Fluoride,
Premature Birth and
Impaired Neurodevelopment

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A global review of recent laboratory, clinical, and ecological evidence
that fluoride is a significant risk factor for premature birth
and long-term neurological disabilities in children

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"Prenatal Fluoride and Autism"

"Placental Fluorosis: Fluoride and Preeclampsia"

Contents

Fluoride, Premature Birth and Impaired Neurodevelopment

Premature or preterm birth is birth prior to 37 weeks (8.5 months) of pregnancy. Not just a temporary problem dealt with during the first weeks of an infant's life, preterm birth is the leading predictor of infant death and long-term neurological disabilities in children.[1] Preterm infants are more likely to have lower IQs and require significantly more educational assistance than children who were born at term. The societal economic burden associated with preterm birth in the United States is estimated to be at least $26 billion per year, or more than $50,000 per infant born preterm.[2]

Preterm birth is the most common pregnancy complication that can seriously compromise the newborn brain's viability and normal development. Many studies have documented the prevalence of a broad range of central nervous system dysfunctions and neurodevelopmental impairments in people who were born preterm, including mental retardation, ADHD, and major depression.

The genesis and wiring of the human brain during fetal development is one of the most remarkable feats in all of biology. During the last trimester, dynamic changes occur in the two brain areas most important to cognitive processes: the cerebellum whose surface area increases 30-fold; and the cerebral cortex whose white matter undergoes striking changes.[3]

Premature birth can interrupt this vital developmental process, as British researchers showed using a novel form of magnetic resonance imaging to track the growing complexity of nerve cells in the fetal brain before the normal time of birth. Maturation was most rapid in areas of the cortex relating to social and emotional processing, decision making, working memory, and visual-spatial processing – functions often impaired after premature birth. Professor David Edwards, Director of the Centre for the Developing Brain at King's College London said:

> "These findings highlight a key stage of brain development where the neurons branch out to create a complex, mature structure. We can now see that this happens in the latter stages of development that would usually take place in healthy babies when they are still in the womb... With this study we found that the earlier a baby is born, the less mature the cortex structure. The weeks a baby loses in the womb really matter."[4]

US Preterm Birth Rate Unusually High

The misconception that preterm birth is a third-world problem was shattered in May 2012 by the first global report to compare premature birthrates in 184 countries. Three years in the making, "Born Too Soon: The Global Action Report on Preterm Birth" was produced jointly by the World Health Organization, Save the Children, March of Dimes, and Partnership for Maternal, Newborn and Child Health.[5]

America lags behind 130 other nations in preterm birth rate. The United States is similar to developing countries in the percentage of mothers who give birth before their children are due. "It does worse than any Western European country and considerably worse than Japan or the Scandinavian countries," reported Donald G. McNeil, Jr. in the *New York Times*. Most European countries are in the 7% to 9% range, while the United States shares the 12% range with Kenya, Turkey, Thailand, East Timor, and Honduras – meaning that one in nine births is early.[6]

"This report offers conclusive evidence that the United States rate of preterm birth has been far too high for far too long," says March of Dimes president Dr. Jennifer L. Howse. "We have failed to do enough to prevent preterm births and help more mothers carry their babies full-term."[7]

"If somebody had a simple explanation of why the UK and Europe do much better, I wouldn't believe them," says preterm birth expert Dr. Gordon C. S. Smith. "The reality is, for most preterm births, we just don't understand the cause."[6]

Residence in the US a Risk Factor for Preterm Birth
A 2012 study involving 2,141 women revealed that duration of stay in the US is associated with increased risk of preterm birth for Hispanic women. Dr. Radek K. Bukowski, an expert on premature birth at the University of Texas Medical Branch in Galveston, found that the longer a woman lived in this country, the greater her chances of giving birth prematurely.

Women living in the US for less than 10 years had a 3.4% frequency of preterm birth. Women living in the US for more than 10 more years had a 7.4% frequency. Furthermore, women born in the US had a 10% frequency of preterm birth.[8]

The findings support the hypothesis that preterm birth is, at least in part, related to environmental, potentially preventable, factors. It remains unclear what specific environmental factors protect or predispose women to preterm birth. Even after controlling for risk factors such as age, poverty, smoking, obesity, and diabetes, Bukowski admitted: "We really don't have an explanation for what's behind it. It's something they acquire here."[6]

Best-Available Science Will Reduce Preterm Birth by Only 5%
Although preterm birth is the leading cause of death for children younger than five years in high-income countries, second leading cause worldwide, and a major contributor to the "global burden of disease," it wasn't until 2013 that the first multi-country analysis of trends in preterm birth rates was published.

The international team of researchers concluded, "The current potential for preterm birth prevention is shockingly small." If five proven interventions were implemented, it would lower the preterm rate from an average 9.6% of live births to 9.1%. The most effective of these evidence-based interventions is decreasing non-medically indicated caesarean deliveries and induced labor. Dr. Joy Lawn of Save the Children, who coordinated the research, says, "The best-available science will allow just 5 percent relative reduction in high-income countries' preterm birth rates by 2015." Note: of the 39 countries with a "very high human development index," the US has the third highest preterm birth rate (after Cyprus and Bahrain).[9,10]

Because the triggers for premature labor are not fully understood, the poor performance by the US is partly a mystery, says Dr. Alan E. Guttmacher, Director of the National Institute of Child Health and Human Development. "This underscores the need for more research," especially because, as the March of Dimes points out, in up to 40% of cases, the cause of preterm birth is unknown.

It also underscores the need to acknowledge and heed research already available: laboratory, clinical, and ecological evidence that fluoride consumption is a significant risk factor for preterm birth – as this report documents. Unfortunately, health agencies and organizations in the United States typically ignore such research.

Fluoride: Ancient Enemy of Biological Systems
Many Americans think there's nothing wrong with fluoride, a chemical added to nearly three-fourths of their public water supplies and now permeates the nation's processed food and beverage chain. Even a National Academy of Sciences award-winning molecular biologist with a doctorate in biochemistry "did not know that biology cared much about this ion."[11]

Ronald R. Breaker, PhD, and his team of experts in microbiology and bioinformatics at Yale University's Howard Hughes Medical Institute study a type of noncoding RNA called a *riboswitch* that helps turn genes on and off. In 2011, they discovered a new riboswitch but could not figure out its function, until a chemistry graduate student "overcame any biases" and quickly demonstrated that pure fluoride indeed triggers riboswitch function that helps cells fight fluoride's "antimicrobial properties."[11-13]

"Despite this evidence, we were still unwilling to accept that fluoride was the natural target," admits Breaker. "It is very likely no one would have solved the mystery of fluoride riboswitches for several more decades, if we had not been lucky enough to receive a contaminated chemical sample spiked with

fluoride." Genes associated with fluoride-sensitive riboswitches are very widespread in biology. In fact, this new riboswitch is "one of the only non-coding RNAs we've ever found that's present in both bacteria and archaea [a recently identified major domain of life]," Breaker says. This suggests an ancient biological system that cells have evolved to deal with fluoride's toxicity.[13,14]

Molecular Mechanisms of Fluoride Toxicity

In a 2010 scientific review, the authors note that until the 1990s, the toxicity of fluoride was largely ignored due to its "good reputation" for preventing dental caries via topical application in toothpastes. In the last decade, however, interest in its undesirable effects has resurfaced due to the awareness that "this element interacts with cellular systems even at low doses."[15]

> "Even though some studies report no clear evidence on the potential negative effects of fluoride exposure at permissible concentrations (e.g., studies that support water fluoridation), others have shown evidence of fluoride's effects on cellular processes at biologically relevant concentrations. When discussing these controversial results, it is important to highlight that fluoride must be actively considered as a potent toxic compound in the field of toxicology...
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> "Fluoride can interact with a wide range of cellular processes such as gene expression, cell cycle, proliferation and migration, respiration, metabolism, ion transport, secretion, endocytosis, apoptosis/necrosis, and oxidative stress, and that these mechanisms are involved in a wide variety of signaling pathways."[15]

Fluoride Inhibits the Enzyme Enolase

"Although the toxicity of fluoride is well known, it has been ignored for a long time... As a result, the consumption of fluoride by humans became uncontrolled and unpredictable, often exceeding its therapeutic window," say the authors of "Molecular Mechanisms of Cytotoxicity and Apoptosis Induced by Inorganic Fluoride," a scientific review published in 2012. The Russian researchers detail the many ways fluoride harms life. One mechanism: "Fluoride is a well-known inhibitor of enzymes of the glycolytic pathway, first of all enolase."[16]

"Inhibition of glycolysis by fluoride is central to the concept that the anti-microbial effect of fluoride has a role in caries prevention," reported Canada's leading dental journal, *Oral Health*. The bacterium that inhabits the human mouth, *Streptococcus mutans*, causes dental caries by converting dietary sugars into enamel-corroding lactic acid. Fluoride interferes with the complete breakdown of glucose by inhibiting enolase, an intermediary enzyme in the pathway. This results in a reduction in the synthesis of lactic acid and in a significant reduction in the metabolic activity of the cariogenic bacteria.[17]

Fluoride's inhibition of enolase, however, is not limited just to the mouth. Exposure of red blood cells (erythrocytes) to fluoride produces a variety of metabolic alterations, most of which are based upon the secondary effects of enolase inhibition.[18] Via its effect on enolase in human red blood cells, fluoride inhibits active sodium transport, aerobic glucose utilization, and lactate formation.[19,20]

Working with red blood cells of rats, researchers found that sodium fluoride leads to impairment of the cellular antioxidant system, severe energy depletion, and triggers rapid progression of cell death in a dose- and time-dependent manner. "Long-term intoxication of the rats with fluoride triggers premature death of their erythrocytes due to intrinsic death-associated biochemical defects and development of anemia."[21-23]

Fluoride, Anemia, and Preterm Birth: A.K. Susheela's Research

Anemia is a condition marked by a deficiency of red blood cells or of hemoglobin, the red protein in blood cells responsible for transporting oxygen in the blood. Anemia is common in pregnancy, because a woman needs to have enough red blood cells to carry oxygen around her body and to her baby.

The leading expert on the connection between fluoride, anemia, and preterm birth is A.K. Susheela, PhD, who has spent more than 25 years researching fluoride toxicity and has over 80 scientific publications in Western and Indian Journals. She is executive director of the Fluorosis Research and Rural Development Foundation in India, winner of the 2013 Spirit of Humanity Award in Women's Health presented by AmeriCares India.

"There is now ample scientific evidence to support the fact that ingestion of fluoride prevents biosynthesis of hemoglobin, leading to anemia in human beings," Susheela says.[24] "Fluoride decreases production of erythrocytes (red blood cells) by the bone marrow and other hemopoietic tissues and increases erythrocyte abnormalities resulting in premature death of red blood cells."[25]

In 2010, Susheela conducted a clinical program that emphasized a greatly reduced intake of fluoride and the inclusion of essential nutrients in the daily diet during pregnancy. "Effective Interventional Approach to Control Anemia in Pregnant Women" was the first report dealing with fluoride, pregnancy, anemia, low birthweight babies and the linkages to act upon for the benefit of maternal and reproductive child health programs.[26]

The 205 pregnant women in the study were all anemic. Their hemoglobin levels were less than 9 g/dl, and their urinary fluoride levels were more than 1 mg/l. Ninety pregnant women formed the sample group, and 115 formed the control group. "The major focus of the investigation of the sample group was to eliminate ingestion of fluoride as much as possible," says Susheela. "The sample group was counseled to avoid consumption of fluoride-containing food, water, and other substances." They even changed their toothpaste to a low-fluoride paste. The women were also counseled to ensure an adequate intake of essential nutrients: calcium, vitamins, and antioxidants from dairy products, fruits, and vegetables. The women in the control group were not counseled, but both groups received the standard iron and folic acid tablets.[25,26]

By the time of delivery, improvements in the women's body-mass index were considerably better in the sample group than in the control group, suggesting that the sample group was absorbing nutrients more efficiently. Also, hemoglobin increased by an average of 78% in the sample group compared to 57% in the controls.

> "A striking impact of these interventions for improving the gestation period was also noted." In the sample group, 32% of the women delivered before 37 weeks – compared to 50% in the control group.[25,26]

At the Global Maternal Health Conference convened in New Delhi in 2010, Susheela presented results of a similar but larger study of 481 pregnant women, further confirming:

> "Maternal and child under-nutrition and anemia is not necessarily due to insufficient food intake, but because of the derangement of nutrient absorption due to damage caused to GI mucosa by ingestion of an undesirable chemical substance, namely fluoride through food, water and other sources."[26,27]

Prenatal Fluoride Linked to Low Birthweight

In Susheela's clinical study, the number of low birthweight babies was reduced to 22% in the sample groups of mothers who avoided fluoride, as opposed to 52% in the control groups.[26]

A 2011 study with 108 pregnant women (17-36 years old) concluded: "With increased serum fluoride in the mother, there is an inclination towards preterm delivery, low birthweight, and poor APGAR count."[28] APGAR evaluates a newborn's appearance, pulse, grimace, activity, and respiration.

A 2012 case-control study found a significant association between fluoride levels in the drinking water consumed, dental fluorosis in mothers, and low birthweight of newborns.[29]

Low Birthweight, Cognitive Problems, Autism, and Obesity
Links between low birthweight and a range of motor and cognitive problems have been well known for some time. The 2007 National Summit on America's Children presented an analysis of 35 years of data on more than 12,000 individuals – the first to link birthweight with adult health and socioeconomic success, using a full nationally representative sample of the US population. Some findings:

> "Compared to their normal birth weight siblings, low birthweight children are 30 percent less likely to be in excellent or very good health in childhood. They also score significantly lower on reading, passage comprehension, and math achievement tests... Low birthweight children are nearly twice as likely as their normal birth weight siblings to be in problematic health by ages 37-52."[30]

In 2011, researchers at the University of Pennsylvania found that the rate of autism spectrum disorder is highly elevated in children and adults who were born at low birthweight. For 21 years, they followed a regional birth cohort of 1,105 children who weighed less than 2,000 grams (4 pounds, 6 ounces) at birth – finding that 5% of the low birthweight children were diagnosed with autism, compared to 1% of the general population.[31]

Low-birthweight infants also have an increased risk for developing adult obesity.[32] Obesity increases the risk of preterm delivery. A 2013 study of 1.5 million deliveries in Sweden found that women with the highest Body Mass Index also had the highest statistical risk of giving preterm birth. Researchers at Karolinska Institutet say that maternal overweight and obesity have replaced smoking as the most important preventable risk factor for adverse pregnancy outcomes in many countries. In the US, where preterm delivery rates are twice as high as in Sweden, 53% of pregnant women are either overweight or obese compared to 34% of pregnant women in Sweden.[33] (Sweden has prohibited water fluoridation since 1971.)

Iron-Deficiency Anemia
Iron is the main constituent of the hemoglobin molecule, hence a deficiency in iron is a major cause of anemia. About half of all pregnant women don't have enough iron in their body. Pregnant women need about twice as much iron as usual, therefore they have a higher risk of iron-deficiency anemia, which can increase the risk of preterm delivery and low birthweight.

As with most mineral nutrients, iron from digested food is absorbed in the intestinal lining by epithelial cells whose microvilli provide the huge surface area needed to efficiently absorb nutrients. "Fluoride not only decreases production of red blood cells by the bone marrow but also destroys microvilli – the microscopic protrusions lining the intestine," notes Dr. Susheela.[34] "Fluoride diminishes beneficial microbial growth in the gut... resulting in poor absorption of nutrients critical for the biosynthesis of hemoglobin."[25]

In June 2013, Susheela and her team submitted to the Indian Council of Medical Research results of a three-year study to correct anemia in more than 2,500 adolescent school children, ages 10 to 17. When fluoride was withdrawn and nutritious food promoted, the children's anemia was corrected. In contrast, anemia continued in the control group that consumed fluoride, even though they ate a nutritious diet.

Microflora in the GI Tract
The human gut is the natural habitat for a large and dynamic bacterial community. Major functions of the gut microflora include metabolic activities that result in salvage of energy and absorbable nutrients. Colonic microorganisms also play a part in vitamin synthesis and in absorption of calcium, magnesium, and iron.[35]

Lactobacillus acidophilus belongs to a group of bacteria that live in the human small intestine. These beneficial microorganisms aid digestion, help maintain a healthy intestinal tract, and prevent harmful bacteria from congregating there. *L. acidophilus* has been shown to increase iron bioavailability in studies with animals.[36]

When children were fed an iron-fortified probiotic milk beverage supplemented with *L. acidophilus*, they "exhibited higher red blood cell status and a positive correlation between iron intake and hemoglobin" – evidence to support the use of *L. acidophilus* to prevent anemias in children.[37]

When fluoride comes in contact with *Lactobacillus acidophilus*, it inhibits this beneficial bacterium that aids in the absorption of iron. Fluoride-containing resin-based dental sealants have proved "capable of contact inhibition of *L. acidophilus* and *S. mutans* growth."[38] A statistically significant 49% reduction in *Lactobacillus* counts was obtained 24 hours following mouth rinsing by Egyptian children with 0.05% sodium fluoride solution.[39]

In a 2013 interview, Dr. Susheela explained why India's Iron and Folic Acid Supplementation Program has failed to prevent anemia. As long as fluoride consumption is high, she said:

> "No amount of tablets is going to solve anything. Withdrawal of fluoride on the other hand permits the regeneration of microvilli in the gut which improves the absorption of nutrients from the diet and hemoglobin levels improve.
>
> "The evidence is there for the scientific community, bureaucrats, and policymakers, but no one has reproduced it nationally or globally. They're simply not willing to accept the truth."[34]

Thyroid Disorders and Preterm Birth

Subclinical hypothyroidism is associated with an increasing number of adverse effects including infertility, miscarriage, and preterm birth.[40] In a 2005 study of 25,756 women, preterm birth was almost two-fold higher in women with subclinical hypothyroidism compared to women with normal thyroid-stimulating hormone levels.[41]

Each year in the US, at least 80,000 pregnant women have thyroid diseases. A 2013 analysis of 223,512 pregnancies in the United States (2002-2008) found that women with thyroid disorders face greater risk of preterm birth and other complications that have short- and long-term consequences for the health of mother and child, including preeclampsia.[42]

Anemia is often the first sign of hypothyroidism,[43] perhaps in part because thyroid hormones modulate the glycolytic enzyme enolase.[44]

Because of its antagonism to iodine, fluoride has long been known to interfere with the function of the thyroid gland.[45] In 2006, the US National Research Council found substantial evidence that fluoride exposure can impact thyroid function in some individuals. Furthermore, in pregnant women, subclinical hypothyroidism is associated with "decreased IQ of their offspring."[46]

A 2015 study found that high rates of hypothyroidism were at least 30% more likely in areas with water fluoride levels above 0.3 mg/l.[47]

An under-active thyroid gland is also associated with obesity, and obesity increases the risk of preterm delivery.[33]

Prematurity and Infant Mortality

The main cause of the high US infant mortality rate, when compared with Europe, is the very high percentage of preterm births in the United States. After identifying the top 20 leading causes of infant death, the CDC determined that preterm birth is the most frequent cause of infant death in the United States, accounting for 36% of infant deaths in 2007.[48] Prematurity is the #1 cause of death in the first month of life. In 2008, nearly 10,000 babies in the US died from preterm birth-related causes.[49]

Preterm birth doesn't just affect the mortality of infants. A study of 674,820 individuals born in Sweden (who survived to age one) found that "low gestational age at birth was independently associated with increased mortality in early childhood and young adulthood."[50]

The severity of all the problems associated with being born early depends on the degree of prematurity. A 2012 study of 128,000 New York kids found that "each week of increased gestation from 37-41 weeks showed an added benefit in both reading and math scores."[51]

Water Fluoridation and Preterm Birth Rates

A 2009 public-health study, Relationship Between Municipal Water Fluoridation and Preterm Birth in Upstate New York, was undertaken by researchers from the Department of Epidemiology & Biostatistics at the State University of New York (SUNY), because:

> "Current literature suggests an association between periodontal disease and preterm birth. Domestic water fluoridation is thought to have lessened the burden of dental disease. Theoretically, one would expect water fluoridation to be protective against preterm birth."[52]

What was found however surprised the researchers, who did not expect fluoridated water to be positively associated with preterm birth rates – yet they had to conclude otherwise:

> "Domestic water fluoridation was independently associated with an increased risk of preterm birth in logistic regression, after controlling for age, race/ethnicity, neighborhood poverty level, hypertension, and diabetes."[52]

Results of this study were presented at the 2009 American Public Health Association Meeting, but subsequently were never published. One can't help but wonder how much other fluoride research goes unpublished, when results don't support expectations. Case in point:

> The 2007 Oregon Smile Survey showed that non-fluoridated Portland had lower rates of tooth decay. After fluoridation promoters were confronted with this reality check, they omitted Portland statistics from their next survey (2012). When a journalist compared tooth-decay rates of children living in fluoridated vs. nonfluoridated areas of Oregon, fluoridated students averaged a 9% higher decay experience than unfluoridated kids living in the Portland water district (52.03% vs. 47.81%).[53]

After the SUNY public health study, a logical next step would have been to look at available data for ecological associations elsewhere in the US. According to CDC data for 2010, in the 25 least fluoridated states[54] (average fluoridation rate = 52%), the preterm birth rate[55] averaged 116 per 1,000 births. In the 25 most fluoridated states (average fluoridation rate = 90%), the preterm birth rate averaged 5% higher: 122 per 1,000 births.

If that difference of six births per 1,000 were extrapolated to the United States, where four million births occurred in 2010 (when 66% of the population was fluoridated), then higher levels of water fluoridation would be associated that year with about 16,000 more preterm births – each one with an annual societal economic burden of more than $50,000.[2]

Although this nationwide statistical association is not adjusted for age, race, poverty, and maternal disease (as the SUNY study was), nevertheless it is the best large-scale population data we have – a snapshot that supports laboratory and clinical studies showing an association between fluoridated water and preterm birth. It should not be dismissed, but after the SUNY study, no further research has been published.

Similar statistical snapshots of America in 2010 reveal that low-birthweight rates averaged 5% higher[56], and infant mortality rates averaged 17% higher in the 25 most-fluoridated states compared to the 25 least-fluoridated states. Neonatal (under 28 days) deaths were 19% higher.[57]

HPA Axis: Link Between Preterm Birth and Brain Disorders

In 2012, researchers at the University of Adelaide discovered a possible mechanistic link between the altered brain physiology of preterm birth and subsequent neurological deficits. Their research provides the first physiological evidence that human adolescents who were born preterm have a "significantly reduced

capacity for cortical neuroplasticity." Dr. Julia Pitcher of the Robinson Institute says plasticity in the brain is vital for learning and memory throughout life. "It enables the brain to reorganize itself, responding to changes in environment, behavior and stimuli by modifying the number and strength of connections between neurons and different brain areas."[58]

"The growth of the brain is rapid between 20 and 37 weeks gestation, Pitcher said. "Being born even mildly preterm appears to subtly but significantly alter brain microstructure, neural connectivity, and neurochemistry." In contrast, the brains of term-born teenagers were highly plastic.[58]

This study's findings also suggested a mechanism. Altered hypothalamic-pituitary-adrenal (HPA) axis function due to preterm birth may be "a significant modulator of this altered neuroplasticity." The HPA axis a complex neurohormone mechanism that regulates metabolic and behavioral reactions to physiological and environmental stress. It is highly susceptible to programming during fetal and neonatal development.

Animal and human studies have demonstrated that the stress associated with preterm birth provokes adaptive changes in endocrine and metabolic processes that become permanently programmed via the HPA axis – affecting later health, memory, learning, executive function, and associated behavior throughout life.[59-61]
Premature birth is a stressful event, not only due to a shortened gestation period, but also because of medical interventions during the first weeks of life (painful procedures, handling, mechanical ventilation, maternal separation).

Abnormal regulation of the HPA axis is commonly associated with a range of affective and stress-related disorders. A 2012 Swedish study of more than a million individuals found that preterm birth was significantly associated with increased risk of psychiatric hospitalization in adulthood across a range of psychiatric disorders.[62]

"The gut microbiota contributes to developmental programming; a process whereby an environmental factor acting during a developmental 'window of vulnerability' can have a potentially life-long impact on physiological function," say researchers at the Brain-Body Institute at McMaster University in Ontario, Canada.[63] Other researchers there note, "The presence of gut microbiota regulates the set point for HPA axis activity."[64] Findings from a 2004 study "suggest that exposure to indigenous microbiota at an early developmental stage, when brain plasticity may still be preserved, is required for the HPA system to become fully susceptible to inhibitory neural regulation."[65]

Attention-Deficit Hyperactivity Disorder (ADHD)
In a study of boys with ADHD and disruptive behavior symptoms, those scoring high on "callous unemotional traits" showed a blunted HPA axis reactivity to the experimentally induced stress.[66]

In the US, ADHD is the most common neurodevelopmental disorder of childhood, affecting about 7% of all children. In 2013, the results of a long-running study – 5,718 children in Rochester, Minnesota born from 1976 through 1982 – found that 29% of the children with ADHD still had ADHD as adults. Of the children who still had ADHD as adults, 81% had at least one other psychiatric disorder, as compared with 47% of those who no longer had ADHD and 35% of controls. Lead investigator, William Barbaresi, MD, says, "We suffer from the misconception that ADHD is just an annoying childhood disorder that's overtreated. This couldn't be further from the truth."[67]

Premature infants have significantly more severe symptoms of ADHD at school age.[68] Another statistical snapshot of America reveals that children's ADHD rates[69] averaged about 14% higher in the 25 most-fluoridated states compared to the 25 least-fluoridated states.

A 2015 study found that for each one-percent increase in artificial fluoridation prevalence in 1992 was associated with approximately 67,000 to 131,000 additional ADHD diagnoses (2003 to 2011).[70]

Prenatal Fluoride and Hyperactivity
A landmark study led by Phyllis Mullenix, PhD, found that rats exposed prenatally to fluoride exhibit higher levels of hyperactivity.[71] After her research was published in *Neurotoxicology and Teratology* (1995), Mullenix was fired from Boston's Forsyth Dental Center, where for 10 years she had been Head of the Toxicology Department. As documented by investigative journalist Christopher Bryson in *The Fluoride Deception*, Forsyth's associate director told Mullenix:

> "You are going against what the dentists and everybody have been publishing for fifty years, that this is safe and effective. You must be wrong. You are jeopardizing the financial support of this entire institution. If you publish these studies, NIDR [National Institute of Dental Research] is not going to fund anymore research at Forsyth." (Forsyth was getting about 90% of its money from NIDR.)[72]

By 2010, more than 80 animal studies had confirmed what Mullenix et al. reported.[73] Also, the Neurotoxicology Division of the EPA had found "substantial evidence" that fluoride is a chemical "toxic to the developing mammalian nervous system."

Note: rat studies involving higher doses of fluoride are relevant to humans, because research shows that when rats consumed 75-125 ppm and humans 5-10 ppm fluoride in their respective drinking waters, the result was equivalent ranges of plasma fluoride levels.[74]

Fluoride, Defective Tooth Enamel, and Prematurity
A major 2011 European review of fluoride's health effects concluded: "Systemic exposure to fluoride through drinking water is associated with an increased risk of dental and bone fluorosis in a dose-response manner without a detectable threshold."[88] Studies show that the prevalence and severity of developmental defects of enamel (DDE) in children increase significantly with the increase in fluoride levels in drinking water, as well as with the ingestion of fluoride tablets.[75-78] (See pages 55-56.)

Premature infants are more frequently affected by tooth enamel anomalies or defects when compared with infants born at term. An Australian study of 8,411 children found the prevalence of DDE in children and adolescents born prematurely was 56.5%, while the control group was 9.3%.[79]

Low-birthweight children more likely than their normal birthweight counterparts to have enamel hypoplasia, a form of DDE in which the tooth enamel is hard but thin and deficient in amount.[80]

Developmental enamel defects in primary teeth have been found at least twice as frequently in children with mental retardation.[81] Another statistical snapshot of America reveals that children's mental retardation rates[82] averaged about 38% higher in the 25 most-fluoridated states compared to the 25 least-fluoridated states.

Genetic Factor
Animal studies show there is a genetic component in the pathogenesis of dental fluorosis and in bone response to fluoride exposure. Different strains of inbred mice demonstrate differential physiological responses to ingested fluoride.[83,84]

In human populations, African Americans appear to be more vulnerable to fluoride's toxicity. They have higher rates of dental fluorosis as well as preterm birth. A study of 83 African American and 109 White children (7-14 years old) found that even though both groups had the same water and saliva fluoride concentrations, dental fluorosis was observed in 63% of White children, but in 80% of African American children.[85]

"Approximately 50% of preterm birth has no clear medical cause, and evidence strongly suggests that genetic factors contribute to some of these cases," says Dartmouth Professor of Genetics Scott Williams, PhD. It's unknown why preterm birth happens in about 10% of pregnancies in Caucasian women nationwide, but in about 20% of pregnancies of African-American women.[86]

When a genetic predisposition is combined with mild inflammation, the rate of preterm birth profoundly increases in mice, according to a 2013 study. Researchers observed aspects of the same molecular signatures in tissue samples of women who had undergone preterm birth: increases in cyclooxygenase-2 (COX-2) signaling.[87] Fluorides have well-established ability to cause and aggravate inflammation,[15] including increased expression of COX-2 in human cells.[88]

We really don't know the racial and genetic factors that determine an individual's resistance to developing fluorosis and susceptibility to fluoride's multiple mechanisms of toxicity[15,16] in the body and brain.

Fluoride Contaminates US Processed Food and Beverage Chain

Americans consume uncontrolled and unknown amounts of fluoride. Water is the predominant source of fluoride in the United States, however, a historically unprecedented array of other sources are responsible for a significant amount of exposure to fluoride, especially in processed foods and beverages. (Fluoride content is missing from food ingredient labels, including pet foods whose very high fluoride content has been implicated in canine bone cancer.[89,90])

Other sources of fluoride exposure include toothpaste, mouthwash, supplements, and other dental products and treatments; fluorinated pharmaceuticals, pesticides, and post-harvest fumigants. The additive effect can be substantial.

In 1993, the National Research Council admitted, "It is no longer feasible to estimate with reasonable accuracy the level of fluoride exposure simply on the basis of concentration in drinking water supply."[91] Therefore, even where fluoride levels in drinking water are claimed to be safe, a woman who is pregnant (or intends to be) should take steps to minimize her consumption of fluoride if she wants to reduce her risk for giving birth prematurely – especially if she has dental fluorosis, visible proof she is susceptible to systemic fluoride toxicity.

Residence in the US is a risk factor for preterm birth, and more people consume artificially fluoridated water (and products made with it) in America alone than in the rest of the world combined.[92]

It is high time we change our long habit of not thinking fluoride consumption wrong and realize that this toxic chemical is a significant risk factor for premature birth and long-term neurological disabilities.

A vibrant fully functioning brain is the most precious gift of life. It is inexcusable to promote, condone, or ignore any substance or policy that threatens this birthright.

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Correlations Between Cognitive Scores and Gestational Age

A major study published in 2002 in the *Journal of the American Medical Association*:

> "We report the first meta-analysis on the cognitive and behavioral outcomes of school-aged children who were born preterm by combining the results from case-control studies published between 1980 and November 2001...
>
> "Among 1556 cases and 1720 controls, controls had significantly higher cognitive scores compared with children who were born preterm."
>
> Conclusions:
> "Children who were born preterm are at risk for reduced cognitive test scores, and their immaturity at birth is directly proportional to the mean cognitive scores at school age. Preterm-born children also show an increased incidence of ADHD and other behaviors."[93]

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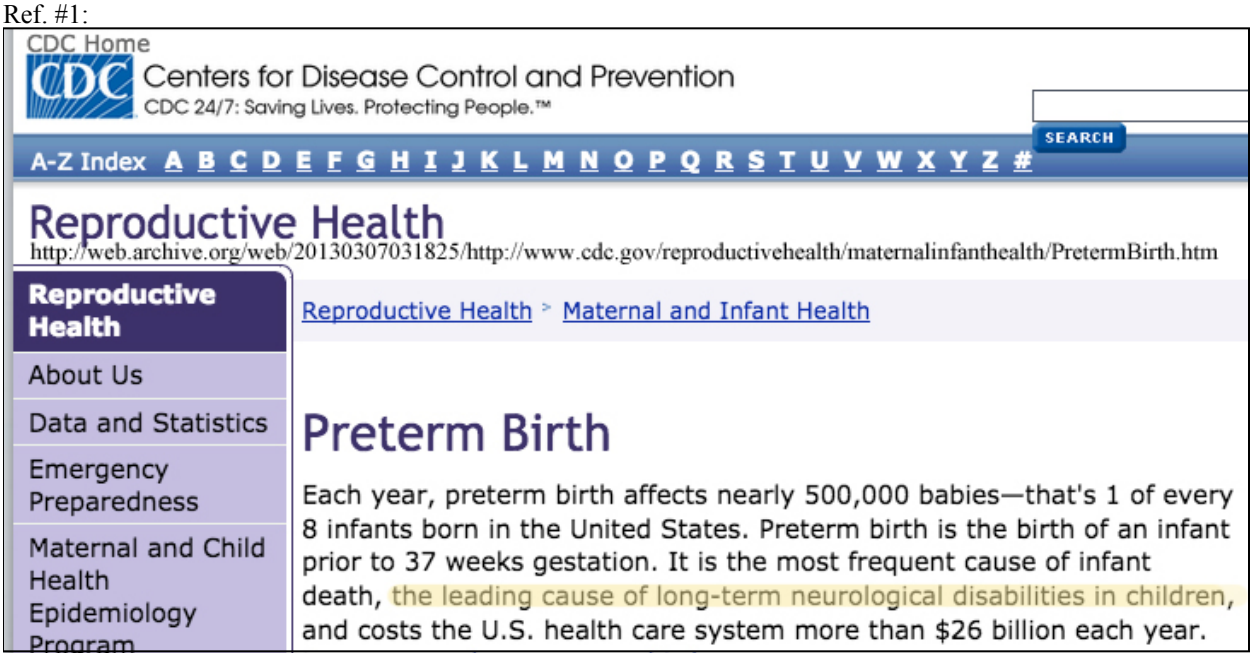
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SEARCH
A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #
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http://web.archive.org/web/20130307031825/http://www.cdc.gov/reproductivehealth/maternalinfanthealth/PretermBirth.htm
Reproductive Health
About Us
Data and Statistics
Emergency Preparedness
Maternal and Child Health Epidemiology Program
Reproductive Health > Maternal and Infant Health
Preterm Birth
Each year, preterm birth affects nearly 500,000 babies—that's 1 of every 8 infants born in the United States. Preterm birth is the birth of an infant prior to 37 weeks gestation. It is the most frequent cause of infant death, the leading cause of long-term neurological disabilities in children, and costs the U.S. health care system more than $26 billion each year.