고지방 식이요법이 여성 생식에 미치는 영향

연세대학교 의과대학 산부인과학 교실
박주현

YONSEI UNIVERSITY

The weight loss epidemic
High fat diet

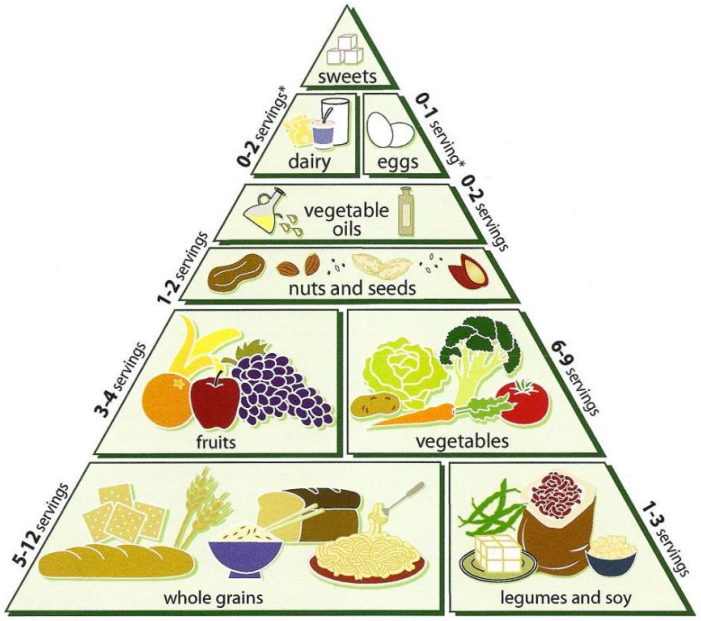
고지방 다이어트 열풍, 버터 품귀현상... 버터·치즈·삼겹살↑ 쌀↓

김수정 기자 | 2016.10.16 10:39

기사공유 f 가 가

“6개월 후 체중감량을 해 오세요”

The classic nutrition pyramid



* A reliable source of vitamin B12 should be included if no dairy or eggs are consumed.

Other Lifestyle Recommendations

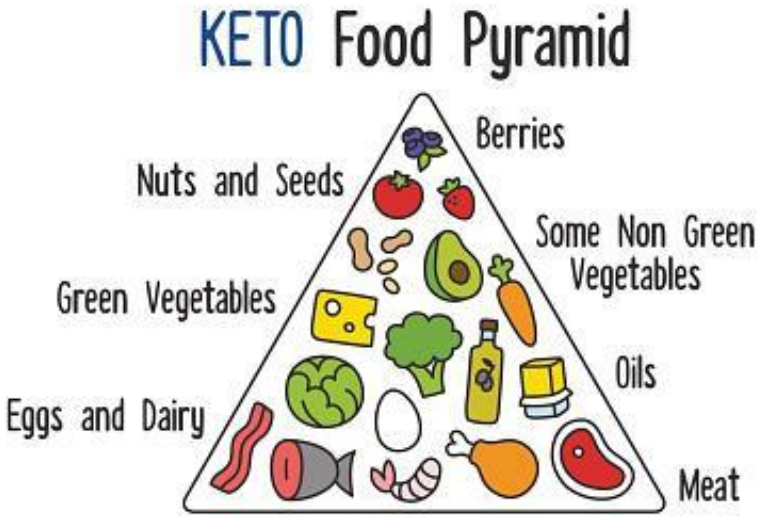
Daily Exercise

Water—eight, 8 oz. glasses per day

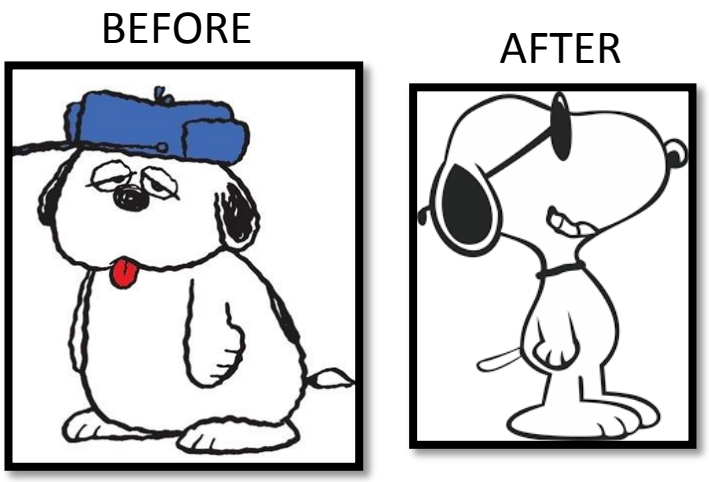
Sunlight—10 minutes a day to activate vitamin D

영양소		2015년		
		1-2세	3-18세	19세+
탄수화물		55-65%	55-65%	55-65%
단백질		7-20%	7-20%	7-20%
지질	총지방	20-35%	15-30%	15-30%
	오메가-6 지방산	4-10%	4-10%	4-10%
	오메가-3 지방산	1%내외	1%내외	1%내외
	포화지방산	-	8%미만	7%미만
	트랜스지방산	-	1%미만	1%미만

The low-carb high fat (LCHF) diet



Does LCHF diet work?



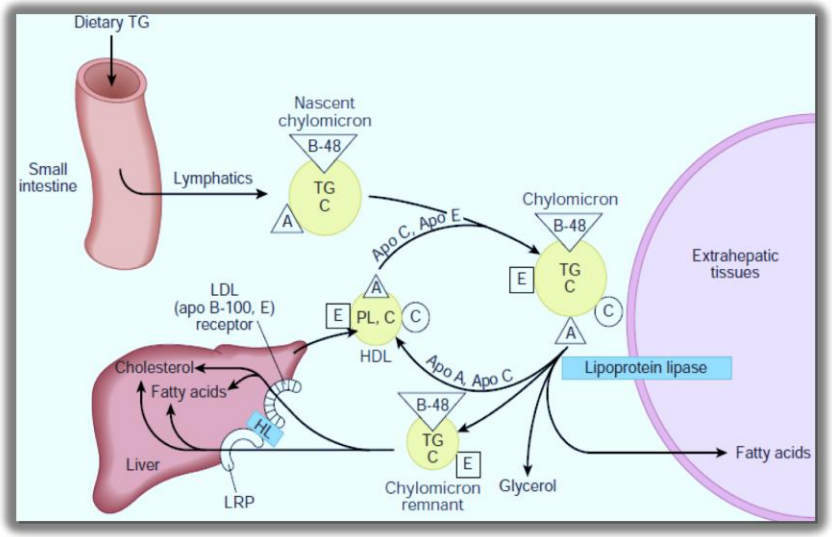
High fat (Low carbohydrate) Diet

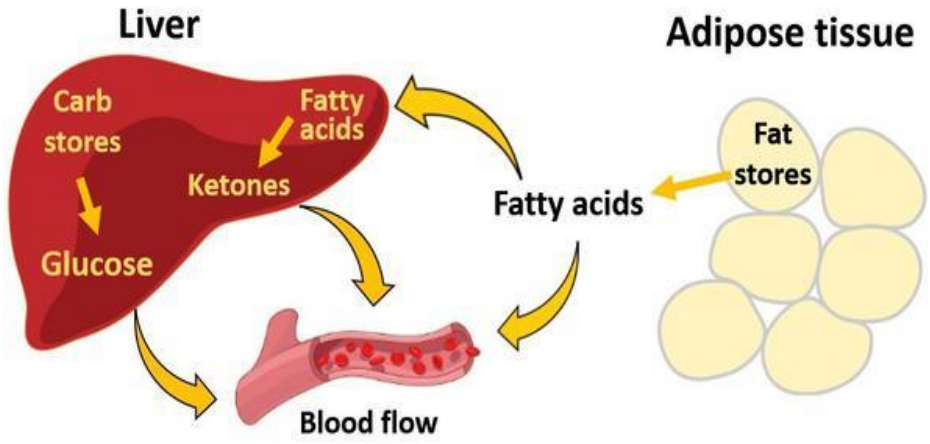
- Increasing fat (~>50%) and lowering carbohydrate in meals
- =Ketogenic diet
  - High fat
  - Moderate protein
  - Low carbohydrate (<50g)

- Body obtains energy from metabolism of ketone bodies vs glycolysis from glucose (*Hans Krebs*)
- Fasting or reducing the intake of carbohydrates in diet induces change in energy metabolism

High fat diet for weight loss

- How does it work?
  - Long chain triglyceride (LCT)-based diet
    - Fat:(Protein,Carbohydrate) = 4:1, 3:1, 2:1, 1:1
  - Medium chain triglyceride (MCT)-based diet
    - Caprylic acid, capric acid, caproic acid, lauric acid

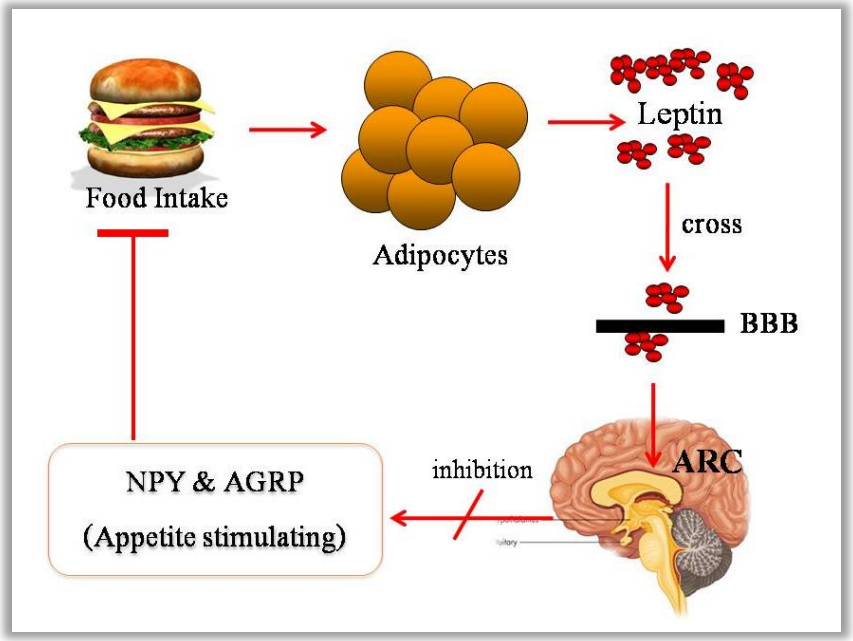




High fat (Low carb) Diet

- Beta oxidation of fatty acids in liver mitochondria to produce ketone bodies in the absence of carbohydrate
- High fat in diet forces the body to use ketone bodies as an energy source instead of carbohydrates

- Leptin regulation, control of appetite

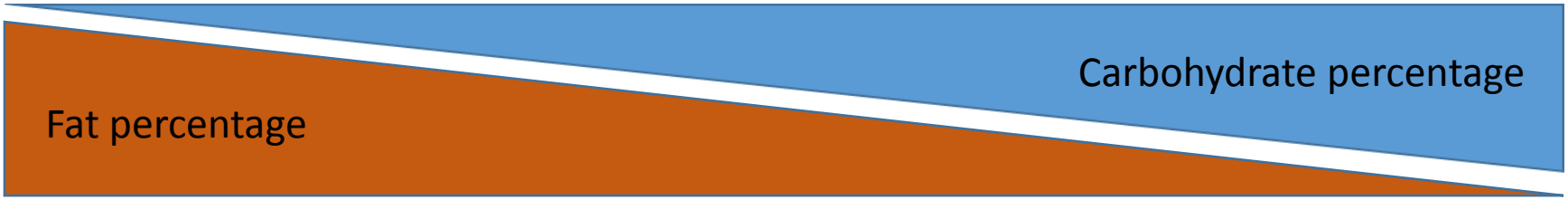


Comparison of the Atkins, Zone, Ornish, and LEARN Diets for Change in Weight and Related Risk Factors Among Overweight Premenopausal Women

The A TO Z Weight Loss Study: A Randomized Trial

- *Gardner et al., JAMA. 2007;297:969-977*

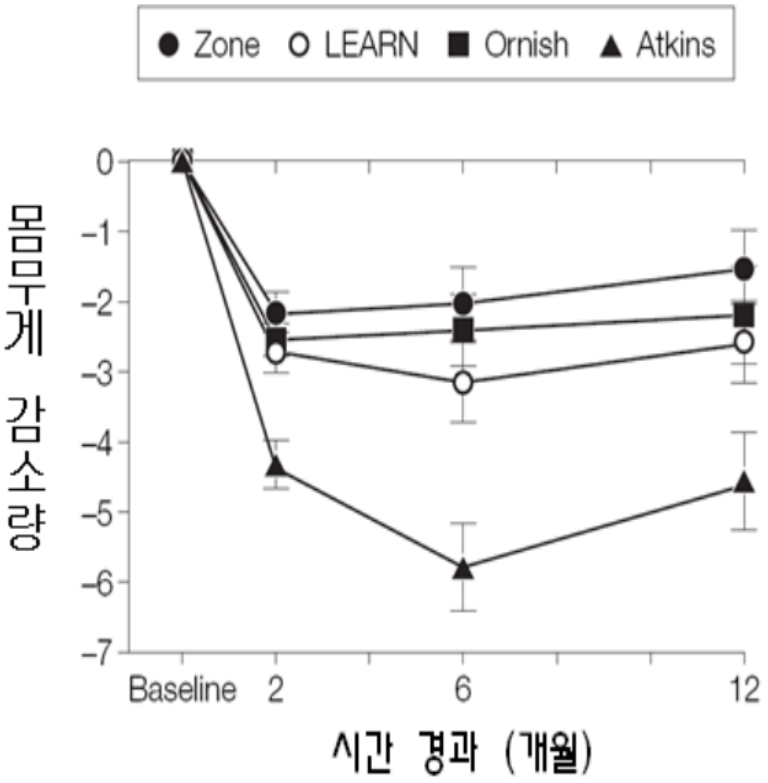
Comparison groups
Randomized control trial of women age 25-50 years



Atkins	Zone	LEARN	Ornish
• N=77	• N=79	• N=79	• N=76

Comparison of weight loss with different fat ratios

- Mean 12-month weight loss
  - Atkins, -4.7 kg (95% CI, -6.3 to -3.1 kg)
  - Zone, -1.6 kg (95% CI, -2.8 to -0.4 kg)
  - LEARN, -2.6 kg (-3.8 to -1.3 kg)
  - Ornish, -2.2 kg (-3.6 to -0.8 kg).



The NEW ENGLAND JOURNAL of MEDICINE

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Comparison of Weight-Loss Diets with Different Compositions of Fat, Protein, and Carbohydrates

Frank M. Sacks, M.D., George A. Bray, M.D., Vincent J. Carey, Ph.D., Steven R. Smith, M.D., Donna H. Ryan, M.D., Stephen D. Anton, Ph.D., Katherine McManus, M.S., R.D., Catherine M. Champagne, Ph.D., Louise M. Bishop, M.S., R.D., Nancy Laranjo, B.A., Meryl S. Leboff, M.D., Jennifer C. Rood, Ph.D., Lilian de Jonge, Ph.D., Frank L. Greenway, M.D., Catherine M. Loria, Ph.D., Eva Obarzanek, Ph.D., and Donald A. Williamson, Ph.D.

- fat, protein, and carbohydrates in the four diets
  - 20, 15, and 65%
  - 20, 25, and 55%
  - 40, 15, and 45%
  - 40, 25, and 35%

Changes in body weight with progression of diet regimen

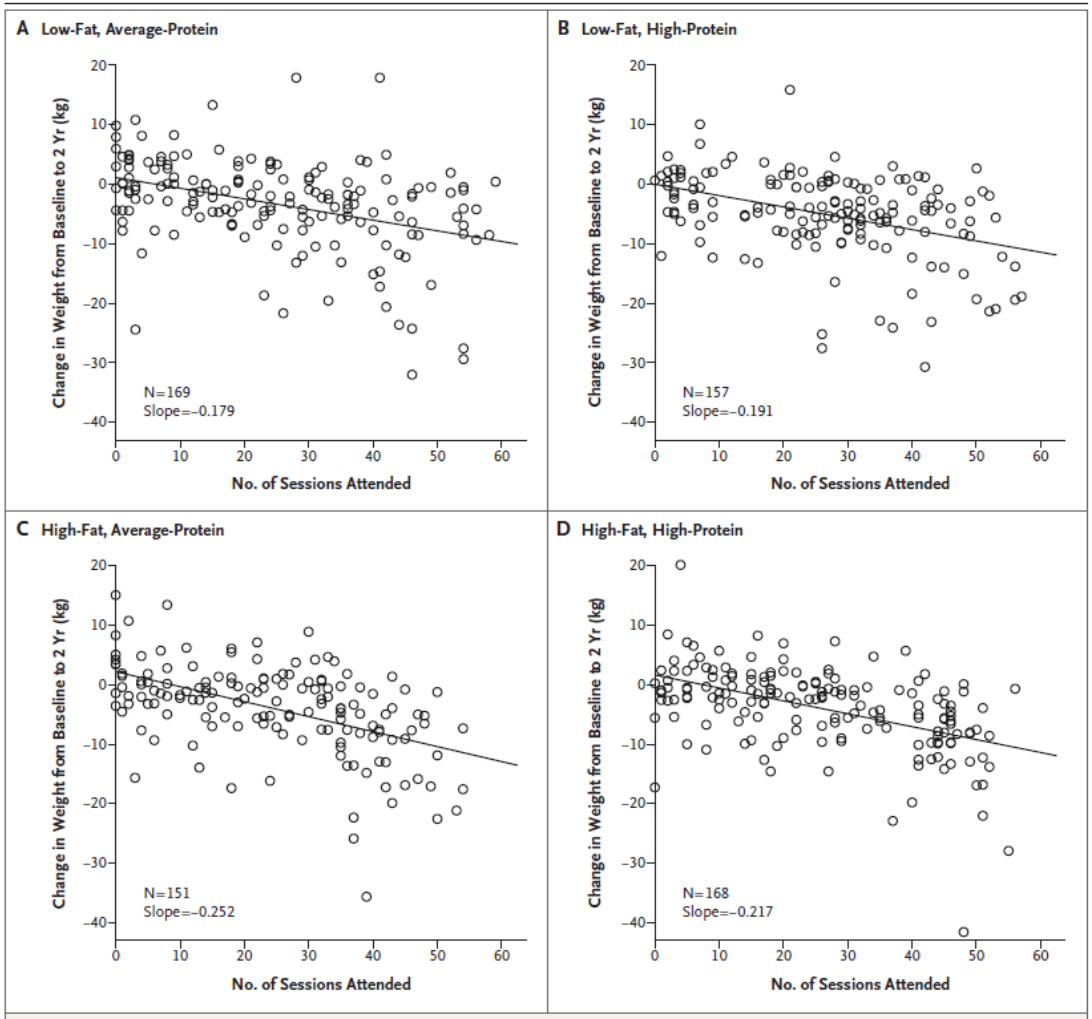

Figure 3. Change in Body Weight from Baseline to 2 Years According to Attendance at Counseling Sessions for Weight Loss,

Changes in metabolic indices with progression of HF diet

Variable	Change with High Fat minus Change with Low Fat			
	At 6 Mo	P Value	At 2 Yr	P Value
Risk factors†				
Cholesterol (mg/dl)				
Total	4.7±1.8	0.01	5.6±1.9	0.003
LDL	4.4±1.6	0.005	5.1±1.6	0.001
HDL	1.1±0.5	0.01	0.7±0.5	0.12
Triglycerides (mg/dl)	−2.8±4.3	0.52	−1.2±4.0	0.76
Blood pressure (mm Hg)				
Systolic	0.4±0.7	0.59	0.3±0.7	0.64
Diastolic	0.1±0.5	0.77	0.1±0.5	0.85
Glucose (mg/dl)	1.2±0.6	0.04	1.1±0.5	0.05
Insulin (μU/ml)	0.2±0.4	0.68	−0.1±0.4	0.77
HOMA	0.13±0.13	0.31	0.03±0.10	0.78
Nutrient intake per day				
Energy (kcal)	11.4±53.9	0.83	−75.6±70.9	0.29
Carbohydrate (%)	−9.5±1.0	<0.001	−6.4±1.5	<0.001
Protein (%)	0.9±0.5	0.06	0.2±0.7	0.77
Fat (%)	8.0±0.8	<0.001	6.7±1.2	<0.001
Saturated fat (%)	1.3±0.3	<0.001	1.7±0.5	<0.001
Biomarkers of adherence				
Urinary nitrogen (g)‡	−0.11±0.39	0.77	0.08±0.42	0.84
Respiratory quotient§	−0.01±0.00	0.005	−0.02±0.00	0.002

Will high fat diet have an impact on female reproduction?

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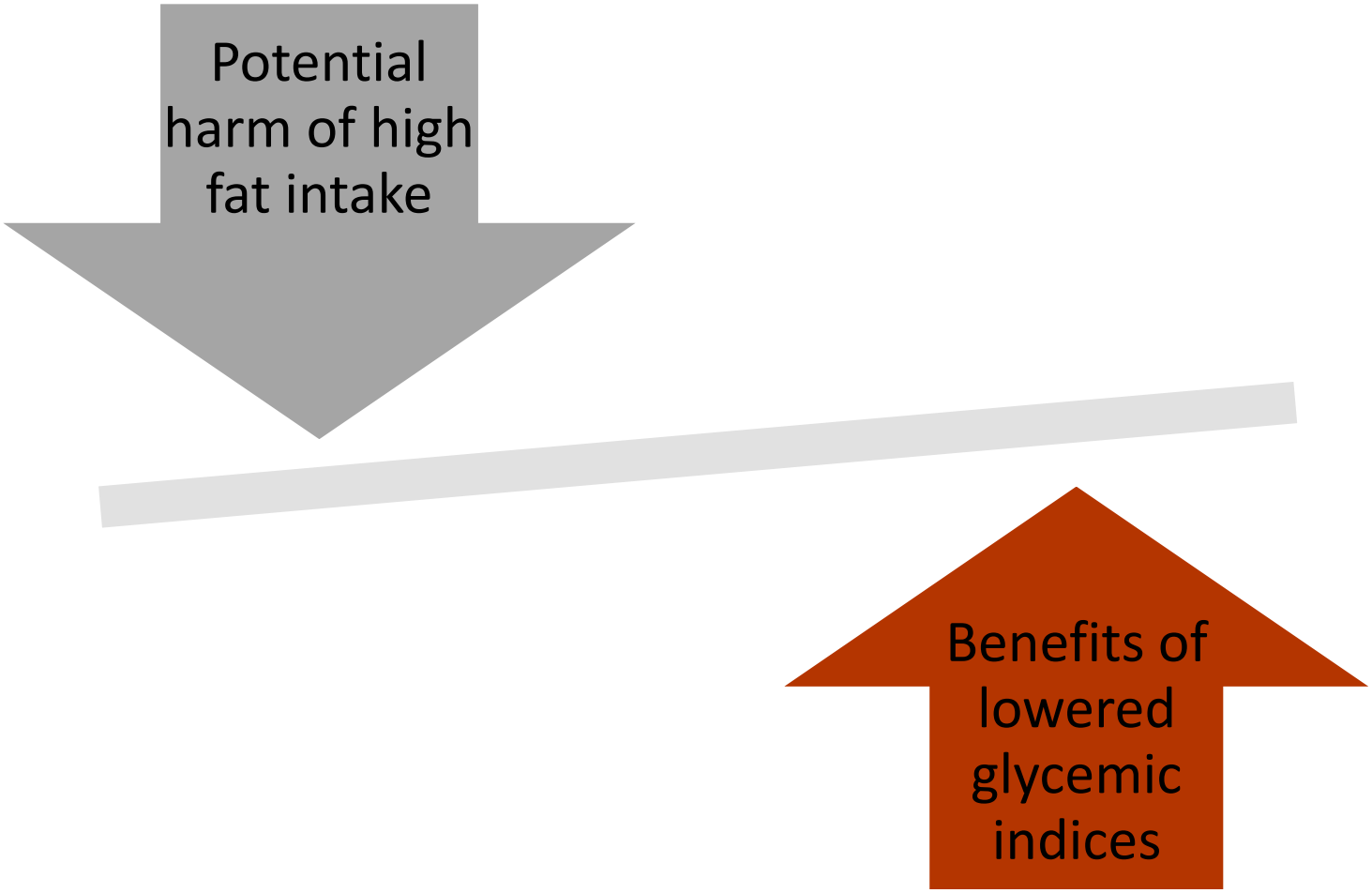
Gain or Loss?


Potential harm of high fat intake
Benefits of lowered glycemic indices

Reproductive effect of high fat diet

- Ovulatory disorders are common in obese animal models
- Neuroendocrine changes that suppress natural ovulation

- *Balasubramanian et al., J Neuroendocrinol. 2012 May;24(5):748-55*

  - Low fat vs high fat (HF) diet (45% calories from fat) for 6 weeks
  - Jugular catheter to monitor luteinising hormone (LH) levels
  - Norepinephrine (NE) concentrations in discrete hypothalamic areas measured using high-performance liquid chromatography directly from brain tissue

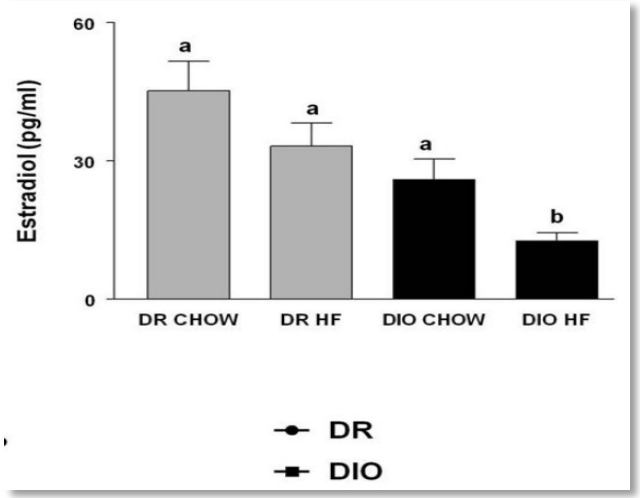
Reproductive effect of HF diet

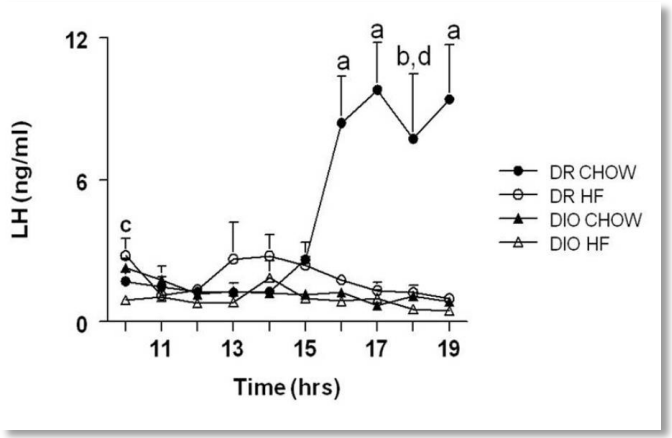
HF diet affected estrous cyclicity in both obese and normal weight rats, with the effect being more pronounced in obese animals

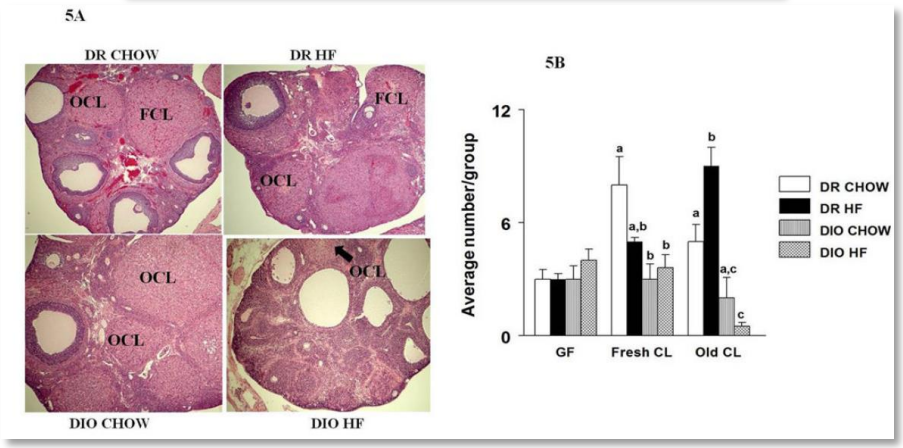
HF diet exposure increased leptin levels in both obese and normal weight rats

NE levels in the hypothalamus unaffected by HF diet or genotype

Obese rats have inherently reduced reproductive capacity and exposure to a HF diet decreases it further







Reproductive effect of HF diet

- Does high-fat diet (HFD) impacts ovarian function, long-term fertility, and local and systemic markers of inflammation independent of obesity?
- *Malgorzata et al., Biology of Reproduction 2016*

- 5 week old mice fed either low-fat diet (control group-LF-Ln) or HFD for 10 weeks and divided based on body weight into high-fat obese (HF-Ob; >25 g) and high-fat lean (HF-Ln; <22 g) to examine reproductive parameters

Reproductive effect of high fat diet

- 10-week and 32-week exposure to HFD resulted in depleted primordial follicles irrespective of obese phenotype
- Macrophage counts revealed increased tissue inflammation in the ovary independent of obesity
- Serum pro-inflammatory cytokines: increased in those under HFD
- Those under HFD-sustained effect on litter production rate and number of pups per litter regardless of obese phenotype

Effect of feeding a high-fat diet independently of caloric intake on reproductive function in diet-induced obese female rats

Mona A. Hussain[1], Noha M. Abogresha[2], Ranya Hassan[3], Dalia A. Tamany[4], Mariam Lotfy[5]

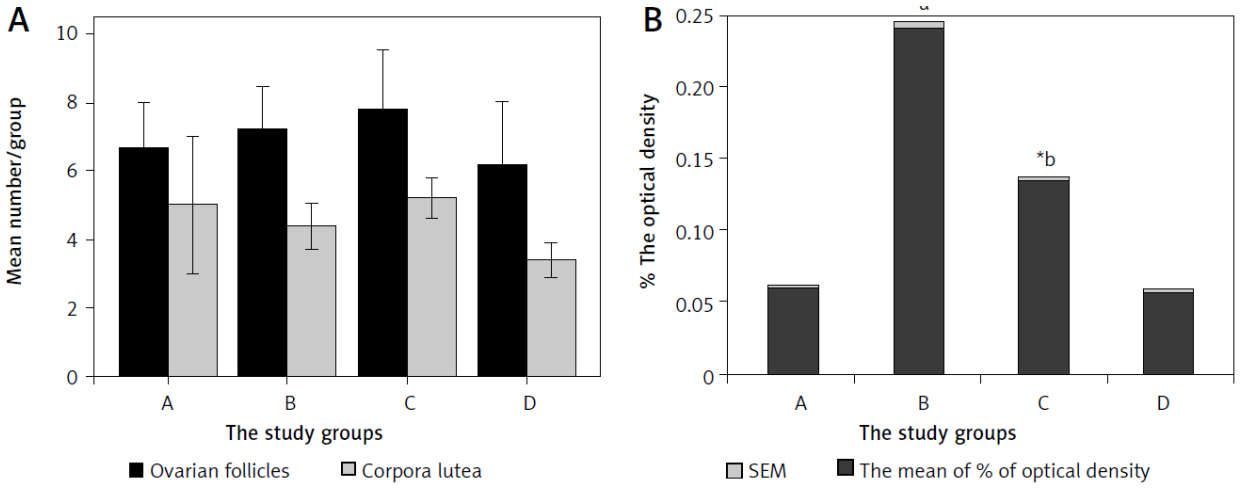


Figure 2. A – The mean of number of ovarian follicles and corpora lutea in the study groups; **B** – the percent of optical density of immunoreactive cells

**[a]Significant increase in the percent of optical density of ovarian caspase-3 immunoreactivity in group B vs. groups A, C and D*
**[b]Significant increase in the percent of optical density of ovarian caspase-3 immunoreactivity in group C vs. groups A and D*

ad libitum HFD group (B),
isocalorically restricted HFD group (C),
hypocalorically restricted HFD group (D)

Glucose; a key substrate for providing energy during oocyte maturation

- Glucose metabolism is crucial for oocyte maturation and development post-fertilization in many mammalian species (Sutton-McDowall et al., 2010; Krisher et al., 2007)
- *In vitro* culture of oocytes in sub-optimal concentrations of glucose results in delayed meiotic maturation, fertilization and embryonic development (Sutton-McDowall et al., 2010; Sato et al., 2007; Zheng et al., 2001)
- Delayed resumption of meiosis in prepubertal cattle oocytes is associated with retarded glucose metabolism (Steeves & Gardner, 1999)

The effects of a low-carbohydrate, ketogenic diet on the polycystic ovary syndrome: A pilot study

John C Mavropoulos[1], William S Yancy[1,2], Juanita Hepburn[1] and Eric C Westman*[1]

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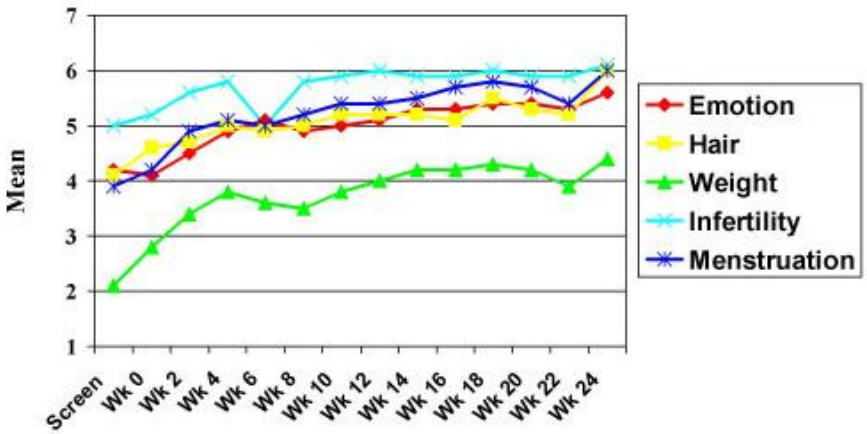
* Corresponding author



Effect of Diet on PCOS-Q Scores The effect of a low carbohydrate, ketogenic diet program on mean polycystic ovary syndrome specific questionnaire (PCOS-Q) domain scores shown over a 24 week period

Carbohydrate 20gm

- unlimited consumption of animal foods (meat, chicken, turkey, other fowl, fish, shellfish), prepared and fresh
- cheeses (up to 4 and 2 ounces per day, respectively),
- unlimited eggs, salad vegetables (2 cupfuls per day),
- low carbohydrate vegetables (1 cupful per day)

Take home message

- High fat diet, under the scientific evidence provided by therapeutic 'ketone diets' may be effective in inducing weight loss short-term
  - May be useful short-term, for disease in gynecology where hyperinsulinemia may play a role

- However, prolonged consumption of high fat diet exposes patients to health risks
  - With conflicting results on dyslipidemia
  - Significant impact on ovulatory dysfunction long-term
  - Significant oxidative stress on developing follicles with high caloric fat diets

THANK YOU!