathione; decreased ability of liver to detoxify heavy metals |
| Causes significant reduction in glutathione peroxidase and glutathione reductase | Abnormal glutathione peroxidase activities in erythrocytes |
| Disrupts mitochondrial activities, especially in brain | Mitochondrial dysfunction, especially in brain |</p>
<table>
<thead>
<tr>
<th>Dysfunction</th>
<th>Mercury Poisoning</th>
<th>Autism</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immune Dysfunction</strong></td>
<td>Sensitivity due to allergic or autoimmune reactions; sensitive individuals more likely to have allergies, asthma, autoimmune-like symptoms, especially rheumatoid-like ones</td>
<td>More likely to have allergies and asthma; familial presence of autoimmune diseases, especially rheumatoid arthritis; IgA deficiencies</td>
</tr>
<tr>
<td></td>
<td>Can produce an immune response in CNS</td>
<td>On-going immune response in CNS</td>
</tr>
<tr>
<td></td>
<td>Causes brain/MBP autoantibodies</td>
<td>Brain/MBP autoantibodies present</td>
</tr>
<tr>
<td></td>
<td>Causes overproduction of Th2 subset; kills/inhibits lymphocytes, T-cells, and monocytes; decreases NK T-cell activity; induces or suppresses IFNg &amp; IL-2</td>
<td>Skewed immune-cell subset in the Th2 direction; decreased responses to T-cell mitogens; reduced NK T-cell function; increased IFNg &amp; IL-12</td>
</tr>
<tr>
<td><strong>CNS Structural Pathology</strong></td>
<td>Selectively targets brain areas unable to detoxify or reduce Hg-induced oxidative stress</td>
<td>Specific areas of brain pathology; many functions spared</td>
</tr>
<tr>
<td></td>
<td>Damage to Purkinje and granular cells</td>
<td>Damage to Purkinje and granular cells</td>
</tr>
<tr>
<td></td>
<td>Accumulates in amygdala and hippocampus</td>
<td>Pathology in amygdala and hippocampus</td>
</tr>
<tr>
<td></td>
<td>Causes abnormal neuronal cytoarchitecture; disrupts neuronal migration &amp; cell division; reduces NCAMs</td>
<td>Neuronal disorganization; increased neuronal cell replication, increased glial cells; depressed expression of NCAMs</td>
</tr>
<tr>
<td></td>
<td>Progressive microcephaly</td>
<td>Progressive microcephaly and macrocephaly</td>
</tr>
<tr>
<td></td>
<td>Brain stem defects in some cases</td>
<td>Brain stem defects in some cases</td>
</tr>
<tr>
<td><strong>Abnormalities in Neuro-chemistry</strong></td>
<td>Prevents presynaptic serotonin release &amp; inhibits serotonin transport; causes calcium disruptions</td>
<td>Decreased serotonin synthesis in children; abnormal calcium metabolism</td>
</tr>
<tr>
<td></td>
<td>Alters dopamine systems; peroxidine deficiency in rats resembles mercurialism in humans</td>
<td>Possibly high or low dopamine levels; positive response to peroxidine (lowers dopamine levels)</td>
</tr>
<tr>
<td></td>
<td>Elevates epinephrine &amp; norepinephrine levels by blocking enzyme that degrades epinephrine</td>
<td>Elevated norepinephrine and epinephrine</td>
</tr>
<tr>
<td></td>
<td>Elevates glutamate</td>
<td>Elevated glutamate and aspartate</td>
</tr>
<tr>
<td></td>
<td>Leads to cortical acetylcholine deficiency; increases muscarinic receptor density in hippocampus &amp; cerebellum</td>
<td>Cortical acetylcholine deficiency; reduced muscarinic receptor binding in hippocampus</td>
</tr>
<tr>
<td></td>
<td>Causes demyelinating neuropathy</td>
<td>Demyelation in brain</td>
</tr>
</tbody>
</table>
Aluminum

Although there are no significant peer-reviewed studies on aluminum as a causative factor for autism, aluminum is a known neurotoxic agent in high enough concentration and has been strongly linked to the degenerative changes found in Alzheimer’s disease. It is detoxified through methylation and may contribute to the toxicity of mercury through loading the same detoxification pathway used to excrete mercury from the body.
Lead

Lead toxicity has been associated with the development of ASD and autistic symptom patterns.\textsuperscript{106} The association is strong enough that testing for lead poisoning is indicated with the presence of ASD or the related symptoms.

Chemicals

One recent study found that in one group of 18 autistic children, 16 had blood levels of toxic chemicals exceeding adult maximum tolerance.\textsuperscript{107}

Medications

Terbutaline, a 2-adrenoceptor agonist, is a drug used to prevent premature births. It is suspect as an ASD causing agent from both observation and in animal model studies.\textsuperscript{108}

Plastics

There is research supporting that some populations are unable to break down the xenobiotic (hormone-disrupting) compounds found in plastics among those with ASD.\textsuperscript{109} Hormone disruption during fetal development has been proposed as a possible mechanism of the developmental neurological impairments seen with ASD.\textsuperscript{110}

Pesticides

Organophosphates (OPs) are routinely used as pesticides in agriculture and as insecticides within the household. A gene-environment interactive model of autism pathogenesis has been proposed, whereby genetically vulnerable individuals prenatally exposed to OPs during critical periods in neurodevelopment could undergo altered neuronal migration, resulting in an autistic syndrome.

Since household use of OPs is far greater in the USA than in Italy, this model was predicted to hold validity in North America, but not in Europe. As predicted by the experimental model, Caucasian-American and not Italian families display a significant association between autism and paraoxonase gene variants. This shows that groups genetically deficient in the enzyme paraoxonase required to break down OPs are susceptible to neurodevelopmental abnormalities from prenatal exposure to organophosphates (OPs).\textsuperscript{111}


\textsuperscript{108} M. Carolina Zerrate, Mikhail Pletniko, et al; Terbutaline Treatment in Rats: Implications for Autism; Journal of Pharmacology And Experimental Therapeutics; March 30, 2007


\textsuperscript{110} Theo Colborn; Neurodevelopment and Endocrine Disruption; Environ Health Perspect. 2004 June; 112(9): 944–949.

\textsuperscript{111} D’Amelio M, Ricci I; Paraoxonase Gene Variants Are Associated With Autism In North America, But Not In Italy: Possible Regional Specificity In Gene-Environment Interactions.; Molecular Psychiatry, advance online publication, 19 July 2005
Organophosphate exposure must be considered a possible cause of the neurodevelopmental defects found in autism. Both avoidance and support for detoxification of organophosphates through clinical nutrition should be considered.