NUTRITION GENOME

12 WEEK PRACTITIONER TRAINING

WEEK 2, TOPIC 3: CLINICAL CONNECTION TO PREGNANCY, MOOD AND MENTAL HEALTH

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Epigenetics, B6, Folate, B12, Choline and Pregnancy

Pregnancy is the most powerful example of epigenetics at work. Geneticists have shown that the epigenetic change could be passed down for up to 4 generations.

One fascinating study looked at how fear associated with a particular smell affects animals and leaves an imprint on the brains of their descendants. When male mice were exposed to a chemical with a sweet almond smell, they were given a mild shock. After three days, the mice would freeze in fear each time they smelled the chemical.

When the mice mated with unexposed female mice, their young were more sensitive to the chemical and more likely to be startled by an unexpected noise when they smelled it. The grandchildren of these male mice were still jumpier in the presence of the chemical. The study, published in Nature Neuroscience, **suggested that chemical epigenetic changes to the genome without altering the DNA made an impression that lasted for multiple generations.**

The implications of this understanding of both our diet and life experience for multiple generations is profound. Educating your patients on all aspects of health is literally paving the way for a better life for your patient and potentially altering the health of their future children.

A mother's eating habits, exercise regime, stress levels and environment **epigenetically have the power to shape the genes passed down and impact the susceptibility of her child to certain health disorders.**

Originally geneticists believed these epigenetic changes only occur only during fetal development. Now we know that this process is fluid and flexible, and can be altered at any point in life. Even if we don't have the best start in life, we can epigenetically strengthen our genes, reduce health risks, and shape the following generations for the better.

Folate, choline, B12, B6, and betaine are required to provide the cofactors that are used to make the methyl groups, influencing DNA methylation of the mother and fetus during pregnancy.

Folate

Digestion Section: SLC19A1, HMNT, APB1

Methylation Section: MTHFR, MTHFD1, DHFR

DNA Repair, Damage and Repair Section: ATM

Analyzing your patient's folate genes can help you determine optimal folate intake for a healthy pregnancy. MTHFD1 encodes for folinic acid, and some patients may benefit from both folinic acid and methylfolate to support downstream and upstream metabolism. Foods high in folate achieve hitting both of these targets. Folate is also depleted by excess sun exposure in light-skinned individuals, making certain times of the year more important for higher levels. One study showed a 20% reduction in folate levels in pregnant women with high sun exposure.

A study from JAMA found that women who took acetaminophen while pregnant had a 37 percent higher risk of having a child who would be later given a hospital diagnosis of hyperkinetic disorder, a particularly severe form of ADHD. Women also had a 29 percent higher chance of having children who were later prescribed medications for attention deficit hyperactivity disorder, and a 13 percent higher chance of exhibiting ADHD-like behaviors by age seven. **NSAID's deplete folate and vitamin C.**

Variants in the **genes ABP1 and HMNT** reveal sensitivities to NSAID's like Aspirin and Tylenol on the Nutrition Genome Report. The sensitivities stem from high histamine release (folate and vitamin C lower histamine) and may help explain why NSAIDs can be especially damaging to people with variants in APB1 and HMNT, especially for those with a high folate need. Studies have found that the adverse effect of food additives on ADHD symptoms was determined by histamine degradation gene polymorphisms in HNMT in 3 and 8 to 9-year-old children, showing that histamine sensitivity may partly explain ADHD etiology.

B6

Digestion Section: NBPF3

Homozygotes (CC genotype) for the NBPF3 gene have approximately 2.90 ng/mL lower vitamin B6 blood concentration, while heterozygotes (TC genotype), have 1.45 ng/mL lower Vitamin B6 blood concentration.

B6 it is a crucial nutrient for the development of the fetus's brain and nervous system. It is one of the most important co-factors for the neurotransmitters and is a very common nutrient deficiency in women.

It has been suggested that low B6 is associated with gestational diabetes and "pregnancy depression"—described as pessimism, crying, tension without sleep, or appetite disorders. The elevation of estrogen during pregnancy increases the need for B6. The deficiency of B6 leads to morning sickness and nausea, which can be treated successfully with B6 supplementation.

It has been shown that oral contraceptives deplete vitamins B2, B6, B12, vitamin C and E and the minerals magnesium, selenium, and zinc. **This means that each gene that encodes for an enzyme that requires this co-factor is affected.** Long-term use (>30 months) of oral contraceptives containing high levels of estrogen was associated with significantly lower maternal and umbilical cord serum vitamin B6 levels than those in women who took no oral contraceptives, and evidence indicates that their vitamin B6 reserves may be decreased in early pregnancy.

If your patient is already prone to low B6 levels genetically and has taken birth control, it would be prudent for them to spend more time building back their reserves before pregnancy. B6 in the P-5-P form is preferable to pyridoxine hydrochloride for improved absorption.

B12

Digestion Section: FUT2

Methylation Section: MTR, MTRR, TCN2

Neurotransmitters and Mental Health: MAO-A

A study from John's Hopkins University looked at 1,391 mother-child pairs in the Boston Birth Cohort, a predominantly low-income minority population. The researchers found that very high circulating folic acid doubled the risk of autism, and B12 levels that were very high tripled the risk of autism. If both levels are extremely high, the risk that a child develops the disorder **increases 17.6 times**.

Since folic acid (not folate) was highlighted and cyanocobalamin, this most likely was due to a diet high in processed fortified foods along with low-quality supplements. In the last folate lesson, I explained why folic acid can be so problematic.

Cyanocobalamin is composed of cyanide and cobalamin and splits off cyanide, which can block the electron transport chain of the mitochondria. Lithium is a carrier of B12 into the mitochondria. A study found that young US children with autism and their mothers had unusually low levels of lithium compared to neurotypical children and their mothers. Excessive cyanocobalamin could theoretically disrupt the electron transport chain into the mitochondria, deplete methyl groups for methylation, increase mitochondrial oxidative stress, and cause very low lithium levels trying to keep up with the high circulating blood levels of B12 to transport into the mitochondria. **Mitochondrial dysfunction is one of the medical disorders that has been consistently associated with Autism Spectrum Disorders.**

B12 from food or in the form of methylcobalamin and/or adenosylcobalamin should be the form used in prenatal vitamins.

Choline

Estrogen can induce the PEMT gene encoding the enzyme catalyzing the production of phosphatidylcholine in liver. This means that young women with good PEMT function are less dependent on dietary intake of choline than are men. **However, almost half of women have a PEMT gene variant that blocks estrogen-induction of the capacity to make their own choline**. These women may be especially sensitive to dietary choline variations during pregnancy. All of your patients that are pregnant and wanting to be pregnant should have genetic testing done for their PEMT and folate genes.

The choline pathway is actually enriched with DHA, which of course also plays a prominent role in brain development. Fish eggs contain both choline and DHA, which is why traditional societies have always prized them for pregnancy. One analysis found that a higher choline intake (930 compared with 480 mg/d) augmented the rise in choline/DHA in nonpregnant women and choline needs are increased during the third trimester of pregnancy. The researchers found that a higher choline intake along with supplementary DHA acted synergistically to **produce the greatest enrichment of choline and DHA in red blood cells. This is a major find for future mental health.**

Results published in 2013 in the American Journal of Psychiatry by Freedman's group show that 76 percent of newborns whose mothers received choline supplements had normal inhibition to the sound stimuli, while 43 percent of the newborns did not. **Those who do not have a normal inhibition to the sound stimuli have been found to have an increased risk for attention problems, social withdrawal and, later in life, schizophrenia.**

These results show that choline might steer the infant brain away from a developmental course that predicted mental health problems.The US RDA recommends 450 mg/day in pregnant and 550 mg/day lactating women, however, this amount does not factor in PEMT polymorphisms or the third trimester of pregnancy. **As of June 17th, 2017, the American Medical Association voted to support evidence-based amounts of choline in all prenatal vitamins, noting that most prenatal supplements currently contain little if any choline.**

Folate, Choline and Mood

Approximately one-third of depressed individuals having a deficiency of folate. 5-MTHF (methylfolate) contributes to the biosynthesis of SAMe. When 5-MTHF is too low, SAMe and neurotransmitter levels decrease in the cerebrospinal fluid, contributing to depression. The MAT1 gene in the methylation section is connected to SAMe levels, requiring more magnesium and boron to boost SAMe.

5-MTHF also stabilizes tetrahydrobiopterin (BH4) and is a co-factor of nitric oxide, which supports MTHFR A1298C. Low levels of BH4 are also linked to low levels of all the neurotransmitters. Interesting enough, depressed individuals with low serum folate also tend to not respond well to selective serotonin reuptake inhibitor (SSRI) antidepressant drugs.

Those with the lowest choline intake have been found to have the highest anxiety in research. Theoretically, low folate and low choline during pregnancy and after pregnancy could severely affect mood.