Upstream Medicine
What Mainstream Medicine Misses that We Need to Know for the Health of the Next Generation
Aviva Romm, M.D.
“Generation Rx”: The New Pediatric Morbidity

Asthma
~ Tripled from 3.6% to 9.4% between 1980 to 2008.

Food Allergies
Increased 18% between 1997 to 2007. Doubling of peanut allergies.

Eczema
Has tripled in the past 30 years. Now affects 15% of children.

Obesity
1 in 3 children is now overweight or obese.

Diabetes
Affects one in 400-500 children. Previously an adult disease. Type 1 increasing as well.

Mental Health
1 in 10 children and young people aged 5 - 16 suffer from a diagnosable mental health disorder - double the rate seen in the 1980s. One in 12 children is diagnosed with ADHD and 1/88 with ASD. 180,000 kids under 2 yo in the US on a psychiatric medication.

Autism
1 in 68 kids is now on the autistic spectrum. Was 1:10,000 15 years ago!

Early Puberty
Girls as young as 8 years old are going through social-sexual risks, stigma, and increased susceptibility to immunologic problems due to toxin exposure.

Cancer
The leading cause of death by disease among U.S. children between infancy and age 15. More than 10,000 new cases are expected to be diagnosed annually.
For the first time in modern history life expectancy in our kids is predicted to be shorter than our own.
Mother as Gatekeeper
The Social Issues Can’t Be Ignored...
- MICROBIOME: The impact of the maternal microbiome on immunity, stress, and disease.

- NUTRITION: The impact of maternal nutrition on chronic disease development in the next generation.

- EXPOSOME: The impact of maternal environmental toxin exposure and genetic alterations on the next generation.

What you can do to help shift these impacts immediately and individually, and in the long run, globally.
The Maternal Microbiome Impact

- Maternal nutrient breakdown
- Metabolism and weight
- Detoxification
- Healthy vaginal flora (PTL, GBS -> ABX use)
- Mood (i.e., prenatal and postpartum depression)
Factors that Impact Healthy Infant Microbiome Development

- Health of mother’s microbiome
- Cesarean section
- Antibiotics at birth
- Separation of infant from mother via HPA mediated stress impact on cortisol production and changes in immune response
- Infant feeding method (breast or formula)
- Medical antibiotic overuse in infancy
Microbiome Damage Infant Impact

- Gut, oral, dermal colonization affected by change in mode of birth, separation of mother-baby at birth, and maternal microbiome health.

- **Increases lifetime risks of:**
  - Allergic rhinitis
  - Anxiety, depression
  - Asthma
  - Autoimmune disease
  - Celiac disease
  - Eczema
  - IBS and IBD
  - Nutritional deficiencies
  - Obesity
  - Oxidative damage
  - Type I Diabetes
Immune Dysregulation

Leaky Gut & Tolerance

Immune Development

• Altered signaling mechanisms affecting Th2 differentiation and/or tolerance induction & leading to Th1 dominance with increased respiratory reactivity.
A Closer Look
Obesity and Gut Flora

- Global escalated in just 2 decades.
- Not just dietary changes but dietary changes, satiety gut and neuropeptide signaling, changes in calorie extraction, and fat metabolism.
- Up to 15% of calories extracted by normal resident gut flora
Intestinal Permeability, Dysbiosis & Obesity

MICROBIAL INFLUENCE
Research by Patrice Cani, at the Université Catholique de Louvain in Brussels, has shown that, in mice, a decrease in the population of bifidobacteria species in the gut causes the tight junctions between the cells of the gut lining to loosen. The loose junctions increase the gut’s permeability and allow lipopolysaccharide (LPS) from these microbes to leak through the gut wall. The resulting metabolic endotoxaemia causes a low-grade inflammation and can induce a number of metabolic disorders – including the insulin resistance that characterizes T2D.

Liver
- Lipogenesis
- Inflammation
- Oxidative stress
- Steatosis
- Insulin resistance

Fat
- Inflammation
- Macrophage infiltration
- Oxidative stress
- Insulin resistance

Muscle
- Inflammation
- Insulin resistance
The Solutions

- Maternal prenatal probiotic use to ensure healthy vaginal and GI flora
- Encourage vaginal birth as a public health (midwives, doulas, evidence-based obstetrics practices)
- Reduce intrapartum and immediate postnatal maternal antibiotic use
- Support breastfeeding exclusively for at least 4 months
- Consider methods of reinoculating newborns:
  - “Gauze in the vagina”
  - Probiotics for newborn
Susceptibility to chronic disease is programmed *in utero*.

“Thrifty genes”

- Mom transmits environmental information to her baby chemically
- “Predictive Adaptive Responses”
- “Decisions” made by the embryo/fetus change the course of development for future advantage
Leads To…

Irreversible alterations in:
- Pancreatic development and insulin secretion/action
- CV responses, vascularity
- Deposition of fat, muscle, bone
- Organ growth and development, i.e., brain liver
- Metabolism and mitochondrial function
- Number of nephrons (reduced)
- Immune function
- HPA axis set points
Preconception & Pregnancy Nutrition Impact

- Fertility challenges
- Miscarriage
- Neural Tube Defects (FA supplementation)
- GDM
- HTN, PIH, PEC
- Risk of Preterm Birth
- Perinatal and Postpartum depression
- Autism, Learning disabilities
- Diabetes, CVD
Optimize Prenatal Nutrition

Start with a nutritional assessment and educate about:

- Nutrient dense foods only – explain Mediterranean diet
- Manage cravings
- Full spectrum eating – Low inflammation, Antioxidant rich Pregnancy specific supplements at critical times
- Supplement for common nutritional deficiencies (location/demographic specific)
- Consider maternal SNPs
Yet…

According to the CDC, based on biomarkers:
• 1 in 4 Americans eats less than 1 serving of fruits and vegetable per day
• 90 million Americans vitamin D deficient
• 30 million American frankly deficient in Vitamin B6

Women are twice as likely as men to be deficient in B6, and OCPs increase this risk.

Pregnant women are especially at risk for deficiencies, for example, iron deficiency as a result of menstrual status.

Pregnant women are known to be frankly deficient in the above nutrients as well as: Protein, Vitamin E, Folate/Folic acid, EFAs, Iodine, Choline, Calcium, Zinc, Magnesium
Teach How Much Food, How Often

- Eating for two a dangerous myth
  - “Overfed and undernourished”

- Caloric needs not increased in 1st trimester

- By 3rd trimester caloric requirement increase = 1 glass of milk + ½ sandwich!
## Prenatal Weight Gain vs. Food Quality

<table>
<thead>
<tr>
<th>Prepregnancy BMI</th>
<th>BMI+ (kg/m²)</th>
<th>Total Weight Gain (lbs)</th>
<th>Rates of Weight Gain* 2nd and 3rd Trimester (lbs/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
<td>28–40</td>
<td>1 (1–1.3)</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5-24.9</td>
<td>25–35</td>
<td>1 (0.8–1)</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0-29.9</td>
<td>15–25</td>
<td>0.6 (0.5–0.7)</td>
</tr>
<tr>
<td>Obese (includes all classes)</td>
<td>≥30.0</td>
<td>11–20</td>
<td>0.5 (0.4–0.6)</td>
</tr>
</tbody>
</table>
Encourage Prenatal Vitamins

↑ Birth Weight
↓ Gestational HTN
↓ Pre-eclampsia
↓ Preterm Birth
↓ Autism risk
The Folate Debate

- **Folate, Folic Acid, or Methylfolate?**
- **How Much?**

- Best choice: 400-800 mcg of methylfolate daily starting 3 mo. prior to conception, continued throughout pregnancy
Prenatal Anemia: Nutritional Status Indicator

- Reflects overall nutrient poor diet (check ferritin and H&H)
- Associated with adverse maternal and fetal outcomes
- Chronic hypoxia leads to chronic stress/ activation of HPA axis, placental CRH release, and increased fetal cortisol production and increased oxidative stress in the maternal-fetal dyad.
- Reduced maternal immunity with anemia increases infection rates; associated with intrauterine infection in PTL.
- Supplementation leads to longer gestation and improved birth weights in offspring
- No need to supplement in the absence of anemia (account for hemodilution) and an iron rich diet
- At risk groups: teens, vegetarians, vegans
Additional Nutrients

- **Iodine**: Commonly low in US women (studies have shown that approximately only 20 percent of women in the U.S. take supplements with iodine); maternal hypothyroid poses significant risks to fetus. Also higher maternal risk of Hashimoto’s postnatally leads to depression and consequences. Rx: PNV with 220 mcg/day iodine.

- **Vitamin D**: 2000 units/day almost universally safe; replete if deficient; insufficiency associated with higher rates of GDM, AI diseases, asthma, and some cancer.

- **Magnesium** (citrate if constipation, glycinate otherwise) – protective against HTN in pregnancy.

- **Calcium**: 1000 mg/day IOM recommendation. Increased intake in pregnancy improves maternal and fetal bone status, and reduces risk of PTL.

- **Selenium**: 200 mcg/day prevents postpartum thyroiditis in women with elevate TPO antibodies in pregnancy.

- **Choline**: 450 mg/day necessary for healthy fetal brain development and learning abilities, protects baby from effects of maternal stress.
EFAs

- Omega 3s essential for cell membranes structure
- Most women low in serum concentrations
- Reduced fish consumption in pregnancy because of mercury and PCB exposure risk, lowers this further.
- Improved visual and cognitive development
- Maturity of sleep patterns, and motor activity in infants of mothers with adequate prenatal intake.
- Mixed evidence on birth weight outcomes with a modest increase in gestational length and reductions in LBW.
- Dose: 200 mg – 1 gm DHA/day preconception and prenatally and 1-2 portions of oily fish/week (12 oz total).
The Exposome: Toxic at Birth

Toxicants include:
- Pesticides, Herbicides, PCBs, PDBE, etc.
- Heavy metals
- Plasticizers, BPA
- Teflon and other non-stick surfaces
- To name just a few…

They act as:
- Mutagens
- EDCs
- Neurotoxins
- Obesogens
- Diabesogens
- Carcinogens
- Immunotoxins
What We Eat, Wear, and Use

- Change to glass or stainless steel water bottles
- Review cosmetic use
- Decrease dairy, eat organic
- Avoid plastic food packaging and storage containers
- Cooking and storage containers
- Pharmaceuticals
- Home/Furnishings
- Cleaning supplies
- Water
Foods to Avoid Starting…Now

- Sushi, high mercury fish, frequent fish consumption (PCBs)
- Raw fish, raw meat, unpasteurized dairy
- Caffeine > 250 mg/d
- Large amounts of rice and concentrated rice products (arsenic risk)
- “Empty calories”
- Alcohol
- Food toxicants
Should Women Detoxify Before Conception?
Perhaps, Yes…

Body burden of multiple pollutants

Of the women of child bearing age studied, more than half had median or higher levels of at least two of three pollutants that can harm fetal brain development.
Exotoxins
*drugs, (prescription, OTCs, recreational, etc)
*chemicals
- agricultural
- food additives
- household
- pollutants/contaminants
*microbial

**PHASE I**
[cytochrome P450 enzymes]

- **toxins** (nonpolar: lipid-soluble)
- **Reactions**
  - oxidation
  - reduction
  - hydrolysis
  - hydration
  - dehalogenation

- **Enzymes, Cofactors & Other Nutrients Used**
  - riboflavin (vit. B2)
  - niacin (vit. B3)
  - pyridoxine (vit. B6)
  - folic acid
  - vitamin B12
  - glutathione branched-chain amino acids
  - flavonoids
  - phospholipids

- **Antioxidant/Protective Nutrients/Plant Derivatives**
  - carotenoids (vit. A)
  - ascorbic acid (vit. C)
  - tocopherol (vit. E)
  - selenium
  - copper
  - zinc
  - manganese
  - coenzyme Q10
  - thiol (found in garlic, onions)

- **Superoxide**
  - Free Radicals
  - Reactive Oxygen Intermediates
  - Antioxidant/Protective Nutrients/Plant Derivatives

- **Intermediary metabolites**
  - more polar: more water-soluble

- **PHASE II**
[conjugation pathways]

- sulphation
- glucuronidation
- glutathione conjugation
- acetylation
- amino acid conjugation
- glycine
- taurine
- glutamine
- ornithine
- arginine
- methylation

- **N-acetyl cysteine, cysteine, methionine are precursors**

- **Excretory derivatives**
  - polar: water-soluble

- **Serum**
- **Kidneys**
- **Bile**
- **Urine**
- **Faeces/stool**
Maternal SNPs & Prenatal Disease

Elevated maternal Hcy levels →
- Miscarriage
- Placental abruption
- PTL
- IUGR
- Hypertension
- Preeclampsia
- NTDs
- Autism

MTHFR, SOD, GSH: One carbon metabolism disorders in pregnancy may establish adult disease in utero
The Future is In Our Hands
References


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