

# Pregnancy Nutrition and Brain Health: *You are what your mother ate*

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# Disclosures

***Errol R. Norwitz, MD, PhD, MBA***

*Neither I nor my spouse has a relevant financial relationship with a commercial interest to disclose*

# Objectives

- To understand that human brain development is a **lifelong process**
- To recognize the importance of **nutrition** (both macro- and micronutrients) as a driver of metabolic health
- To devise **evidence-based guidelines** to optimize nutrition and health for the mother-fetal dyad before, during, and after pregnancy

# Human brain development is a lifelong process

- **Structural** brain development begins shortly after conception
  - *Neural tube forms between days 18-28 (weeks 2-4) postconception*
  - *Folds into forebrain, midbrain, and hindbrain*
  - *New neurons develop (neurogenesis), cells migrate to their final locations*
  - *At birth, the brain is 80% its adult size, doubles in first year, 90% of adult size by age 5*
- **Functionally**, the brain development continues our entire lives
  - *Synapses (connections) form rapidly, peaking in the first year*
  - *Myelination increases speed/efficiency of communication between brain regions*
  - *Pruning (elimination of unused neurons/synapses) refines connections and enhances brain function*
  - *Prefrontal cortex continues to develop/mature through adolescence and early adulthood*
  - *Although the brain ages, neuroplasticity (ability to form new connections) persists*

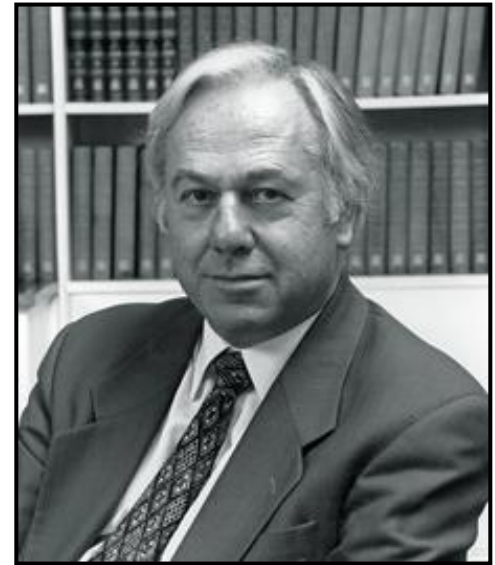
# The most important 9 months of your life

 **Massachusetts General Hospital**  
Founding Member, Mass General Brigham  
Psychiatry Academy



# “All diseases begin *in utero*”

- **Intrauterine environment** has profound effect on what chronic diseases you are going to get, how long you are going to live, and what you are going to die of
- Described in 1980s by **David Barker**, who showed that people with LBW are at greater risk of CVD in later life
  - *In 1995, BMJ coined “Barker hypothesis” (in utero epigenetic fetal programming, DOHaD/Developmental Origins of Health & Disease)*
- **Association exists** for CVD (HTN, CAD, stroke), obesity, type 2 diabetes, cancer, asthma → also affects F2 generation



David Barker, MD, PhD  
Prof of Clinical Epidemiol,  
Southampton, UK  
(1938-2013)

Barker DJ, Osmond C. *BMJ* 1988;297:134; Barker D, et al. *BMJ* 1989;298:564; Barker DJ. *Lancet* 1989;2:577; Hales CN, Barker DJ, et al. *BMJ* 1991;303:1019

# Mechanisms underlying DOHaD

- Chronic diseases in adulthood result directly from **fetal metabolic/hormonal adaptive responses** to intrauterine insults, such as undernutrition
  - *Uteroplacental insufficiency → reduced nutrients to fetus → FGR → adaptive response, e.g. altered gene expression, changes in tissue/organ development → increased weight gain, inflammation, and chronic diseases later in life*
  - *Having experienced deprivation in utero, fetus is ‘primed’ (‘programmed’) to expect a lifetime of deprivation → after birth, the child’s behavior/metabolism is primed to conserve energy stores (overeat, not exercise) → leads to metabolic syndrome, obesity, type 2 diabetes, and chronic diseases*



Identical twins with unequal placental sharing (discordant nutrient supply)

# Pregnancy health is established prior to conception

- We **can't prevent** most pregnancy complications
  - *Including PTB, GDM, FGR, stillbirth*
  - *Possible exception is preeclampsia (LDA, effect is limited)*
- **Overlapping clinical syndromes** and part of same biological continuum → same underlying pathology
  - *Common risk factors; overlapping biomarkers*
- Grand unifying explanation: (1) **defective decidualization** → (2) defective implantation/placentation → (3) clinical syndrome
  - *Decidua is primed during menstrual cycle hormonally, biochemically, immunologically (“the soil is more important than the seed”)*



# Implications for pregnancy health



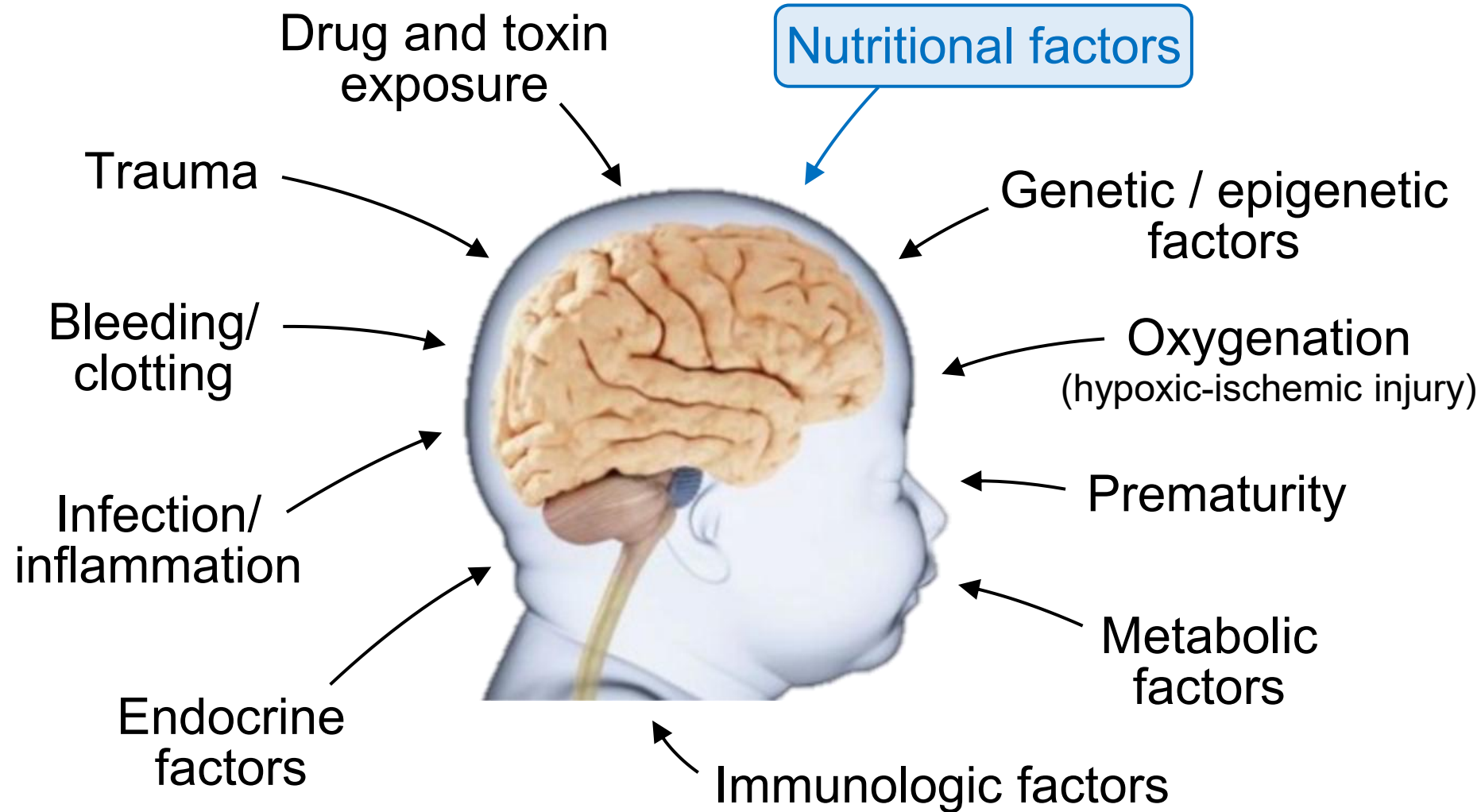
- The health of the pregnancy is determined by the health of the woman—the health of the endometrium—**around the time of conception**

# Risks of under / overnutrition at conception

- Nutrition is **modifiable risk factor** for pregnancy health → it's **actionable**
- **Total caloric restriction** results in LBW with life-long consequences
- **Total caloric excess** (obesity) is assoc. with multiple adverse events
  - *For pregnancy: GDM, HTN/preeclampsia, PTB, stillbirth, cesarean, PPH, infection*
  - *For fetus: congenital anomalies (NTD, cardiac anomalies, omphalocele, cleft lip/palate), fetal macrosomia (EFW  $\geq 4,500$ g), shoulder dystocia/birth injury, childhood obesity*
  - *Pre-pregnancy weight (BMI) more important than weight gain in pregnancy → dose-dependent*
- **Micronutrient deficiencies (excesses)** can lead to adverse events
  - *e.g., (i) folic acid → NTD; (ii) iodine → hypothyroidism; (iii) vitamin A → LBW (excess causes birth defects); (iv) L-arginine, calcium, PUFA → PTB, ?PE; (v) fluoride → bone/teeth health*
  - *Most evident in LMICs (but also 50% of patients in HIC)*

Stephenson J, et al. *Lancet* 2018;391:1830; WHO. [www.who.int/publications/i/item/9789240007789](http://www.who.int/publications/i/item/9789240007789)

# Factors affecting brain health





Think like a fetus

*If I could choose, I  
would like to have  
\_\_\_\_\_ for dinner*

# General principles

- Perform **detailed assessment** at 1<sup>st</sup> prenatal visit (ideally pre-pregnancy)
  - *History: incl. behaviors and medical/surgical conditions that pose nutrition-associated health risks (e.g., alcohol, illicit drugs, bariatric surgery); consider dietary questionnaire*
  - *Exam: BMI, clinical evidence of nutritional deficiency*
  - *Labs: HCT, GDM screening (no benefit to routine testing for vit D <sup>#^</sup> or iron deficiency\*)*
- Consider **referral** to a nutrition professional (e.g., registered dietitian)
  - *Possible indications: DM, hyperemesis, food insecurity, bariatric surgery, elevated BMI, eating disorders, self-imposed dietary restrictions (vegan, gluten free, paleo)*
- ACOG recommends counseling at first prenatal visit “**regarding benefits of appropriate weight gain, nutrition, and exercise**”<sup>\*\*</sup>

<sup>#</sup> WHO. Vitamin D in pregnancy. [www.who.int/publications/i/item/9789240008120](http://www.who.int/publications/i/item/9789240008120); <sup>^</sup> ACOG Committee Opinion 495. *Obstet Gynecol* 2011; 118:197 (reaffirmed 2024);

<sup>\*</sup> U.S. Preventative Services Task Force. Iron deficiency in pregnancy. Aug 2024; <sup>\*\*</sup> ACOG Committee Opinion 548. *Obstet Gynecol* 2013; 121:210 (reaffirmed 2023)

# Recommended weight gain in pregnancy: IOM / NAM guidelines

| Category     | BMI (kg/m <sup>2</sup> ) | Recommended total weight gain |
|--------------|--------------------------|-------------------------------|
| Underweight  | <18.5                    | 12-18 kg<br>(28-40 lbs)       |
| Normal       | 18.5-24.9                | 11.2-16 kg<br>(25-35 lbs)     |
| Overweight   | 25-29.9                  | 7-11.2 kg<br>(15-25 lbs)      |
| <b>Obese</b> | <b>≥30</b>               | <b>5-9 kg<br/>(11-20 lbs)</b> |

Institute of Medicine, National Academy Press 1990. pp. 27; Institute of Medicine, National Academies Press 2009; ACOG Practice Bulletin 156. *Obstet Gynecol* 2015;126:e112; ACOG Practice Bulletin 230. *Obstet Gynecol* 2021;137:e128

# General principles (cont.)

- Counsel patients to eat **healthy diet** before, during, and after pregnancy\*
  - *Encourage consumption of fruits and vegetables, proteins, whole grains, low-fat dairy*
  - *Avoid consumption of ultra processed foods and sugary drinks*
  - *Organic foods are not nutritionally superior (and are more expensive, less accessible)*
- Avoid ingestion of **potentially toxic foods, environmental pollutants**
  - *e.g., fish with high mercury levels (swordfish, shark), excess caffeine (>300mg/day, >3 cups), herbal products (except ginger), liver-based foods (vit A), bisphenol A/phthalates, pesticides*
- Prevent **foodborne infections**
  - *Unwashed fruit/veg (toxins), uncooked meats (listeria), unpasteurized dairy goods (brucellosis)*
- Note: **No association** between ingestion/avoidance of specific antigens in pregnancy (e.g., milk, peanuts) and risk of atopic disease in offspring

Gardner CD. *UpToDate*. Oct 2024; \* U.S. Dept Agriculture/DHHS. Dietary Guidelines for Americans, 2020-2025, 9<sup>th</sup> ed. [www.dietaryguidelines.gov/](http://www.dietaryguidelines.gov/)

# Macronutrient recommendations

- **Total caloric (energy) requirements** depend on:
  - *Maternal age*
  - *Level of physical activity*
  - *Gestational age → no increase in 1<sup>st</sup> trimester; small increase in 2<sup>nd</sup> tri (+340 kcal/day); larger increase in 3<sup>rd</sup> tri (+450 kcal/day)*
  - *Pre-pregnancy BMI → +300 kcal/day for underweight BMI, +200 kcal/day for normal BMI, +150 kcal/day for overweight BMI, -50 kcal/day for obese BMI*
- For patients with normal pre-pregnancy BMI, typical caloric requirements in pregnancy range from **2,200-2,900 kcal/day** in 2<sup>nd</sup> and 3<sup>rd</sup> trimester
  - *10-30% protein, 20-35% fats, 45-65% carbohydrates (<10% added sugar)*

U.S. DHHS. Dietary Guidelines for Americans, 2020-2025, 9<sup>th</sup> ed. [www.dietaryguidelines.gov/](http://www.dietaryguidelines.gov/)  
Calculator for individualized caloric needs: <https://www.nal.usda.gov/human-nutrition-and-food-safety/dri-calculator>  
Personalized diet: <https://wicworks.fns.usda.gov/resources/tips-pregnant-moms>, [www.myplate.gov/life-stages/pregnancy-and-breastfeeding](http://www.myplate.gov/life-stages/pregnancy-and-breastfeeding)

# Micronutrient recommendations

- Most micronutrient requirements are **unchanged** in pregnancy/lactation and will be met by a healthy diet<sup>\*</sup>
  - *RDA exist for a range of micronutrients in pregnancy (WHO, IOM/NAM, U.S. DHHS)*
- Dietary requirements of **some micronutrients** increase in pregnancy<sup>\*\*</sup>
  - **Folic acid** (0.4-0.8 mg/day) is recommended for all pregnant women to prevent NTD → high-dose (4 mg/day) in certain circumstances (e.g., history of NTD, antiseizure meds)<sup>^</sup>
  - **Iron** (30 mg elemental iron/day) is recommended for all pregnant women → higher dose (60 mg/day) in LMIC with high prevalence of anemia; not recommended by USPSTF<sup>#</sup>
  - **Iodine** requirements increase 150-200 ug/day; critical for fetal thyroid development/ function (congenital hypothyroidism/cretinism) → consider supplementation only in LMIC without adequate diet and food fortification (even here, benefit is unclear)

<sup>\*</sup> U.S. DHHS. Dietary Guidelines for Americans, 2020-2025, 9<sup>th</sup> ed. [www.dietaryguidelines.gov/](http://www.dietaryguidelines.gov/); <sup>\*\*</sup> WHO. [www.who.int/publications/i/item/9789240007789](http://www.who.int/publications/i/item/9789240007789);

<sup>^</sup> U.S. Preventative Services Task Force. Aug 2023; <sup>#</sup> U.S. Preventative Services Task Force. Aug 2024

# Micronutrient recommendations

- **Omega 3 fatty acids (n-3 PUFAs)** and brain health
  - *Fetus relies on transplacental transfer of DHA for optimal visual and cognitive development*
  - *Adequate servings of fish (2-3 times/week; 8-12 oz/week) will cover requirements*
  - *Other foods (yogurt, milk, eggs, fish oil, some PNV) or omega-3 supplements can be used to achieve an intake of 200-300 mg/day of DHA/EPA <sup>^</sup>*
  - *Supplementation has not been shown to improve childhood neurodevelopment <sup>@</sup>*
- High levels of **glucose** may be toxic to developing fetus
  - *Certainly true for early pregnancy (e.g., diabetic embryopathy)*
  - *Dietary restriction of sugar from conception through 1000 days reduces risk of DM, HTN <sup>\*</sup>*
- Routine supplementation of **vitamin B6, C, D, and E <sup>\*\*</sup>** and **probiotics <sup>#</sup>** are not recommended in pregnancy

<sup>^</sup> Oken E. *UpToDate*. March 2024; <sup>@</sup> Middleton P, et al. *Cochrane Database Syst Rev* 2018; 11:CD003402; <sup>\*</sup> Gracner T, et al. *Science* 2024; 10.1126/science.adn5421; <sup>\*\*</sup> WHO. [www.who.int/publications/i/item/9789240008120](http://www.who.int/publications/i/item/9789240008120); <sup>#</sup> Grev J, et al. *Cochrane Database Syst Rev* 2018; 12:CD012519

# Key points

- Human brain development is a **lifelong process**
- A ‘healthy diet’ (appropriate macro-/micro-nutrients) is a key driver of metabolic health, both for the pregnancy and the offspring
- Pregnancy health is determined by the health of the mother **around the time of conception** → focus on pre-pregnancy health; once the pregnancy is established, it is largely too late
- **Opportunity:** identify interventions (lifestyle, diet, drugs) to optimize maternal health, decidual health, and pregnancy outcome