Nutrition During Pregnancy and Lactation: Reflections on the Workshop

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State of Science on Nutrition

Equity in Access of Nutritional Care

Today's Context Differs

- Moms now
  - Older, but fewer adolescents & fewer smokers
  - More overweight, obese & diabetic,
  - More excess WG
- Births now
  - More PTB, TB & LBW
- Shifting dietary patterns & food values
  - More intermittent fasting, Paleo/low-carb, & organic/natural/sustainable foods

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Cross-cutting Themes

- Clearly new evidence & emerging issues since 1990 & 1991 IOM Reports*: Nutrition & Pregnancy* and *Nutrition & Lactation*
  - *Protein, Energy (obese), Type of Carbohydrate, One-C metabolism (folate, choline, B-12), Iron, Vitamin D, Iodine, Antioxidants, DOHaD , Obesity/GDM*
- Biomarkers & physiological adjustments
  - Omega 3 FA, Iron, Vitamin D, folate (for high status), choline, vitamin B-12, antioxidants, iodine (pregnancy & lactation)
- Dosage, form, bioavailability & timing of supplements vs quality diet/dietary pattern
  - Folate, choline, iron, vitamin D, carbohydrate/fiber, omega 3 FA, protein/AA, iodine (lactation)
- Interaction between baseline status & supplement: omega3 FA, folate , iron, vitamin D, iodine, energy, antioxidants
  - low – benefit?,
  - adequate- unresponsive ,
  - high – adverse?

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Cross-cutting Themes

- Preconception-pregnancy-postpartum/lactation continuum
- DOHaD
  - Human Milk Oligosaccharides (including fructose) modified by maternal dietary fat/carbohydrate affect microbiome, growth, body composition, & brain development
  - Obesity/GDM/Nutritional Status alter placental function & direction of mother & fetus, lactation to ‘program’ microbiome, chronic disease risk & DOHaD, stress response, etc.
  - Sexual dimorphic responses of fetus/placenta to maternal nutrition, obesity & GDM

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Cross-cutting Themes

- Chronic Disease Outcomes & Expanded DRI
  - Adequacy health outcomes – no longer can be chronic disease
  - Toxicologic Outcome for UL now – no longer chronic disease.
  - Moderate level of evidence required for CDDR for BOTH outcome & dose-response.
  - Inconsistent or Discordant Observational associations & RCT results for many outcomes & nutrients
    - Vitamin D, antioxidant nutrients, omega 3 FA (immune)
    - Challenges in synthesizing the evidence & in consistency of results stem from variability in study design, variability in dosing, timing, baseline status considerations, biomarkers used
    - Balance of benefit & risk: Omega 3 FA, Iron, Vitamin D, Iodine
  - Developmentally-validated surrogate endpoints (maternal & offspring)

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Cross-cutting Themes

- Disparate outcomes, status & intakes for at-risk populations
  - At risk populations often for many nutrients & use of supplements: lower income & education, multiple fetuses, obese/overweight pregravid, non-European/NH-black, unplanned pregnancies, adolescent, younger (supplement use) vegans, gluten avoidance
  - Social injustice, stress, obesity/GDM, poverty, food insecurity drive disparities.
    - Focus intervention trials on reducing stress response.
    - WIC addresses vulnerable at-risk population, supports improved breastfeeding inequities & nutritional risk.
  - Systems approach informed by implementation science needed to improve food & physical activity systems & ↓ food insecurity for optimal Pregnancy & Lactation.

Key Selected Issues from State of Science on Macronutrients

- **Omega 3 LCFA** – large number of trials since 1990/91
  - ↓ early & later PTB (Cochrane SR; primarily fish oil & diverse risk population) in singleton pregnancies, but also ↑ prolonged gestation.
    - Raises issue of screen & treat strategy that needs testing.
  - Conflicting evidence on allergies & asthma
  - Little evidence of clinically meaningful benefit pregnancy outcomes (neurodevelopment & growth) in TB including neurodevelopment & growth
- **Protein**
  - Newer. more precise stable-isotope approach (driven by rate protein synthesis) suggests higher & dynamic requirements than current static DRI based on N-balance & factorial approach
    - ↑ during pregnancy; early & further ↑ later in gestation (13-17% energy, within macronutrient recommended range
  - Energy-balanced protein supplementation (<25%) shown to reduce reduced LBW.
    - Observational evidence suggests U-shaped risk with low)<10% energy) and high)>25% energy) for LBW.
  - Quality of protein & differential need for EAA requires further study.
    - Differential pattern of increase for LYS & PHE

Key Selected Issues from State of Science on Macronutrients

- **Carbohydrate** (based on brain glu utilization) & **Energy**
  - Quality of CHO intake a concern with excess added sugar & insufficient fiber intakes US pregnant women
  - Evidence on type/amount of CHO or low GI diet limited & low for GDM, T2DM, PE, PTB, SGA, LBW. .
  - Energy DRI not based on weight gain guidelines, but recent studies suggest requirement differs based on pregravid weight.
    - Obese women may not need to increase energy intake & may meet additional E needs by mobilization of fat stores.
    - Implications for greater nutrient density diet.

Key Selected Issues from State of Science on Micronutrients: One Carbon Micronutrients

- **Folate**
  - Mandatory folate fortification in 71+ countries decreased NTD 31-46%, but compliance with preconceptional folate supplements low
  - Long-term benefit of supplementation 3 trials concordant with associations in observational studies for neurodevelopmental. cognitive outcomes & DNA methylation), but emerging concerns about those with high folate status but evidence (largely observational) inconsistent & lacking D-R.
- **B-12**
  - **Low** status associated with adverse maternal (GDM, PE, anemia) & pregnancy outcomes (NTD, LBW/IUGR/SGA, spontaneous abortion, DOHaD), but need dose-dependent functional trial.
- **Choline**
  - Supplementation during pregnancy improves maternal DHA & Me-donor status, placental methylation, & pregnancy outcomes (↓ NTD, infant stress response & sFLT1 & improves cognitive function & choline content in HM), but most pregnant women (92%) consuming choline << AI
  - Physiologic adaptation of choline & PC metabolism with alterations in biomarkers & supplementation enhances PEMT derived PC preferentially enriched in n-3 LCFA & preferentially transferred to fetus
  - Most prenatal supplements have not contained choline or only small amounts, but AAP, etc. urges increased choline in prental supplements.

Key Selected Issues from State of Science on Micronutrients: Iron, Vitamin D, Calcium, Antioxidants Iodine

- **Iron**
  - Fe supplementation reduces risk of maternal anemia & improves maternal & neonatal hematologic indices, but evidence for other clinical outcomes conflicted or uncertain
  - Prevalence ID anemia low in pregnant women even though Fe stores decrease even to high prevalence of Fe 'deficiency' based on ferritin cutoff. (US/CN)
  - Applicability of established Hb cutoffs to diverse population with greater obesity/overweight.
  - Many issues interpreting data – dose, form, baseline Fe status, timing & compliance supplements, plad,s volume expansion, best biomarkers with physiologic adjustment, obesity/overweight, Hb cutoffs - & insufficient data on maternal & pregnancy outcomes
- **Vitamin D**
  - Adaptations in D homeostasis such that best biomarker during pregnancy not fully established & biological function of these adaptations uncertain
  - Maternal vitamin D supplementation increases maternal and neonatal 25OHD, but outcomes less clear due to conflicted & inconsistent &evidence with some evidence that it reduces HOMA IR (but not pl glucose) and probably reduces risk of GDM, PE, LBW.
- **Calcium**
  - Supplementation with Ca ↓ PE risk if low Ca diet
  - Future needs to study bone morphology across pregnancy

Key Selected Issues from State of Science on Micronutrients: Iron, Vitamin D, Calcium, Antioxidants Iodine

- **Antioxidant Nutrients: Viminal C, Vitamin D, Selenium, plus beta-carotene, carotenoids, lycopene, etc.**
  - Discordant observational evidence associates some pregnancy outcomes (primarily premature rupture of membranes, etc.) with low status except for higher risk with higher alpha tocopherol whereas RCT do not demonstrate effect (largely in replete).
  - Observational evidence associates high vitamin E status with Congenital Heart Defects.
  - Pro-oxidants gamma tocopherol appears to have some pro-oxidant and pro-inflammatory properties.
- **Iodine.**
  - Low maternal I Iodine associates with impaired cognition, verbal, autism, etc.; SR maternal I supplementation benefits IQ. Some evidence of
    - D-R from low to moderate/mild on cognitive/neurodevelopment subsequent
    - U-shaped risk for low verbal skills.
  - AAP & others recommend I supplement, but few pregnant women comply

Key Selected Issues from State of Science on Nutritional Supplements

- Dietary Supplements help pregnant & lactating women meet needs, but also increase those exceeding UL.
  - High prevalence supplement use by pregnant & lactating that increases from T1 to T3
  - Prevalence of Iodine-containing supplements low throughout pregnancy.
- Standardization on label & content needed
- Different bioavailability & characteristics.
  - Nutrient interaction – Fe/Zn, vit C-Fe, Mg/Ca-Fe
  - Inactive ingredients can also affect bioavailability
  - Drug-nutrient interaction
- Concerns about contaminants including heavy metal & other environmental contaminants

Key Selected State of Science for Emerging Topics on Pregnancy & Lactation

- Decreasing caffeine is strategy to optimize fetal growth, but challenging to assess intakes.
  - Inconsistent evidence on safety in pregnancy,& scant for lactation (but may be lower risk for baby).
  - Expansion of caffeinated products including energy drink, cosmetics, dietary supplements & OTC medications, content & synergistic botanical components
  - Physiologic adjustments in pregnancy, genetic variation of rate of metabolism (fast/slow) & responsiveness & food, drug interactions modify caffeine effects.
- Human milk oligosaccharides (also found in amniotic fluid at lower concentration than HM)
  - enable postnatal tolerance of & ecology of differential commensal microbes
  - modified by maternal diet especially amount of fat with persistent changes in fetus (primate) & offspring GI microbiome (humans & primates).
  - affect infant body composition, growth, appetite regulation/food responsiveness and cognitive outcomes.
    - sialic-acid HMO dynamic over lactation & play role in brain development
    - Includes effects of fructose (present in HM at variable concentration & influenced by maternal fructose consumption)

Key Selected State of Science for Emerging Topics on Lactation

- Human milk content of some vitamins (A,D, E, K, B1, B2, B6, B12, choline) and minerals (Iodine, Selenium) responsive to maternal diet & supplementation whereas HM content of folate, calcium, iron, copper, zinc are not
  - Limited evidence on HM micronutrient content complicated by interaction with maternal status & analytical limitations.
  - New evidence emerging using state of art analytic approaches with evidence that current AI set on past content data likely outdated for some (thiamin, B-6, Iodine, B-12)
    - Iodine highly variable, dynamic (↓) & responsive to maternal diet, but historic evidence based on inaccurate analytic technique
      - Weaning may need Iodine-fortified formula or complementary foods
- Maternal obesity & GDM adversely affects lactation, alters HM FA, alters HM factors that regulate appetite, growth & body composition as well as infant microbiome ('locational programming'), but evidence is limited on functional outcomes.
- Lactation reduces risk of maternal diabetes making postpartum period a 'critical period', but challenging limitations in body of evidence.
  - Two newer, better designed, longitudinal repeated-measure studies across child-bearing years and later find strong & inverse association of duration of lactation with incident T2D.

Key Selected State of Science for Emerging Topics on Pregnancy & Lactation

- Placental role in DOHaD & fetal programming
  - Placenta - ‘directors’, sexually dimorphic, adapts to maternal nutrition/malnutrition, ‘selfish’ organ
  - Type & level of maternal nutrition, as well as obesity, GDM & oxidative stress (especially in male), important for placenta & DOHaD through epigenetic regulation
    - Placenta regulates nutrient transfer, fetal growth & development, adaptive response to altered supply (regulatory signals, etc.)
    - Timing of ‘nutritional insult’ critical for placenta & its adaptation
    - Me-donors, folate, altered glucose, caloric restriction & many micronutrients alter DNA methylation & modify histones
    - Obesity & GDM ↑ glu/aa oxidation with loss of metabolic flexibility only in male, shift to SCFA/MCFA oxidation in male & ↓ DHA/PC-DHA in male
    - Placental biomarkers may prove useful for predicting placental stress/health.

Key & Selected Issues for Equity in Access of Nutritional Care

- Strong inequities exist due to social injustice that require systems approach across the life course.
  - Implementation science basis for design of approach to pregnancy & lactation
- Poverty induces stress known to affect DOHaD.
  - Need to know if nutrition intervention helps reduce impact
    - Pilot omega 3 FA supplementation ↓ maternal stress response @ 30 wk GA & offspring..
  - Must understand ecological/social factors across life course, impact on nutrition & informed framework relevant to this understanding & population's context.
  - Inform scale-up models by implementation science such as the Breast-feeding Gear Model, behavioral economic approaches to develop policies & agent-based modeling for food system improvement.
- Food Insecurity also induces stress & influences nutrition, eating behavior & metabolism during and subsequent to pregnancy.
  - Food insecurity exists in WIC participants as well.
  - Mindfulness intervention reduced stress & ↓OGTT
  - New SF systems level approach to multiplicity of factors related to food insecurity in pregnant women through colocation of federal food programs, additional WIC food voucher,

Key & Selected Issues for Equity in Access of Nutritional Care

- WIC expanded support for breastfeeding beginning in 1992 with revisions of food package for exclusive breastfeeding & implementing Famer's Market Program & in 2004 to implement peer counseling for breastfeeding.
- 2007 food package revision with CVV, whole grains, etc.
- Health equity in WIC
  - NWA shifting to health equity approach to inform programs, research & advocacy.
  - Benefit of peer-counseling BF model & nutrition support helps address disparities of breastfeeding gap.
  - Policy & advocacy
    - WIC Act, CARE Act, Public Charge Rule WIC excluded but still adversely impacting participants