

FROM PRECONCEPTION TO INFANCY: ENVIRONMENTAL AND NUTRITIONAL STRATEGIES FOR LOWERING THE RISK OF AUTISM

BY DAVID BERGER, MD, FAAP

INTRODUCTION

Autism spectrum disorders (ASDs) represent a cluster of neurobehavioral-developmental conditions characterized by varied levels of impairment in communication, behaviors, social interactions, and sensory integration. To date, no single medical hypothesis has adequately explained the increasing prevalence of ASDs as well as the wide range and intensity of symptoms. There is a growing belief in the medical world that ASDs have both genetic and environmental triggers, and there is growing interest in how the environment (both internal and external to the body) interacts with the genetic code as well as the various body organs to produce symptoms of ASDs.

At a glance, it is obvious that ASDs cannot have a purely genetic cause. There are multiple documented cases of identical twins where one child is severely affected by autism, while the other twin is neurotypical and indistinguishable from his or her peers. I have seen identical twins where one child received multiple courses of antibiotics while the other did not, and the antibiotic-exposed child (but not the unexposed twin) is now on the autism spectrum. I have also seen identical twins where one child received vaccines in accordance with the recommended schedule and subsequently developed signs of being on the autism spectrum, while the other twin did not receive early infant vaccines at 2 or 4 months of age due to illness at time of check-up and remained unaffected by autism. On the other hand, genetics play some role. It is well known that there is an increased

prevalence not only of ASDs but also of allergies, asthma, and autoimmune and hyperinflammatory conditions in children for whom there is a family history of such conditions. Families with such histories may be particularly interested in strategies to prevent these conditions in their future children.

The purpose of this review article is to explore how environmental exposures and nutritional factors may play a role in the development of ASDs in children. This implies that there are also certain precautions and steps that may be taken to minimize the risk of having a child who develops an ASD (and other chronic/disabling medical conditions). These measures include avoidance of environmental exposures and implementation of nutritional testing and optimized nutrition. Since I began using these strategies 10 years ago with families, to the best of my knowledge, not a single child born into my medical practice has gone on to develop an ASD. Furthermore, of the more than 500 patients who joined my practice at birth, none have developed diabetes, just one has developed asthma, and only one family (of 3 children) has developed recurring ear infections.

Some of the recommendations listed below are not specific to and may have never been studied in relation to ASD. However, strategies intended to decrease antibiotic exposure, *Candida* development, and the incidence of allergies, asthma, and autoimmune diseases likely are relevant to lowering the incidence of autism as are strategies to increase cognitive development and optimize nutrition.

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PRECONCEPTION AND PREGNANCY

Many families of ASD children have asked me throughout the years if there are things that they could do even prior to conception to decrease the likelihood of having another child develop an ASD. Few formal studies have looked into this issue, and with so many different variables in play, it would be very difficult to perform good research on this. Nonetheless, the approach I have taken over the past 10 years seems to be successful. I have not had any subsequent siblings develop an ASD, although the incidence in siblings has otherwise been documented to be high (close to 1 in 5)¹ when compared with 1 in 91 for the general population.² Most of the concepts that I take into account when evaluating and treating a woman prior to conception are similar for women who are pregnant. Factors that I consider both preconceptionally and prenatally are summarized in Table 1 and described in greater detail in the rest of the article.

Table 1. Preconceptional and prenatal considerations in autism prevention	
Concept	Examples
Genetics	Genetic mutations Methylation/transsulfuration pathway Maternal single nucleotide polymorphisms (SNPs)
Cellular environment	Maternal nutrition Toxic exposures (i.e., bisphenol A)
Nutrition-related	Celiac disease Gluten and casein opioid peptides Maternal allergies
Intestinal flora	<i>Candida</i> <i>Clostridia</i>
Heavy metals	Mercury (thimerosal, amalgams, and environmental) Lead
Thyroid health	Hypothyroidism Thyroid autoantibodies
Nutrients	Vitamin D Iron Folate Calcium Omega-3 fatty acids

GENETIC FACTORS

Although there are genetic abnormalities that have been associated with ASD, no genes have been identified that are present in even close to a majority of children with ASD (and most of these gene tests are not commercially available). For

example, the abnormal gene sequence found between the cadherin 9 and 10 protein on chromosome 5, which was widely reported in 2009, was only present in 15% of children with ASD.³ Fragile X is present in about 2% of children with autism.^{4,5} While this incidence of fragile X in ASD children is significantly higher than the 1 in 4000 males who carry the full fragile X mutation and the 1 in 1000-2000 who carry the premutations,⁶ it still represents a very small percentage of children with autism.

Genes involved with methylation and transsulfuration (see Figure 1), the pathway that breaks down homocysteine and produces glutathione, may contribute to autism. Genes code for various enzymes, and these genes and enzymes often have the same name. Cystathionine β -synthase (CBS) is the enzyme that metabolizes homocysteine to cystathionine, and methionine synthase (MS) is the enzyme that converts homocysteine back to methionine. CBS and MS genes may play a role in the abnormal biochemistry that can be observed in ASD, although most labs do not run these tests. MTHFR (methylene tetrahydrofolate reductase), the enzyme that converts 5,10-methylene tetrahydrofolate to 5-methyl tetrahydrofolate (a substrate in the homocysteine-to-methionine methylation reaction), is commercially available at most labs. As abnormal nucleotide sequences have been associated with fetal miscarriage^{7,8} and cardiovascular disease,^{9,10} MTHFR has become a particularly useful test.

The biochemical abnormalities that can occur due to these atypical genes may be at least partially overcome with the use of methylcobalamin (M-B12) and activated folate (folinic acid or L-methylfolate).¹¹ Supporting the methylation/transsulfuration pathway with proper B vitamin supplementation may be particularly important for a mother of a child with ASD as parents of children with autism have often been found to have similar abnormal biochemical markers to those of the children.¹² Interestingly, one study found that mothers of children with autism were less likely than those of typically developing children to report having taken prenatal vitamins during the 3 months before pregnancy or the first month of pregnancy.¹³ Significant interaction effects were observed for maternal MTHFR 677 TT, CBS rs234715 GT + TT, and child COMT 472 AA genotypes. Children were 4.5 times more likely to be diagnosed with autism if their mothers had the homozygous MTHFR C677T single nucleotide polymorphism (SNP) (SNPs are DNA sequence variations) and 7 times more likely with the COMT SNP.¹³ Because of the greater risk for autism when mothers did not report taking prenatal vitamins, the authors suggest that the B vitamin component of prenatal vitamins may protect against fetal brain development deficits.

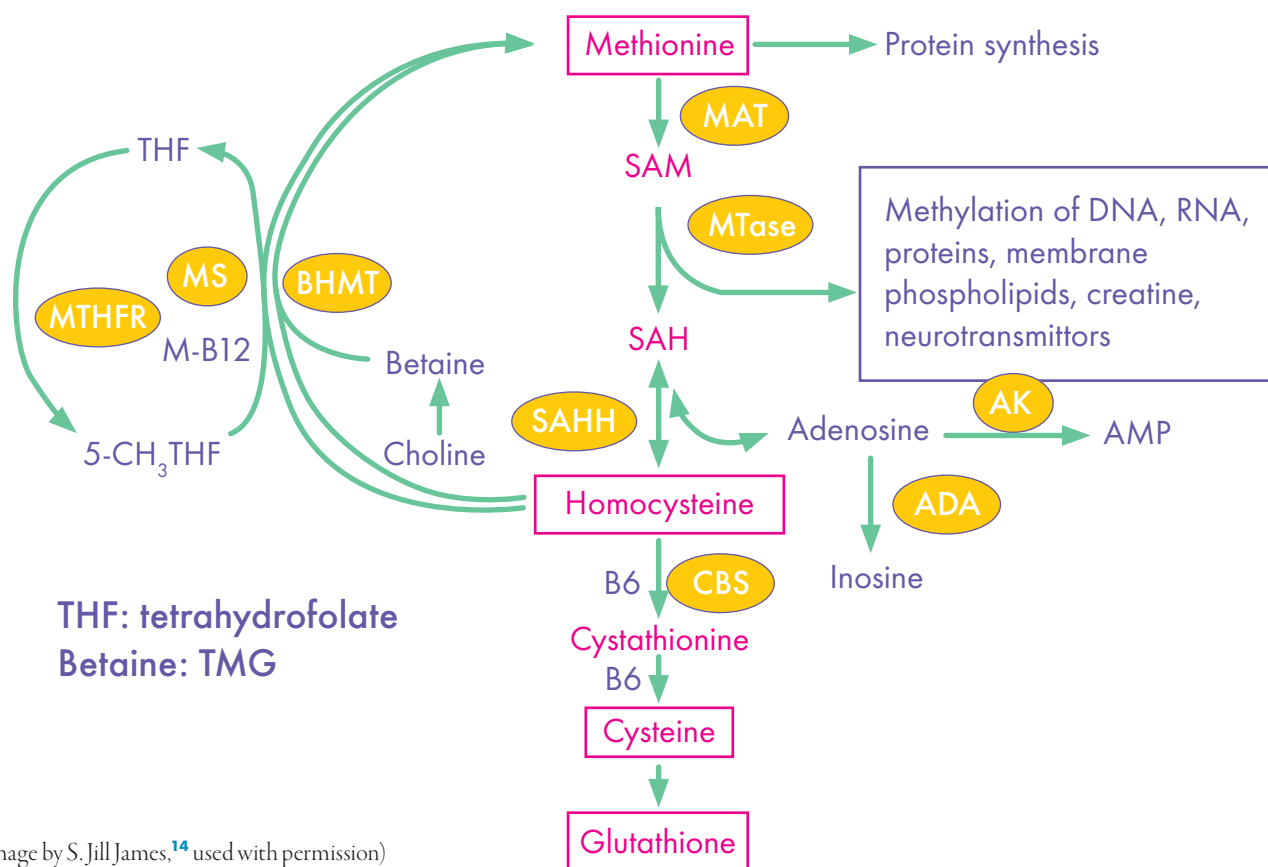
Although vitamins for pregnancy are referred to as “prenatal,” for an optimal pregnancy I propose the use of “preconceptional” vitamins, a product still under development. While waiting for a preconceptional product to become available, I suggest that women start taking prenatal vitamins prior to getting pregnant to ensure that adequate nutrition is provided from the moment of conception. A recently identified concern about multivitamins, in general, however, is the possibility that chromium, an essential mineral, could be present in its carcinogenic chromium VI (hexavalent chromium) form.¹⁵ Unfortunately, most manufacturers do not test for the different forms of chromium to make sure that the hexavalent form is not present. I would, therefore, ask the manufacturer if they are testing for and rejecting hexavalent chromium and only use companies that do this.

EPIGENETICS AND THE CELLULAR ENVIRONMENT

An emerging hypothesis for potential causes of ASDs is related to epigenetics. An epigenetic trait is a stably heritable phenotype resulting from changes in a chromosome without alterations in the DNA sequence.¹⁶ The environment within the cell can affect the way that genes are expressed. An example of this

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Figure 1.
Methylation/transsulfuration pathway



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is found in Prader-Willi and Angelman syndromes, where there is abnormal imprinting of the ubiquitin protein ligase E3A (UBE3A) gene.¹⁷ In fragile X syndrome, the epigenetic effects result in a CGG-repeat expansion that triggers hypermethylation and silencing of the FMR1 gene.¹⁸ I expect that in coming years, research will reveal specific alterations in the cellular environment that lead to these epigenetic changes. Ultimately, epigenetics may be the map that explains how the body and its environment interact in a manner that prevents or causes disease. While this is being figured out, we already know enough to minimize toxic exposures and enhance maternal nutrition to give cells an optimal environment in which to develop and reproduce.

NUTRITIONAL ISSUES

Certain laboratory tests that can be run on a woman preconceptionally or during pregnancy may be helpful in providing the information needed to support an optimal fetal environment. I often run a celiac panel because untreated celiac disease can cause nutritional deficiency.¹⁹ And, although not well studied in humans, mammalian studies have suggested that celiac disease could increase intestinal permeability (leaky gut), which could, in turn, permit gluten-based opioid peptides and other toxins to gain access to the maternal bloodstream^{20,21} and, thus, the fetus. In addition to testing for celiac disease, I often also test for

the presence of opioid peptides derived from gluten and casein. Just as we would not want to have morphine or other pharmacological opiates present during fetal development, I presume that opioids derived from foods containing these two proteins could also have a negative effect on the developing fetus.

Circulating maternally derived antibodies may have a negative impact on the future health of children. The intake of foods that a woman is allergic to during pregnancy may increase the risk of allergy in the offspring.²² Taking this into account, performing maternal IgE and IgG antibody testing for various foods and avoiding those foods during pregnancy may bring an immunological advantage to the child later in life.

CANDIDA

As many families who have explored biomedical treatments for ASD have discovered, controlling *Candida* (yeast) can significantly reduce many of the symptoms of autism. Unfortunately, most of the research performed by gastroenterologists has yet to support these clinical findings. Nonetheless, especially for women who have a significant history of frequent antibiotic exposure or recurring yeast infections, I test for the presence of *Candida* species using stool microscopic evaluations and cultures as well as the urine Organic Acids Test. If the woman is not pregnant, I often treat with systemic antifungal

medications (fluconazole, ketoconazole, itraconazole, or terbinafine), probiotics, and dietary control (low-carbohydrate diet or Specific Carbohydrate Diet™).

I do not use most systemic antifungal therapies during the first two trimesters of a pregnancy. However, the oral form of the antifungal medications nystatin and amphotericin B are not absorbed into the bloodstream, meaning that both can be considered safe to use orally at any point during pregnancy. Systemic amphotericin B is the antifungal medication that has been most studied during pregnancy. It is in the FDA's pregnancy risk category B (the second safest category but only recommended for use during pregnancy when the benefit outweighs the risk), and there have been no reports of fetal abnormalities from its use, even when administered intravenously.²³ Fluconazole is the most studied azole antifungal medication during pregnancy; abnormal fetal development has been seen at high doses (> 400 mg/day) but not at lower doses (150 mg).²⁴ Because herbs that are used to treat *Candida* have not been studied, in general, I avoid these during pregnancy.

CLOSTRIDIA

Multiple species of clostridia bacteria have been implicated in contributing to symptoms of ASD. Elevated levels of a measurable clostridia metabolite, HPHPA, have been found in some individuals with autism and schizophrenia; use of a treatment appropriate for eliminating clostridia (vancomycin) reduced HPHPA levels and simultaneously improved symptoms.²⁵ Treatments for clostridia that are safe to use during pregnancy include *Saccharomyces boulardii* and certain strains of lactobacillus. Vancomycin oral capsules are a FDA risk category B pregnancy medication.

BISPHENOL A

Bisphenol A (BPA) is used in many different products to harden plastics. It also can be found in or on tin can linings, dental sealants, and cash register receipts. It is believed that BPA is an estrogen hormone disruptor, and there is mounting evidence that exposure during pregnancy may lead to negative outcomes. Prenatal BPA exposure has been linked to aggression in 2 year olds²⁶ as well as anxiety, depression, and poor emotional control in girls.²⁷ Avoidance of BPA-containing products is the best strategy to minimize the impact of BPA on a fetus or young child.

HEAVY METALS

Heavy metals such as mercury and lead are well established to be toxic to fetuses and young children, and all efforts should be made to minimize exposure in these populations.^{28,29} Although there is no consensus on what defines increased heavy metal exposure or toxicity, I recommend that a woman consider performing a single dose chelation challenge with baseline urine metal testing *prior to getting pregnant* to determine if heavy metals are present. If there is a significant increase in heavy metals following this single dose, I would recommend that she consider chelation therapy with the agent that brought about the increased metal excretion. Chelation therapy should *not* be used during pregnancy, however.

Vaccines that contain thimerosal (a mercury compound), such as certain flu shots, should not be given to pregnant women. Consumption of fish that have significant mercury levels should also be avoided. (A list of the mercury levels in commercial fish and shellfish is available at the US Food and Drug Administration website.³⁰) Women found to have high levels of mercury and who have amalgam (50% mercury) fillings should consider having the fillings replaced (except during pregnancy), but this should only be done by a dentist who is knowledgeable and experienced in safe removal procedures. Improper amalgam removal can lead to increased mercury exposure. Living in close proximity to coal-fired power plants also can increase exposure to mercury. An increased incidence of autism has been associated with communities that have high levels of mercury-releasing coal plants^{31,32} (see Figure 2).

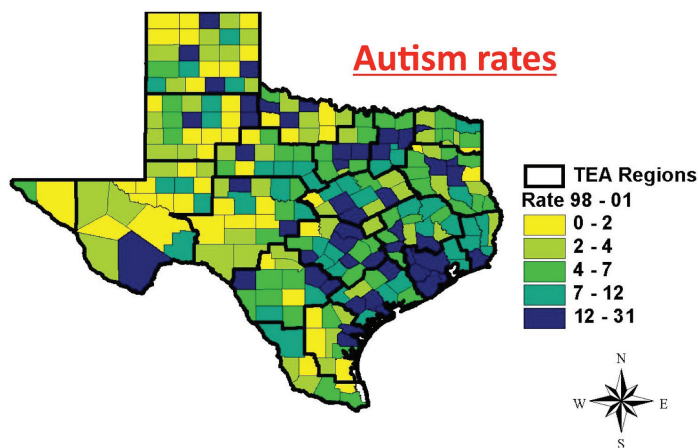
HYPOTHYROIDISM

Testing for hypothyroidism is one of several other tests that I perform before and during pregnancy, with correction of the abnormality if present. Hypothyroidism is a known cause of developmental delay in children,³³ and thyroid hormone is also a growth factor for fetuses and young children.³⁴ The prevalence of hypothyroidism in pregnant women has been estimated at 5%, and thyroid autoantibodies can be seen in 12% of pregnant women.³⁵ My personal observation is that the actual percentages are higher. Women with true hypothyroidism and those with positive antibodies (especially those with consistently low basal body temperatures under 97°F) should receive consideration for thyroid hormone supplementation and be closely monitored during both pregnancy and lactation.

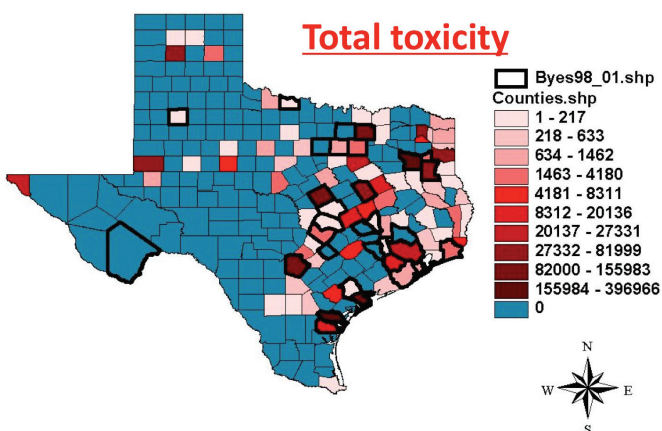
Figure 2. Environmental mercury release and autism

Observed rate of autism 1998 - 2000 by county of Texas

Aggregated from school districts
with Texas Education Agency (TEA) districts



Levels of total toxicity by Texas county for 2001
with top two deciles of Bayesian autism rates (1998-2001)



On average, for each 1000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism.^{31,32}

VITAMIN D

Vitamin D has long been established to be essential for bone health, and emerging evidence is showing its importance for proper immune development. Children born to women who are low in vitamin D have an increased incidence of allergies and severity of asthma³⁶ and a greater incidence of type I diabetes.³⁷ The Vitamin D Council has hypothesized that vitamin D deficiency may be contributing to the increased incidence of autism.³⁸ Most recently, in *Pediatrics*, Whitehouse et al. demonstrated a link between maternal vitamin D insufficiency during pregnancy and offspring language impairment at 5 and 10 years of age. In the study, women with 25-hydroxyvitamin D levels under 18 ng/ml were twice as likely to have a child with language impairment when compared with those above 33 ng/ml. The Vitamin D Council recommends that pregnant women get their level of 25-hydroxyvitamin D (the storage form of vitamin D, also called calcidiol) above 50 ng/ml and suggests a dose of 5000 IU of vitamin D3 a day for pregnant women who cannot get their level checked.³⁹

IRON

Iron is an essential mineral not only for the production of hemoglobin, but it also may affect a person's cognitive function. While a low hemoglobin level (anemia) is one indicator that a patient may be iron-deficient, a low blood ferritin level (<30 ng/ml) is a better early indicator of low iron stores.⁴⁰ Iron deficiency without anemia has been associated with autism,⁴¹ attention-deficit/hyperactivity disorder (ADHD),⁴² and lower math scores in children.⁴³ Correcting non-anemic iron deficiency has been shown to correct verbal learning and memory⁴⁴ as well as symptoms of ADHD.⁴⁵

During pregnancy, a hemoglobin level under 10.5-11.0 g/dl (depending on trimester) is considered anemia. When I document that a woman has a low ferritin level, I try to correct the level to above 50 ng/ml.⁴⁰ During pregnancy, 40 mg of elemental iron per day is usually sufficient to prevent iron deficiency,⁴⁶ and doses of between 60-120 mg are recommended if there is already iron deficiency present.⁴⁰ Some forms of iron can cause intestinal discomfort and constipation, especially during pregnancy. I find that iron in the ferrous bisglycinate chelate form is best tolerated by the GI tract and has very good absorption. Iron absorption can be enhanced if taken at the same time as vitamin C but should be taken away from thyroid hormone supplementation. I have also found that using a cast iron skillet for pan frying and sautéing can increase food's iron content.

FOLATE

Folate is known to be essential for fetal brain development. Folate deficiency has been associated with spina bifida and other neural tube defects. All pregnant women should get a minimum of 400 mcg of folic acid daily. However, because women who have the abnormal *MTHFR* gene sequence may not be able to efficiently complete the conversion of folic acid to methylfolate, they may have issues if taking only folic acid. In such cases, I recommend that women not take folic acid but rather L-methylfolate or folinic acid or possibly a combination of both. These two forms bypass the faulty *MTHFR* enzyme and provide the fetus with activated folate.

Another potential complication of faulty folic acid metabolism is cerebral folate deficiency (CFD) and the presence of cerebral folate receptor antibodies. CFD has been associated with low-functioning autism, mitochondrial disease or dysfunction, Rett syndrome, epilepsy or seizures, and an abnormal electroencephalogram.⁴⁷ While this disorder is not something that I routinely check for in all preconception or pregnant women, testing for the presence of folate

receptor I antibodies may be indicated if there is a significant family history of any of the above conditions. If CFD is identified, folic acid should be stopped and high doses of activated folate (i.e., folinic acid or L-methylfolate) taken, working up to 25 mg twice a day.⁴⁷

ADDITIONAL CONSIDERATIONS DURING PREGNANCY

Beyond folate, iron, and vitamin D, there are two additional nutrients (calcium and omega-3 fatty acids) that I focus on with pregnant women to ensure that there are no deficiencies.

CALCIUM

Adequate calcium intake is essential for bone growth and long-term health. A pregnant woman should take between 1000-1200 mg daily. If a woman is avoiding dairy, this may be difficult to accomplish through the diet, and calcium supplementation may be needed. As lead has recently been found to be present in some calcium supplements, it is essential to use supplements from manufacturers who are testing for lead and rejecting calcium raw materials that have increased amounts of lead. (This means verifying that the manufacturer is screening for lead in the raw material or in each batch produced.) When taking calcium supplements, I suggest that women also take magnesium in a 2:1 ratio of calcium to magnesium.

OMEGA-3 FATTY ACIDS

Omega-3 fatty acids are essential for brain and cardiovascular development and growth. The DHA form of omega-3 fatty acid (available in certain sea algae and other marine sources but not plant-based sources of omega-3 fatty acids) is the one that is best utilized by the developing brain. It is recommended that pregnant and lactating women take at least 300 mg per day of DHA,⁴⁸ and some studies have suggested that significantly higher doses may be even more beneficial. Children of mothers who took 3.3 grams of combined EPA and DHA during pregnancy demonstrated greater hand-eye coordination,⁴⁹ and children of mothers who took about 2 grams of combined EPA/DHA (as 2 teaspoons of cod liver oil) had increased mental processing.⁵⁰ Fish oil supplementation during pregnancy has also been associated with lower potential for allergies and possibly other immune-mediated diseases.^{51,52}

BIRTH AND POSTNATAL CONSIDERATIONS

An increased prevalence of autism has been identified in children born by both emergency and elective cesarean section (C-section).⁵³ It is logical to suspect that when an emergency C-section is performed due to fetal distress, this stress could be related to a lack of blood flow to the fetal brain that could lead to brain injury with resulting autism symptoms. Because the prevalence of autism is also higher with elective C-sections, however, all efforts should be made to avoid C-sections whenever possible. Although many women are told that they need to have a C-section if they had a previous C-section, the American Congress of Obstetricians and Gynecologists (ACOG) recently declared, "Attempting a vaginal birth after cesarean (VBAC) is a safe and appropriate choice for most women who have had a prior cesarean delivery, including for some women who have had two previous cesareans."⁵⁴

I instruct parents that a baby is not considered past due until after 42 weeks. There is no reason to artificially rush the delivery of a baby before the baby and placenta indicate that it is time for delivery. If there is any concern, an ultrasound can be performed to ensure that the baby is healthy and not under stress. Induction of pregnancy itself may have a negative role on a child's development.

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In one study, there was almost a 2-fold increase in ADHD diagnosis in children born to mothers who were induced.⁵⁵

Some families express concern about exposing their newborn to the antibiotic ointment that is placed in newborns' eyes soon after delivery. This is used specifically to prevent neonatal infection from sexually transmitted diseases (STDs) such as chlamydia and gonorrhea that can be contracted during passage through the birth canal. Therefore, this has to do with the STD status of the mother. (It should be remembered that these STDs can be asymptomatic or missed on vaginal screening.) While I am not overly concerned about a topical one-time exposure to an antibiotic (using a route that would not have an effect on the baby's intestinal flora), it is the case that the ointment may cause chemical irritation or interfere with the initial eye contact and bonding that happens when the mother is first holding the baby. Parents should evaluate the pros and cons and decide what they think is best for their baby.

Vitamin K is routinely administered by intramuscular injection soon after birth. This is done to prevent a rare newborn condition called hemolytic disease (a condition where the baby's blood cannot clot and the baby has a hemorrhage). The injected form does not contain thimerosal. Deficiency in vitamin K can cause the hemorrhagic condition in about 1 in 10,000 births, and the bleeding can occur up to 12 weeks after birth. For families who have concerns about the injected form of vitamin K, there are protocols available for its oral use from the Canadian Pediatric Society,⁵⁶ the Pediatric Society of New Zealand,⁵⁷ and the Australian government.⁵⁸

Babies are routinely given the first dose of hepatitis B vaccine on the first or second day of life. I discuss vaccines at greater length below. Many parents question why they should give a newborn a hepatitis vaccine at birth if the mother tests negative for the virus during pregnancy and babies do not engage in activities that would spread hepatitis B. While the administration of the vaccine along with hepatitis B immunoglobulin may be effective in preventing the acquisition of hepatitis B in babies born to infected mothers, all pregnant women should have been tested for hepatitis B, meaning that their infection status should be known at the time of delivery. If the mother is not infected with hepatitis B, I see little benefit to vaccinating a baby for this at birth.

After birth, I advocate for discharging mother and baby from the hospital as soon as possible. Hospitals are known to harbor higher levels of certain infections (such as *Candida*, methicillin-resistant *Staphylococcus aureus* [MRSA], and clostridia) than most of the outside world, including most people's homes.

INFANCY BREASTFEEDING

The importance of breastfeeding is now universally accepted. The American Academy of Pediatrics (AAP) recommends that babies be breastfed for at least the first year of life, and longer if desired by the mother and baby.⁵⁹ Babies who are breastfed have been suggested to have higher IQs and cognitive development,^{60,61} and a lower incidence of type 1 diabetes,⁶² allergies (when compared with cow's milk and soy formulas),⁶³ asthma,⁶⁴ and ear infections.⁶⁵ Babies who receive cow's milk-based formula may have increased intestinal permeability (leaky gut) when compared with babies who receive breast milk,⁶⁶ especially if they were born prematurely.⁶⁷ Although some families express concern about feeding any form of milk to their babies due to the casein content,

the amino acid composition of human milk is different from that of cow's milk.⁶⁸ For these and other reasons, I encourage adherence to the AAP breastfeeding recommendations.⁵⁹

Babies who are breastfed are provided antibodies through the milk to fight off infection within hours of a mother being exposed to a virus or bacteria. This can protect the baby against a host of different pathogens that could otherwise lead to the baby being exposed to antibiotics. Another advantage of breastfeeding is that a mother who continues to optimize her nutrition (as already discussed with regard to pregnancy) provides the nutrients to her baby through the breast milk.

INTRODUCTION OF SOLID FOODS

Infants who are fed solid foods too early are prone to developing food allergies. In general, the American College of Allergy, Asthma, and Immunology recommends that solid foods not be introduced until 6 months of age, with dairy products introduced at 12 months, eggs at 24 months, and peanuts, tree nuts, fish, and seafood not introduced until at least 36 months of age.⁶⁹ For younger siblings of children on the autism spectrum, I also recommend waiting at least until 1 year of age before introducing gluten. When foods are finally introduced, only small amounts should be offered for the first few days, and one new food should be introduced every 4 days to watch for negative reactions.

VACCINES

Much controversy surrounds the potential connection between vaccines and ASD. I find it interesting that pediatricians routinely tell parents that to prevent an undesirable immune reaction (allergies) they should wait six months to introduce a foreign substance (food) to their baby and advise parents to give foods one at a time to watch for reactions, yet recommend that vaccines be given starting at birth (hepatitis B) and continuing with another 21 antigens given simultaneously at 2 months of age: diphtheria, tetanus, pertussis, 3 strains of polio, 13 strains of pneumococcus, *Haemophilus influenzae* type b (HiB), and rotavirus. This displays a significant disconnect between pediatricians' feeding and vaccine advice.

In my pediatric practice, I follow the true meaning of informed consent, explaining vaccine benefits, risks, and alternatives to families so that they are fully and meaningfully informed when making their decision. Ultimately, parents have both the right and responsibility to make medical decisions and decide what is best for their child. They can choose to give vaccines according to the recommended Centers for Disease Control and Prevention (CDC) schedule, or they can split vaccines, delay them, or not give any at all. The AAP recommends that pediatricians listen carefully and respectfully to parents' concerns about vaccines, convey respect for continued refusals that follow adequate discussion,⁷⁰ and not discharge families who refuse vaccination from their pediatric practice. Notwithstanding these recommendations, almost 40% of pediatricians said they would not provide care to a family that refused all vaccines, and 28% said they would not provide care to a family that refused some vaccines.⁷¹

Although thimerosal is a known neurotoxin with no natural biological role, concerns about vaccines go beyond the mercury in vaccines. With the exception of flu shots and tetanus vaccine (DT has trace thimerosal and tetanus toxoid may have the full 25 mcg of mercury), thimerosal was removed from most

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vaccines in the early 2000s, yet the prevalence of autism has continued to climb. One possible explanation is that exposure to injected antigens from vaccines can cause undesirable immunological effects with or without the presence of mercury. The diseases that children are vaccinated against (with the exception of tetanus and hepatitis B) are not contracted in the natural world through injection but through the respiratory tract or the gastrointestinal (GI) tract, and, therefore, the immune system's first line of defense, which sets in motion the rest of the natural immune response, is bypassed. Both of these systems (respiratory and GI) have specific white blood cells and antibodies residing on their surface that serve as a first line of defense against invading organisms. The injection of vaccines prompts an artificial immune response. Abnormal shifts in white blood cells following vaccination were suggested to be the reason why children who were given the DTwP vaccine (note that this had a different form of pertussis antigen than the current vaccine and did contain thimerosal) at 2 months of age were significantly more likely to develop asthma than children who did not start receiving this vaccine until 4 or 6 months of age.⁷² The authors of this study hypothesized that the vaccinations can be viewed as promoters of asthma development, perhaps by stimulating a Th2-type immune response and shifting the cytokine balance.⁷³ They also note that at birth the newborn immune system has a limited ability to produce Th1 cytokines, but levels increase over the next 6 months.⁷⁴

More research is warranted to examine possible subtypes of autism relative to vaccine exposure and vaccinated versus unvaccinated children. Nonetheless, existing medical literature makes it clear that a role between autism and vaccines is biologically plausible. To cite a few examples:

- Some children with ASD have been found to have mitochondrial dysfunction.⁷⁵ In the case of Hannah Poling, the United States Court of Federal Claims decided that there was enough evidence to show that vaccines may have aggravated her mitochondrial disorder and triggered problems consistent with autistic-like behavior.⁷⁶ Some people even argue that vaccines can be the trigger for secondary mitochondrial issues.⁷⁷

- Vaccines are documented to have the potential to induce autoimmune diseases,^{78,79} and although rare, MMR vaccine has recently been associated with immune thrombocytopenic purpura.⁸⁰ As a subset of children with ASD has documented autoimmunity against the brain,⁸¹⁻⁸³ it is plausible that vaccines could induce autoimmunity against the brain with resulting symptoms consistent with autism.
- Large epidemiologic studies have been published that found statistically significant evidence to suggest that boys in the United States who were vaccinated with the triple series hepatitis B vaccine during the time period in which vaccines were manufactured with thimerosal were more susceptible to developmental disability than were unvaccinated boys.⁸⁴ In addition, a study based on vaccine records suggests that US male neonates vaccinated with the hepatitis B vaccine prior to 1999 had a threefold higher risk for parental report of autism diagnosis when compared with boys not vaccinated as neonates during that same time period.⁸⁵

CONCLUSION

There is considerable interest in developing strategies to try and prevent autism, especially for families who are at higher risk by having one child on the spectrum already. In this article, I reviewed a variety of possible strategies that can be considered beginning at the time of preconception and beyond. These include supporting the methylation/transsulfuration pathway with proper B vitamin supplementation; avoiding or minimizing toxic exposures (including BPA and heavy metals); enhancing maternal nutrition (including supplementation, as appropriate, with vitamin D, iron, folate, calcium, and omega-3 fatty acids); assessing maternal food allergies and intolerances; screening for maternal hypothyroidism; controlling maternal fungal and bacterial infections; breastfeeding newborns and introducing solid foods with care; and carefully weighing the pros and cons of postnatal interventions including vaccines. Further study is warranted to examine the issues raised in this review article so that we can determine if the prevalence of autism can be reduced by correcting imbalances and insults that can occur preconceptionally, during pregnancy, and during early childhood.

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