What You Eat During Pregnancy Matters

COGS VIPs
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FATS
Placenta

• Organ
• Connects fetus to uterine wall
• Contains umbilical cord
• Essential for Oxygen and Nutrients
• Secretes hormones
Nutrients Delivery

Intervillous space

• Nutrients and oxygen
• Waste and Carbon Disposal
**Placenta Hormone Secretion**

**Human Chorionic Gonadotropin (hCG)**
- Detection of pregnancy
- Stimulates progesterone and estrogen release

**Progesterone**
- Helps the embryo to implant

**Estrogen**
- Essential for proliferation

**Human Placental Lactogen** (Anti-insulin properties)
- Fetal metabolism development and general growth and development
- Provides fuel for the fetus by breaking down fats from mother
- Acts on Lactogenic receptors
**FATS**

**Unsaturated Fats** (monounsaturated and polyunsaturated) essential
- Contains more than one or more double bonds
- Liquid at room temperature
- Primarily plant products (olive oil) and animal produces (salmon)

**Saturated Fats**
- No double bonds between the molecules because they are saturated with hydrogen
- Solid at room temperature
- Primarily animal produces (beef) or plant produces coconut oil/palm oil

**Trans Fats**
- Partial Hydrogenation
- Vegetable oil and margarine
- Packaged and frozen foods
Trans Fats
Trans Fatty Acids

What are they?

• Unsaturated fats become saturated during the process of partial hydrogenation. This results in the cis double bonds to convert into trans double bonds - which eventually yields trans fat

• Fats that the body are unable to break down

What do they do?

• Increase the levels of Lipoprotein LDL “Bad cholesterol”
• Lower the levels of Lipoprotein HDL “good cholesterol”
• Increase triglyceride
• Promote systematic inflammation
• Increases the risk of coronary disease and heart disease
• Over 30,000 deaths in the US were attributed to Coronary deaths (consuming Trans Fats) – in a 1994 study

Note: trans fat is also produced naturally – meats and dairy produces!
Long-chain polyunsaturated fatty acids (LCPUFA)

- Essential for normal brain growth and development
- Thought to play a dominant role in infant cognition

Trans fat and Fetal LCPUFA

- LCPUFA levels and Trans Fat inversely related
- Trans fat impairs the metabolism of LCPUFA
- This affects the fetal secretion of LCPUFA (3rd trimester)
- Not good news for infant development

Trans fat and pregnant women

- LCPUFA are provided through breastmilk
- Mother’s diet affects the levels of LCPUFA
- Higher levels of Trans fat means lower levels of LCPUFA
Formation
Gestational weight gain and child adiposity at age 3 years

- Point: determine the strength of the influence of maternal weight gain during pregnancy on their children’s BMI at age 3
- Gestational weight gain: the difference between the mother’s prepregnancy weight and the last recorded weight before delivery
- Net gain: infant birth weight subtracted from the total weight gain
- Adequate gain by prepregnancy BMI:
  - BMI < 19.8: 27.5 - 39.7 lbs
  - Normal BMI: 25.4 - 35.2 lbs
  - BMI between 26.0-29.0: 15.4 - 24.3 lbs
  - BMI > 29.0: 13.2 lbs
Participants

- 1044 mother/infant pairs from Project Viva
- varied in age and socioeconomic background
  - Greater external validity
- Weight was self-reported
  - Validity test found the weights to be accurate ($r = 0.99$)
Results

- 14% of mothers gained inadequate weight
  - 64, 53, 26
- 35% of mothers gained adequate weight
  - 114, 162, 93
- 51% of mothers gained excessive weight
  - 143, 234, 155
- Gestational weight gain is directly associated with BMI in infants
- Women with adequate or excessive gain were around x4 more likely to have overweight infants
- Infant’s diet had no significant effect on their BMI

Note:
- no correlation between maternal leptin and fetal leptin
- Strong correlation between umbilical leptin and fat mass

Other Findings from Project Viva

- Increasing “leisure time physical activity” through mid-pregnancy is not conductive of lower body fat in mid-childhood
- Faster GWG in 1st and 2nd trimester associated with higher BMI in mid-childhood (effect stronger with higher prepregnancy BMI)
- No association between low-quality diets during early pregnancy and gestational diabetes mellitus (but exercise may lower the risk!)
- BUT a good diet and physical activity is associated with a lower risk of having an excessive GWG
- Exposure to glucocorticoids reduces overall fetal growth and contributes to central adiposity
FRUCTOSE
Glucose

- simple sugar
- body's preferred energy source
- body processes most carbs into glucose which are **immediately** used for energy or stored for later
- unlike fructose, insulin is secreted primarily in response to elevated blood glucose concentrations in order to facilitate the entry of glucose into cells

Fructose

- simple sugar (found naturally in fruits and vegetable, also added to drinks, candies, etc.)
- not the preferred energy source for muscles or the brain
- only metabolized in the liver, then directed toward **replenishment** of liver glycogen and triglyceride synthesis
- more lipogenic than glucose
- does not cause insulin to be released or stimulate production of leptin, which is concerning in large amounts because there is less orexic/anorexic signalling going on to regulate consumption
fructose= a sugar (“fruit sugar”) that is absorbed directly into the bloodstream during digestion; it can be derived from corn and combined with glucose to create high fructose corn syrup

fructokinase= an enzyme which initiates the transfer of a phosphate group from ATP to fructose

xanthine oxidase= enzyme involved in breakdown of (hypo)xanthine

xanthine= increases alertness in CNS

uric acid= often excreted in the urine (high levels can lead to gout; also linked to Type II diabetes, kidney stones, and metabolic syndrome)

gout= a type of arthritis; needle-like crystals of uric acid in joint, capillaries, skin, etc.
Maternal fructose drives placental uric acid production leading to adverse fetal outcomes

Extracellular Uric Acid...

- **Normal**: beneficial, a potent antioxidant
- **Excess**: oxidative stress, cellular dysfunction, increased de novo lipogenesis causing lipotoxicity promoting oxidative stress and inflammation, can promote accumulation of intrahepatic (in the liver) triglyceride in both healthy and Type II diabetic subjects and led to development or worsening of non-alcoholic fatty liver disease
<table>
<thead>
<tr>
<th>CAUSE</th>
<th>Mechanism</th>
<th>EFFECT</th>
<th>Treatment (given allopurinol)</th>
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</table>
| high fructose consumption by pregnant mother | | 1. placental inefficiency  
2. fetal growth restriction  
3. de novo uric acid synthesis in placenta, thus uric acid accumulation  
4. elevated fetal serum glucose and placental triglyceride level  
5. increased lipids  
6. altered expression of genes that control oxidative stress  
7. smaller litter size  
8. had lower levels of ATP in the placenta | 1. prevented placental inefficiency  
2. improved fetal weights  
3. reduced placental uric acid levels  
4. improved serum triglycerides in fetus |
Definitions:

**de novo lipogenesis** = simple sugars converted into fatty acids

**de novo [uric acid] synthesis** = making complex molecules [uric acid] from simpler molecules [fructose,...]

**triglycerides** = made of glycerol and 3 fatty acids, it is present in body fat, the blood (to transfer adipose fat and blood glucose to/from the liver), and skin oils

**oxidative stress** = imbalance that impairs body’s ability to detoxify, peroxides and free radicals damage every part of the cell from proteins to lipids to DNA...including strand breaks in DNA

**allopurinol** = a xanthine oxidase inhibitor
Treatment

1. prevented placental inefficiency
2. improved fetal weights
3. reduced placental uric acid levels
4. improved serum triglycerides
Preeclampsia

**Definition:** abnormal formation of blood vessels in the placenta, characterized by high blood pressure and protein in the urine

At risk when either...

- mother does not have metabolic syndrome and **consumes excess** simple sugars, including those from sugar-sweetened beverages...often with high fructose corn syrup
- mother has metabolic syndrome
High Fructose Corn Syrup

- sweetened yogurt
- soda
- candy
- frozen meals
- breads
- canned fruit
- juice
- granola/protein bars
- sauces and condiments
- salad dressing

“Palatability” and the Cephalic Phase

- familiarity with the food, expectations
- meal plate size
- colors
- linked to hedonic reward systems in brain
- amygdala
fructose (excess)
uric acid
oxidative stress
de novo lipogenesis
inflammation
impaired glucose tolerance
cellular dysfunction
Fruit
What happens with fruit consumption?

**Phytochemicals** (Beta Glucan, Lycopene): non-nutritive plant chemicals that have protective or disease preventive properties.

- Antioxidant
- Hormonal Action
- Stimulation of Enzymes
- Interference with DNA Replication
- Anti-bacterial Effects
- Physical Actions

M cells transport beta-glucan particles from the intestine to macrophages. The beta-glucan binds with macrophages and starts a chain of reactions.
M Cells:

- Component in Circadian “CLOCK”
- Helps regulate “stressors” by signaling (HPA) Axis, ANS, and CNS
- Feedback from “slave” clock can alter “master” clock function
Prenatal & Postnatal Fruit Consumption

- Nutrients required for optimal cognitive development in humans is unknown
- Fragile X syndrome = altered cAMP signaling
- Research on *Drosophila* (fruit fly) suggest a link between (cAMP) and element binding protein (CREB) pathway to learning and memory
  - *Rutabaga* - mutated gene that encodes for calmoduline dependent adenylate cyclase converts (ATP) to (cAMP)
  - Isolated genetic screen linked to learning

*Study used Drosophila Learning and Memory Model to test whether cognitive enhancement in healthy individuals following high prenatal fruit intake persisted across species and test the molecular mechanism with a focus on cAMP*
Cognitive Performance & Genetic and Environmental Factors

- 100 flies, 3 days old; wild & rutabaga
- 15 % OJ: fructose, low lycopene
- 15 % TJ: lycopene
- 841 Participants
- Food frequency questionnaire

**Results:**

Only wild drosophila given 15/15 showed an increase in performance

Increased fruit intake during pregnancy lead to 2.38 point increase of cognitive development of children 1 year old
But...

Though the classical conditioning method showed a learned association with fruit juice intake prior to birth as well as an increase in prenatal and childhood development, the study determined there was not enough evidence to determine if the cAMP pathway alone contributed to learning.

Fruit may improve learning and memory due to antioxidants. Increased antioxidants (phytochemicals) IS associated with improved learning and memory in adults!
FARE... your child is what you eat

Paper: Offspring from mothers fed a ‘junk food’ diet in pregnancy and lactation exhibit exacerbated adiposity that is more pronounced in females
Background

- Obesity rates on the rise, and so is “away-from-home” food consumption
  - Manufactured foods are high in fat, sugar, salt, and calorically dense
  - Qualified as “junk foods”

- Already established in previous research:
  - Junk food consumption = rise in obesity in all ages
  - Exposure to junk food during fetal & suckling lives → more overeating/overweight
  - Pups exposed to junk food diet during pregnancy and lactation → increased adiposity

- Current study: long term influence of maternal junk food diet
  - Examines adiposity in both males and females at the end of adolescence
  - Examine gene expression involved in adipocyte growth
Methods

● Four groups:
  ○ JJJ group = junk food diet during pregnancy, lactation, and during weaning
  ○ JJC group = junk food only fed during pregnancy and lactation. A balanced “chow” diet was fed during weaning
  ○ CCJ group = Junk food only fed during weaning
  ○ CCC group = control

● Various analyses
  ○ Transcriptional analysis of genes involving adipocyte regulation
  ○ Sex differences in glucose, insulin, and lipids
Results

- **JJJ group** → offspring with increased adiposity, raised glucose levels, higher insulin levels, triglycerides, and cholesterol by the end of adolescence

- **JJC group** → increased perirenal fat pad mass, adipocyte hypertrophy
  - Did not reduce to control levels
Adiposity effects

- Both males and females exhibited increased adiposity in junk food groups
- JJJ group adiposity was much higher than CCJ, indicating the role of maternal junk food on adiposity
- However, the JJC group had less adiposity than JJJ or CCJ, indicating that a balanced diet later in life can control far
- However, JJC levels are still higher than CCC indicating perhaps the effects can be controlled to some degree but there is still irreversible damage

**KEY:**
- White = CCC
- Light grey = CCJ
- Dark grey = JJC
- Black = JJJ
More results...Males vs. Females

- Increased adiposity more enhanced in females
  - Increased IGF-1: pre-adipocyte proliferation
  - Perirenal fat pads more transcriptionally active
  - In JJJ and CCJ groups
    - Higher leptin levels
    - Hyperglycaemia
    - Normal Insulinemia

- In males...
  - No dramatic IGF-1 increase
  - In JJJ and CCJ groups
    - Leptin transcription not markedly affected
    - Normal glycaemia
    - Raised insulinemia

**KEY:**
White = CCC
Light grey = CCJ
Dark grey = JJC
Black = JJJ
Significance

- Differences between male/female metabolic regulation of fat from junk foods
  - Both CCJ and JJJ groups had similar leptin effects $\rightarrow$ maternal diet has no long term effect on leptin
  - Males had higher insulin
  - Females had higher leptin
  - Different signaling and regulation between the sexes?

- For both sexes, long-term, irreversible effects of junk food during pregnancy + lactation on adolescence
  - Alteration of protein signaling, higher transcription of adipocyte genes
  - Effects were not completely reversible by eating a balanced diet during weaning
  - These genetic and epigenetic effects are irreversibly changing gene expression!!!
Genetic Significance

- **FRUCTOSE**: high fructose consumption in mother leads to altered expression of genes that control oxidative stress
- **FARE**: high fat, sugar, and salt (junk food) diet throughout pregnancy and lactation has long-term influences on the mRNA expression of genes involved in adipocyte growth

Some genetic modifications can be passed down from generation to generation! We need further research exploring whether maternal diet can affect future generations as well.
FORMULA
**Breast Milk Composition**

**Colostrum** is the first pale yellow milk that breasts produce after giving birth. It’s higher in protein, minerals, salt, vitamin A, nitrogen, white blood cells, and certain antibodies, and has less fat and sugar than mature milk. Colostrum also has a slightly laxative effect and helps a newborn rinse his gastrointestinal tract of meconium, the waste product accumulated before birth, thereby reducing the risk of jaundice. Protein content is markedly higher and carbohydrate content lower in colostrum than in mature milk.

**Mature milk** comes in approximately two to four days after the birth of a baby and is produced in greater amounts than colostrum. Mature milk contains water, fat, carbohydrates, protein, vitamins and minerals, amino acids, enzymes, and white cells.

Mature human milk contains 3%--5% fat, 0.8%--0.9% protein, 6.9%--7.2% carbohydrate calculated as lactose, and 0.2% mineral constituents expressed as ash. Its energy content is 60--75 kcal/100 ml. Over the course of a feeding, breast milk changes from foremilk, high in water and lactose, to hindmilk, high in fat and calories.

After the first few weeks of nursing, breast milk contains fewer white cells and more of another antibacterial enzyme, lysozyme, the level of which stays high as long as breastfeeding continues.
Diet and Breast Milk

Race, age, or diet do not greatly affect milk composition and there is no consistent compositional difference between milks from two breasts unless one is infected? Breast milk is naturally very high in lactose. The foods you eat while breastfeeding can affect the taste and smell of your breast milk. Breast-fed babies might have a more adventurous palate, willing to try different types of food, because they experience different flavors and smells in their daily meals.

Human milk fatty acids are among the nutrients that show extreme sensitivity to maternal nutrition and are implicated in neurological development. The types of food you eat don't affect the total fat content of your milk but can affect the type of fats you produce. A few nutrients relevant to infant neurological development, however, do vary in human milk as a result of maternal nutrition. These nutrients include the following: vitamin A; several water-soluble vitamins including vitamin B-6, vitamin B-12.; and fatty acids.
Metabolic programming effects initiated in the suckling period predisposing for adult-onset obesity cannot be reversed by calorie restriction.

Srinivasan M¹, Mahmood S, Patel MS.

Main Idea: Altered nutritional experience during critical periods of development are an important factor in etiology of obesity and related metabolic diseases in later life

- High Carbohydrate (HC) milk: 56% carbohydrate, 20% fat, 24% protein
- Ad Libitum (AL) feeding: “free feeding,” as much as one desires
- Mother-fed (MF) milk: 8% carbohydrate, 68% fat, 24% protein
- Pair Feeding (PF) technique: amount of food given to control group of mice is matched to that consumed by the experimental group
- Metabolic phenotype: body weight, serum hormone levels, insulin secretory capacity of islets and hypothalamic characteristics
- HC phenotype: chronic hyperinsulinemia and adult onset obesity
- Calorie Restriction (CR): restriction of energy intake without malnutrition

- HC
- HC/PF
- HC/PF/AL
- MF
Methods

- HF milk formula reared a similar phenotype of MF, therefore, MF used as the control
- Postnatal Day 24: MF, HC, HC/PF to MF regimen
- Postnatal Day 90: subgroup HC/PF/AL
- Brain and Pancreas dissected; Serum was separated for analysis of insulin and leptin; blood glucose concentrations determined by glucometer
- Pancreatic islets were isolated by collagenase- islets handpicked under dissecting microscope
- Hypothalamus-enriched region was dissected from frozen brain. mRNA levels of NPY, POMC, Lepr, STAT3, SOCS3 determined via real-time PCR assay
Results

- Body weight: From postnatal day 94 to 108, there was an increasing trend which leveled off after, indicating catchup growth of HC and HC/PF/AL rats.
- Food Intake: Postnatal Day 42 increase in consumption of HC rats compared to MF rats. Postnatal Day 90 HC/PF/AL (within one week) rats closely approximated the amount consumed as HC rats during the same period. ~15% more than MF rats.
- Serum hormone levels: Serum Insulin- Increased with HC, reduced with HC/PF (normalized levels to those in MF). Rapid increase to HC levels in HC/PF/AL rats. Serum leptin levels similar to serum insulin.
- Insulin secretion from islets: HC rats had increased response to cholinergic stimulation (ACh stimulates PNS), reduced sensitivity to adrenergic inhibition (NE inhibits SNS).
- Suggests altered ANS regulation effect on hypersecretory capacity of HC islet ß cells.
- Energy circuitry of hypothalamus -> body weight homeostasis- ARC produce orexigenic (NPY) and anorexigenic (POMC) neuropeptides which were altered in HC rats.
First Hypothesis

- CR is beneficial for improvement of metabolic parameters in overweight/obese individuals. (HC/PF normalization)

HC milk diet until time of weaning: chronic hyperinsulinemia plus HC phenotype
CR caused a reduction in body weight and normalization of blood glucose and hormone levels in obese animals as well as in nonhuman primates
Meaning: Lepr/serum leptin had effects on body weight reduction, normalized serum pattern due to caloric restriction

Second Hypothesis

- Although serum levels were normalized in adult HC/PF rats, insulin secretory capacity of HC/PF islets was similar to the HC islet
  PF technique could not change predisposition for hypersecretory capacity of islets and hypothalamic hyperphagic response in HC rats
  Pancreatic Islets and neurons are not fully mature at birth, development extends to immediate postnatal (suckling) period—altered nutrition in this period can make a change in programming effects
Although serum levels were normalized in adult HC/PF rats, insulin secretory capacity of HC/PF islets was similar to the HC islet
Meaning: programming effects of the HC diet change on insulin secretory capacity could not be reversed by PF technique on HC rats in the post weaning period
Further shown by reappearance of hyperinsulinemia in HC/PF/AL rats
Why? perhaps low serum insulin levels from reduced amount of food in HC/PF diet (suppressed programming), increase in food consumption with AL (HC/PF/AL) means increase in serum insulin levels (resurfaced from suppressed state)
PATERNAL INFLUENCES... How much?

- What the father eats affects the child’s formation too!
- Paternal BMI correlates with infant BMI
- Paternal nutritional/toxological exposures, and age can have transgenerational effects on offspring

Are these directly connected, or do paternal habits affect maternal habits? “Paternally induced maternal influence”
Question for Audience:

Why is the fetus unaffected by the mother’s leptin levels during pregnancy?

How can socio-economic status of the family affect their child’s development?
Basically...
Don’t F your baby up!