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How to Optimize A Baby’s Epigenetics In a Toxic World

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Disclaimers

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Objectives

After participating in this Webinar participants will be able to:

1. Define epigenetics in one simple sentence

2. Recount three ways that genes can be “turned off”.

3. Recommend 3 ways for pregnant women to decrease their exposure to environmental toxins.

There are photos presented in this Webinar which are in the public domain.
What I’ll be covering today

- Genetics review and epigenetic highlights
- A screening tool to help the busy Obstetrician
- Evidence based advice for our patients
A physicist walks into a pub
“We have discovered the secret of life.”

“It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.”

DNA is the blueprint

- DNA is unwound and transcribed to a ribonucleic acid messenger
- mRNA carries information outside of the nucleus
mRNA – nucleotides are read three at a time to line up amino acid chains
Limited gene expression in every organ
April 14, 2003
The human genome project is complete!

- National Human Genome Research Institute
- 23 pairs of chromosomes
- 3 billion base pairs/
  $2.7$ billion dollars
- 30,000 genes
- Each makes an average of 3 proteins

www.genome.gov
If the human genome was a book -
Only a small fraction of our DNA codes for proteins.
The book analogy is misleading

- The letters are not all available to be read.
Epi – on, above like Epidural
Epigenetics is

The study of changes in an organism related to modification in gene expression—rather than a change in the DNA.
So how can something “on or about” the DNA block genes from being expressed?

- Methyl groups
- Protein spools (histones)
- RNA that doesn’t make proteins!

So called microRNA = miRNA = non-coding RNA = ncRNA
Methyl groups turn genes off and it’s a normal event in all cells

- It only has a single carbon so you’ll hear about the influence of single carbon donors

- Vitamins/chemicals involved with single carbon transfer:
  - Folic acid
  - B 6
  - B 12
  - Methionine - amino acid
  - S – adenosyl methionine (SAM)
S – adenosyl methionine (SAM) - a universal donor of methyl groups

Loss of methylation returns embryo to a totipotent state

Most epigenetics are scrubbed out through reprogramming. In mammals about 1% of genes escape epigenetic reprogramming through imprinting. 1% of epigenetic changes are passed on to the next generation.

In mammals about 1% of genes escape epigenetic reprogramming through imprinting.
Two classic examples of epigenetics

- The mice with the agouti gene
- Nurturing behavior in rats
The agouti gene

- Affects pigment in several different types of mammals.
- The color of the fur of the agouti mouse is determined by the degree of methylation of a particular gene.
- Hypomethylation – yellow fur
- Methylated – black

What you fed the mother of these two mice changed the degree of methylation!

- Folic acid is a methyl donor. In this particular circumstance **methylation is better**!

Diet supplemented with folic acid  Normal diet without supplemental folic acid
Not only a phenotypic difference but a physiologic difference!

Yellow – unmethylated mouse. Adult-onset obesity, diabetes and tumorigenesis

Black – methylated mouse. Adult – thin, normal blood sugars
So maternal diet had an epigenetic effect on offspring. How about parenting after birth?

- In rats, good parenting for 10 days leads to lower circulating cortisol levels!
- In this example hypomethylation is a good thing.
Good mothering vs. bad mothering

There is a normal variation in how much mothering a dam does. Quantifiable groom/licking and arched back nursing. With arch backed the mother can be most involved with the pups.
Hypothalamus
Corticotropin releasing hormone (CRH)

Pituitary
Adrenocorticotropin hormone (ACTH)

Adrenal glands
Cortisol:
- increases glucose
- vasoconstriction
- activates autonomic nervous system
  (part of the flight or fight response)
If you’re a rat you would like to have more cortisol receptors. That way when stress occurs your adrenals release cortisol, your brain senses that and the hypothalamus stops stimulating the HPA.
Mothers split into two groups
Observation for 7 hours a day for first 10 days of life
Time with pups was identical
High L/G - ABN
Low L/G - ABN

The most active position a dam can take during nursing
Epigenetic change is in the brain of the offspring

- At birth the gene related to the cortisol receptor is highly methylated and inactive.

- Licking/high nurturing mother leads to demethylation – increase in cortisol receptor - lower cortisol levels, less anxiety.

- The brain shuts down the stimulation to the adrenals quicker.

Offspring had different responses to stress dependent on how their mother treated them!

- **Blood levels of stress hormones (Good mom)**
  - Lower CRH mRNA
  - Lower ACTH
  - Lower cortisol levels

- **Behavior in novel environments (Good mom)**
  - Decreased startle response
  - More open-field exploration
  - Quicker to eat in a novel environment
Does child abuse affect epigenetics?

- 24 males who committed suicide/ 12 male controls accidental death
- Suicide cases half abused/half not abused
- Hippocampus sampled
- If abused significant decrease in glucocorticoid receptor expression $P = 0.05$.
- If abused total glucocorticoid receptor mRNA significantly reduced $P < 0.05$.

Demethylation allows expression of the gene making the cortisol receptor

- Study of 25 women some of whom had been subjected to intimate partner violence.
- Physical abuse, emotional abuse, harassment.
- Did it occur prior to conception, during pregnancy or after.
- Their children were 10-19 years of age.
- Level of methylation of the GR gene was studied.

First study that showed that psychological stress can result in sustained alteration of methylation in this regulator gene.

Transgenerational effect

Do you personally need to be worried about epigenetics/environmental toxins?

- DES is off the market
- I don’t smoke
- I drive a Prius
- I shop at Natural Foods, Inc.
Chemicals are ubiquitous
A growing business in the United States
Make possible many of the conveniences of modern day life
One simple way to determine the extent to which we all carry chemicals in our bodies is through testing of urine samples
Nationally representative survey and physical examination

To assess the health and nutritional status of the civilian non-institutional US population

268 pregnant women

Urine samples screened for 163 chemicals

Some of chemicals/categories (NHANES) 2003-2004

- Tobacco exposure – Cotinine
- Metals
- Pesticides
- Flame retardants (polybrominated diphenyl ethers - PBDE)
- Waste from burning fossil fuels (polycyclic aromatic hydrocarbons - PAH)
- Chemicals to soften plastics, dissolving agents - Phthalates
All sorts of chemicals that don’t belong in us!
Chemicals Detected in Every Pregnant Woman in the US

DARN... I DON'T LIKE THE GREEN ONES...
A single serving of a “good fish” - 6 ounces of salmon
ACOG recommends 8-12 ounces/wk = 2-3 servings
Bad fish

Shark

Tile fish

Swordfish

King Mackerel
Three additional “bad fish” added - Jan 2017, EPA guidance

Orange roughy  
Big eye tuna  
Marlin
Fish/seafood – low in mercury

- Salmon
- Tilapia
- Tuna (canned light)
- Cod
- Catfish
- Shrimp

http://www.nrdc.org/health/effects/mercury/sushi.asp
24,204 fellows

2,514 responded and included in analysis

78% - counseling would help reduce exposures

50% - take an environmental health history

< 20% routinely ask about environmental exposures

1 in 15 reported any training on the topic

Do you routinely discuss this issue as part of your prenatal care?

National data 2014

Do you routinely discuss this issue as part of your prenatal care?

State of GA data - 2017

Barriers for Obstetricians screening?

- Lack of knowledge
- Uncertainty about evidence
- Patients can’t make changes
- Might increase anxiety in patients

An assessment tool that is coming!

- Prenatal Assessment of Environmental Risk (PAER)
- Has the backing of the Agency for Toxic Substance and Disease Registry (ATSDR)
- Online
- Mother fills it out ahead of time and brings in printout
- Focuses on 5 areas
Prenatal Assessment of Environmental Risk

Providers and Clinic Staff
Send the assessment to patients, view secure results, and access key environmental health resources. Learn more about using the assessment in your clinic.

Create an account

Pregnant Women
Find out which chemicals you need to watch out for — and get personalized tips and questions to ask your doctor. Learn more about the assessment.

Take the assessment
Take the Assessment

It only takes about 5 minutes — and you’ll get personalized tips when you’re done.

Your personal information is kept private.

You need to do the whole assessment at once. You can’t do part of the assessment now and finish it later.

When you’re finished, you can print out results and share them with your doctor.

Learn about our privacy policy.
4 questions on lifestyle – work, smoking, personal care products

Section 1: Lifestyle

1. Do any of these describe the type of work you do outside your home? Check all that apply.
   - Cleaning or maintenance
   - Construction or building renovations
   - Cosmetology (beauty or nail salon)
   - Dry cleaning
   - Farming or gardening
   - Health care chemotherapy
   - Manufacturing or factory work
   - Painting
   - Pest control
Section 2: Home

5. Was your home built before 1978?
   - Yes
   - No
   - I don't know

   Why are we asking about this? 

6. Do you have a working carbon monoxide detector in your home?
   - Yes
   - No
   - I don't know

4 questions on home - 1978?, CO monitor
Section 3: Food and Water

9. How often do you eat locally caught fish? This includes local fish sold in markets and fish that you (or people you know) catch nearby.
   - Never or rarely
   - A few times a year
   - Once a month
   - Once a week
   - A few times a week

Why are we asking about this?

10. How often do you eat largemouth bass, tuna, shark, tilefish, king mackerel, or swordfish?
    - Never or rarely
    - A few times a week

Section 4: Cans, Bottles, and Containers

13. Do you microwave food on plastic plates or in plastic containers?
- Yes, often
- Sometimes
- No, never

Why are we asking about this?

14. How often do you drink beverages from plastic bottles?
- Every day
- Most days
- Sometimes
- Rarely or never

Examples: Bottled water, soda or pop, iced tea, juice
Section 5: Getting Ready for your baby

16. Before you have your baby, are you planning to make changes to your home (like painting or remodeling)?
   - Yes
   - No
   - I'm not sure

Why are we asking about this?

17. Are you buying new furniture before your baby arrives?
   - Yes
   - No
   - I'm not sure
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What should I eat?
What supplements should I take?

Evidence suggests that maternal nutrition does not largely influence global methylation patterns, particularly in nutrient-replete populations.

There is a link between maternal nutrition and methylome of the offspring but ... more research is needed.

So it’s not going to be as easy as diet and supplements

Geraghty AA. Nutrition During Pregnancy Impacts Offspring’s Epigenetic Status- Evidence from Human and Animal Studies. Nutrition and Metabolism Insights. 2015:8(S1)
“The rich get richer and the poor get poorer”

Wealthy educated parents live in environments with less environmental toxins.

Walking down the street in my neighborhood is an enjoyable relaxing experience. Most patients do not have that pleasure.

I’m able to afford organic fruits and vegetables. Significant portions of the population do not have that luxury.

Pick good parents and a supportive, kind partner

Don’t live near industry, roadways

Smoking, substance abuse, breast feeding correlate with zip code/income.
“The rich get richer and the poor get poorer”

- Income inequality is worse then when I was a child.

- President Obama’s final state of the union address
  - “How can we give everyone a fair shot at opportunity and security in this new economy”
  - “The American people must decide government’s role in making sure ‘the system is not rigged in favor of the wealthiest and biggest corporations’.”

I’ll close with 6 things to consider to decrease you and your families exposure to environmental toxins.
5. Eat low mercury fish twice a week

- Salmon
- Tilapia
- Tuna (canned light)
- Cod
- Catfish
- Shrimp
4. Don’t microwave plastic

- Heating increases leaching of chemicals
- Glass lid or paper to cover food
- Use glass, porcelain, stainless steel especially for hot foods and drinks

3. Take your shoes off at the door

- Professional applicators – yes
  - Clothes and shoes carry the pesticides
  - Doormats don’t trap enough

- If you have children crawling on the floor

- Active children and indoor/outdoor pets increase transfer from lawn to indoors

2. Avoid tobacco smoke

- First and second hand
1. Support politicians who will act to decrease our ever growing exposure to toxins

- We need to switch to the European model where the onus is on industry

- The City of San Francisco

- The Erin Brockovich approach to changing company behavior is impractical
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