Preparing for Pregnancy: Pre-conception Nutritional Advice

Victoria Maizes MD
Executive Director
Arizona Center for Integrative Medicine
Professor of Medicine, Family Medicine and Public Health
University of Arizona

Is fertility declining?
- Delayed child bearing
- Obesity
- Dietary changes
- Environmental pollutants
- Psychological stress

Definitions:
- Fertility = the capacity to produce offspring
- Clinical infertility = the inability to become pregnant after 12 months of unprotected intercourse
- Affects approx. 15% of the population in industrialized nations

Sponsored by the University of Arizona College of Medicine at the Arizona Health Sciences Center.
Nothing to disclose.

Defini8ons:
 Fertility = the capacity to produce offspring
 Clinical infertility = the inability to become pregnant after 12 months of unprotected intercourse
 Affects approx. 15% of the population in industrialized nations

Human Reprod Update 13(3) 209-223 2007
Can ART solve all?

- IVF was 47% effective overall in women who received three IVF cycles
  - Women in their twenties: 58% success
  - Women aged 40-44: 22% success
The Nurse’s Health Study II on Fertility:

- Onset 1989
- 116,000 female registered nurses ages 24–42
- Followed every 2 years
- Diet first measured in 1991 and updated every 4 years
- 18,555 married women attempting to conceive; 438 women reported ovulatory infertility

Epidemiology • Volume 20, Number 3, May 2009

Carbohydrates and Infertility

Total carb intake not related to ovulatory infertility

- High glycemic index (GI) foods
  - risk: RR was 1.92
  - (CI =1.26-2.92)
- Low GI foods associated with ↓ risk
- Specific foods: only cold breakfast cereal intake statistically significant
  - (P = 0.02)


Protein and Fertility:

- Protein type matters in ovulatory infertility:
  - RR comparing highest and lowest quintiles of animal protein intake was 1.39 (1.01 to 1.90; 0.03)
  - RR for vegetable protein intake was 0.78 (0.54 to 1.12; 0.07)
  - Consuming 5% of total energy intake as vegetable protein rather than as animal protein was associated with >50% lower risk (P = .007)

Chavarro JE. et al, Protein intake and ovulatory infertility. Amer J of Ob Gyn. 198(2);2008

Age Matters

- For women <32 years, consuming 5% of energy as vegetable protein rather than as carbs was unrelated to ovulatory infertility
- For women >32 years,
  - 50% lower risk if eating vegetable protein rather than carbs (RR 0.48; CI 0.27-0.86; P =.01).
  - lower risk if 5% of energy consumed as vegetable protein instead of animal protein

Victoria Maizes, MD, Preparing for Pregnancy: Pre-Conception Nutritional Advice
Insulin Sensitivity:

- High glycemic index/load increases insulin
- Insulin decreases SHBG
- SHBG preferentially binds testosterone = less SHBG means more free testosterone

Dairy and Fertility:

- Hormone free
  - Full fat vs low-fat
  - Lipophilic hormones
  - Water-soluble hormones
  - Milking pregnant cows

Dairy and Fertility:

- Inverse relationship between dairy fat intake and ovulatory infertility (P, trend = 0.05).
  - women consuming low-fat dairy foods ≥2 servings per day compared to ≤1 serving per week was 1.85 (1.24-2.77; 0.002)
  - Intakes of lactose, calcium, phosphorus and vitamin D were unrelated to ovulatory infertility.
- RR comparing women consuming ≥1 serving per day of high-fat dairy foods to those consuming ≤1 serving per week was 0.73 (0.52-1.01; 0.01).

Caffeine:

- Multiple trials and data is mixed
- Retrospective trials – recall bias?
- Caffeine improves insulin sensitivity which improves ovulatory function in women with PCOS

Epidemiology 20(3) May 2009
**Soda and Fertility:**

- NHS: Intake of caffeinated soft drinks, was associated with a higher risk of ovulatory infertility among women consuming ≥ 2 caffeinated soft drinks per day
  - 47% greater risk than women who consumed < 1 caffeinated soft drink per week
- Similar associations were observed for noncaffeinated, sugared, diet, and total soft drinks.
- Mechanism: impaired fasting glucose and metabolic syndrome?

**Fat and fertility:**

- Trans fat reduce PPAR-gamma
  - PPAR-gamma responsible for activating insulin
  - The average amount of trans fat in American’s diets (6 g) cuts PPAR-gamma in half
- Trans fats increase inflammation in the body which interferes with ovulation, conception, and early embryonic development

**Trans fats and Ovulatory Infertility:**

- NHS: Trans fat vs Carbs: each 2% increase in energy intake from trans fats as opposed to carbs was associated with a 73% greater risk of infertility
- Trans fat vs mono unsat: obtaining 2% of energy from trans fats rather than monounsaturated fats was associated with > double risk of infertility (RR = 2.31; 95% CI: 1.09, 4.87).

**Alcohol:**

- NHS: positive association between alcohol intake of ≥1 drink per day and ovulatory infertility
  - Association disappeared after accounting for parity and other factors
- Drinking < 1 drinking per day was unrelated to ovulatory infertility in all analyses
- 16 studies on association between alcohol intake and fertility
  - Only 5 of the studies prospective
  - Divided between null and positive studies

---


2004 EPA warning

- Do not eat shark, swordfish, king mackerel, or tilefish because they contain high levels of mercury.
- Eat up to 12 ounces (2 average meals) a week of fish and shellfish that are lower in mercury.
- Shrimp, canned light tuna, salmon, pollock, and catfish.
- Albacore ("white") tuna max of 6 ounces per week.
- Check local advisories about the safety of fish caught in local lakes, rivers, and coastal areas.
  If no advice is available, eat up to 6 ounces per week but don’t consume any other fish during that week.

Fish facts

Avon Longitudinal Study of Parents and Children (ALSPAC) - 11,875 pregnant women FFQ assessing seafood consumption at 32 weeks’ gestation.

- Compared developmental, behavioral, and cognitive outcomes of the children (aged 6 mos - 8 yrs) in women consuming none, some (1-340 g per week), and >340 g per week.
- Maternal seafood intake during pregnancy <340 g per week associated with children in the lowest quartile for verbal IQ
  - (no seafood consumption, odds ratio 1.48, CI 1.16-1.90; some, 1.09, 0.92-1.29; overall trend, p=0.004)

Fish Facts continued

- The Seychelles Child Development Study
  - 779 mother-infant pairs recruited in 1989–1990 on the island of Ma’he followed to age 9
  - Selected because fish consumption in mothers averaged 12 fish meals a week
  - No consistent adverse developmental effects in the children
  - Presumption: protective nutrients in fish including long-chain polyunsaturated fatty acids, iodine, iron, and choline

Politics and Food Policy

- The 2010 U.S. Dietary Guidelines for Americans recommend at least eight ounces of seafood per week
- Yet, seafood consumption has dropped to 1.89 ounces per week (2008 FDA survey)
- Senator Kirsten Gillibrand (D-New York) joined Senator Tom Coburn, M.D. (R-Oklahoma) in urging the FDA to raise the maximum amount of seafood it recommends for young children and pregnant or nursing mothers


Multi-vitamin use

- NHS: compared with women who did not take multivitamins, RR of ovulatory infertility was:
  - 0.88 for women consuming ≤ 2 tabs/week
  - 0.69 for 3-5 tabs/week,
  - 0.59 for ≥ six tabs/week,

- Micronutrients impact fertility, embryogenesis and placentation


Percent of U.S. Population Not Meeting the DRI For Specific Nutrients

http://www.ba.ars.usda.gov/cnrg/services/cnmaph.html

Are women supplementing appropriately?

- Pilot study: 176 pregnant women's use of omega-3, multivitamin, and other supplements
- Surveyed women in prenatal clinics:
  - 6 women in first trimester, 82 in the second trimester, and 87 were in the third trimester
- 159 respondents (90.3%) reported taking a multivitamin - none were taking a supplement that contained omega-3
- only 20 (11.4%) were taking omega-3

Fertility Blend

- A proprietary combination of chasteberry, green tea extracts, L-arginine, vitamins E, B6, B12, folate, iron, magnesium, zinc, and selenium

- Two RCTs
  - 2004 pilot: 30 women, aged 24 - 46 who were unsuccessful at conceiving over 6 - 36 months, Fertility Blend tid vs placebo for three cycles
    - At 5 months, 5 women in the treatment group were pregnant vs 0 in control (33% versus 0%, P < .01).
    - Four of the five women had healthy live births
  - 2006: 93 women, aged 24-42
    - At 6 months, 17 vs 10 women pregnant. (P < .01)

Folic Acid

- NHS: women who consumed >700 mcg/day from food and supplements were 40% more likely to get pregnant.
- Methyl donor needed during DNA replication.
- Methionine is made from homocysteine.
- Folic acid helps metabolize homocysteine into methionine.
- Women with high homocysteine are more likely to miscarry and to have preeclampsia.
- Folic acid may stimulate ovulation (more dizygotic twins)
- Methylenetetrahydrofolate reductase genetic variant associated with poorer response to IVF

Folic Acid

- NHS: women who consumed >700 mcg/day from food and supplements were 40% more likely to get pregnant.
- Methyl donor needed during DNA replication.
- Methionine is made from homocysteine.
- Folic acid helps metabolize homocysteine into methionine.
- Women with high homocysteine are more likely to miscarry and to have preeclampsia.
- Folic acid may stimulate ovulation (more dizygotic twins)
- Methylenetetrahydrofolate reductase genetic variant associated with poorer response to IVF

Folate

- 3 commercially available forms

Vitamin C

- RCT of 150 women with luteal phase defects
  - 750 mg/day of vitamin C vs placebo.
  - After 6 months of treatment fertility in the vitamin C group was significantly higher than in the placebo group (25% versus 11%, P = .045).
  - Progesterone levels were also significantly increased in the treatment group (52.6% versus 21.7%, P < .01).
- Potential Mechanism: effects of oxidative stress in oocyte maturation and fertilization.
Iron and Fertility:

- NHS: Women who consumed iron supplements had a significantly lower risk of ovulatory infertility than those who did not (RR 0.60, CI 0.39-0.9)
- Ideal dose appears to be 40-80 mg of iron
- Heme iron intake did not reduce ovulatory infertility


Iodine intake recommendations:

- WHO: 150 mcg/d for adults & adolescents, 200 mcg/d for pregnant or lactating women
- IOM recommends 150 mcg/d for adults, 220 mcg/d for pregnant women, and 290 mcg/d for lactating women
- Historical levels:
  - NHANES I (1971-1974): median urine iodine was 320 mcg/L, reflecting adequate dietary iodine intake
  - NHANES III (1988-1994): median urinary iodine had fallen to 145 mcg/L
  - NHANES 2001-2002: iodine intake 167.8 mcg/L
- The risk for insufficient dietary iodine intake in reproductive-aged women (15-44 y) increased 3.8-fold:
  - 11.7% of adult women are iodine deficient
  - 7% of pregnant women in 1994 were deficient (compared to 1% in 1974)

Not all multivitamins contain iodine. Those that do typically contain 150 mcg of iodine per tablet.

Food sources include:
- Milk
- Egg yolks
- Saltwater fish
- Garlic
- Lima beans and soybeans
- Mushrooms
- Seaweed, dulse and kelp
- Sesame seeds
- Asparagus, spinach, summer squash, Swiss chard, Turnip greens

Historical levels:
- NHANES I (1971-1974): median urine iodine was 320 mcg/L, reflecting adequate dietary iodine intake
- NHANES III (1988-1994): median urinary iodine had fallen to 145 mcg/L
- NHANES 2001-2002: iodine intake 167.8 mcg/L

Iodine intake recommendations:

- WHO: 150 mcg/d for adults & adolescents, 200 mcg/d for pregnant or lactating women
- IOM recommends 150 mcg/d for adults, 220 mcg/d for pregnant women, and 290 mcg/d for lactating women
- Historical levels:
  - NHANES I (1971-1974): median urine iodine was 320 mcg/L, reflecting adequate dietary iodine intake
  - NHANES III (1988-1994): median urinary iodine had fallen to 145 mcg/L
  - NHANES 2001-2002: iodine intake 167.8 mcg/L
- The risk for insufficient dietary iodine intake in reproductive-aged women (15-44 y) increased 3.8-fold:
  - 11.7% of adult women are iodine deficient
  - 7% of pregnant women in 1994 were deficient (compared to 1% in 1974)

Flax seed

Pilot trial: 18 normally cycling women, randomized cross-over design.

Methods:
- Each woman consumed her usual omnivorous, low fiber (control) diet for 3 cycles and her usual diet supplemented with flax seed for another 3 cycles.
- 2nd and 3rd flax cycles compared to 2nd and 3rd control cycles.

Results:
- 3 anovulatory cycles occurred during the 36 control cycles - none during the 36 flax seed cycles.
- Ovulatory flax cycles were consistently associated with longer luteal phase (LP) (12.6 vs. 11.4 days; P = 0.002).
- No significant differences between flax and control cycles for estradiol or estrone during the early follicular phase, mid follicular phase, or LR.
- The LP progesterone/estradiol ratios were significantly higher during the flax cycles.


Victoria Maizes, MD, Preparing for Pregnancy: Pre-Conception Nutritional Advice
Male Factors

Fertility in men

- Obesity
  - alterations in hormonal profiles
    (reduced inhibin B and androgen levels accompanied by elevated estrogen levels)
  - increased scrotal temperature
  - contributes to erectile dysfunction
  - reduces semen quality
  - changes sperm proteomes


BMI in men

- Despite major differences in reproductive hormone levels with increasing body weight, only extreme levels of obesity influence male reproductive potential
- Obesity in father does predicts obesity in pre-menarchal daughter

Chavarro JE. et al. Fertility & Sterility. 93(7):2222-31, 2010
Ng Nature Oct 2010

Fertility in men

- 80% of men don’t get 5 servings of fruits and vegetables per day
- Vitamin D and autism

Cochrane Review of Anti-oxidants in Men
- 30-80% of male subfertility due to effects of oxidative stress on sperm.
- 34 RCTs, 2876 couples
  - antioxidant supplements (single or combined) taken by the male partner of a couple seeking fertility assistance compared with placebo, no treatment, or another antioxidant
- Outcomes:
  - live birth, pregnancy, miscarriage, stillbirth, sperm DNA damage, sperm motility, sperm concentration and adverse effects.
  - Live birth: 3 trials. Antioxidant use associated with increase in live birth rate (OR 4.85, 95% CI 1.92 to 12.24; P = 0.0008)
  - Pregnancy rate: 15 trials. 96 pregnancies in 964 couples. Antioxidant use was associated with increased pregnancy rate (OR 4.18, 95% CI 2.65 to 6.59; P < 0.00001)

Paternal age and autism
- Increases genetic mutations – increases risk for autism
- Autism Spectrum Disorder 5.75 times more common for fathers >40 rather than <30

Environmental influences
- Endocrine disruptors
  - Pesticides
  - Plastics
  - BPA
  - Phthalates
- Environmental Working Group – ewg.org
- UCSF – Program on Reproductive Health and the Environment: prhe.ucsf.edu/prhe/pubs/shapingourlegacy.html

Does changing your diet help?
- 25 people, 5 days, vegetarian diet, at a Buddhist temple
- Measured levels of urinary excretion of antibiotic residues, phthalate metabolites and oxidative stress biomarkers
- Reduction in antibiotics and phthalates and oxidative stress biomarker

Victoria Maizes, MD. Preparing for Pregnancy: Pre-Conception Nutritional Advice
Eat more
- Vegetable protein
- Foods with rich amounts of omega 3
- Vitamin D foods
- Whole dairy products
- Low glycemic index carbohydrates

Eat less
- Trans fats
- High mercury fish
- Animal protein
- Sodas (eliminate)
- Pesticide laden
- Alcohol

Supplement Wisely:
- Multivitamin
- Iron
- Folic acid
- Vitamin C
- Iodine
- Vitamin D
- Omega 3

Integrative Approaches
- Reduce environmental exposures
- Use conventional and alternative medicine wisely
- Maintain normal weight
- Dietary change
- Take Supplements
- Use Mind-Body Strategies