

Hormones regulating lipid and carbohydrate metabolism in premenopausal women: modulation by dietary lipids¹⁻³

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ABSTRACT The effect of high- and low-fat diets with different levels of fatty acid unsaturation on plasma hormones involved in lipid metabolism was studied during different phases of the menstrual cycle in 31 premenopausal women. Subjects were divided into two groups and were fed controlled diets containing 39% fat with a ratio of polyunsaturated to saturated fatty acids (P:S) of either 0.3 or 1.0 for four menstrual cycles and then switched to a 19% fat diet with the same P:S for another four cycles. Blood samples were analyzed during both the follicular and luteal phases. A significant direct effect of level of dietary fat was observed on plasma cortisol and dehydroepiandrosterone-sulphate whereas an inverse relationship was seen for plasma insulin. Both plasma insulin and growth hormone levels were higher during the luteal compared with the follicular phase of the menstrual cycle. None of the hormones was affected by the level of unsaturation of dietary fats. *Am J Clin Nutr* 1989;49:752-7.

KEY WORDS Insulin, glucagon, growth hormone, cortisol, DHEA-S, P:S, high-fat diet, low-fat diet, menstrual cycle

Introduction

The composition of plasma lipids in man and animals is a reflection of the type and amount of dietary lipids consumed (1-6). Lipid metabolism is also endogenously controlled by pancreatic, pituitary, and adrenal hormones. Thus, insulin promotes lipogenesis whereas glucagon, growth hormone, cortisol, and epinephrine oppose insulin action and stimulate lipolysis (7). Furthermore, the levels of these hormones appear to regulate lipid metabolism in different metabolic conditions such as obesity and diabetes (7). In addition, dietary carbohydrates are also known to affect plasma lipid levels and lipid metabolism in man and animals (8-10), possibly through control of the secretion of these regulatory hormones.

Although dietary carbohydrates are known to alter plasma hormone levels in man and animals (11-14), a similar effect of dietary lipids is less well defined. In healthy volunteers a low-fat, high-carbohydrate diet was reported as significantly more effective than a high-fat, low-carbohydrate diet in stimulating insulin secretion whereas the opposite was true for glucagon release (15). In contrast, noninsulin dependent diabetes mellitus (NIDDM) subjects did not show a significant insulin response to the high-carbohydrate, low-fat diet although glucagon response remained unaffected.

The effect of dietary lipids on dehydroepiandroster-

one-sulphate (DHEA-S) has not been well studied. Hill and Wynder (16) reported increased levels in subjects fed a low-fat vegetarian diet. DHEA-S is involved in carbohydrate metabolism because it inhibits glucose-6-phosphate dehydrogenase, a rate-limiting enzyme of the pentose cycle (17, 18). However, data on the effect of dietary carbohydrates on plasma DHEA-S levels are lacking. The question of dietary lipid effects on plasma hormone levels becomes more complex in premenopausal women, where the menstrual cycle itself affects hormone secretion.

This report critically examines the effects in premenopausal women of the type and quantity of dietary fat and carbohydrates on the follicular- and luteal-phase levels of plasma insulin, glucagon, growth hormone, cortisol, and DHEA-S. We studied the effects of high-fat diets (40% of energy) and low-fat diets (20% of energy) at low

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TABLE 1

Effect of level and unsaturation of dietary lipids on plasma immunoreactive insulin levels in premenopausal women*

P:S†	Menstrual-cycle phase‡	Dietary period§		
		Self-selected (SS)	High-fat, low-carbohydrate (HF-LC)	Low-fat, high-carbohydrate (LF-HC)
		<i>pmol/L</i>		
0.3	Follicular	64.6 ± 5.2	64.9 ± 5.2	81.4 ± 5.0
0.3	Luteal	81.6 ± 5.7	79.1 ± 5.2	81.4 ± 5.0
1.0	Follicular	66.7 ± 4.8	78.2 ± 4.8	80.1 ± 4.8
1.0	Luteal	85.6 ± 4.8	83.9 ± 4.8	95.6 ± 5.7

* Least-square means ± standard error of least-square means.

† Ratio of polyunsaturated to saturated fatty acids in the experimental diets.

‡ The mean value during the luteal phase (84.5 ± 2.2 pmol/L) was significantly higher according to least-square means than during the follicular phase (72.7 ± 2.0 pmol/L); $p < 0.05$.§ The mean value during the LF-HC diet (84.6 ± 2.6 pmol/L) was significantly higher according to least-square means than during the SS and HF-LC periods (74.6 ± 2.6 and 76.6 ± 2.5 pmol/L, respectively); $p < 0.05$.

(0.3) and high (1.0) ratios of polyunsaturated to saturated fatty acids (P:S) on levels of plasma insulin, glucagon, growth hormone, cortisol, and DHEA-S.

Methods

The experimental protocol was approved by the institutional review boards of Georgetown University School of Medicine, the US Department of Agriculture, and the National Institutes of Health. Premenopausal women aged 20–40 y were recruited from the Beltsville, MD, area for the study. Ninety-seven women volunteered; 40 were considered eligible (no history of metabolic or chronic disease, no regular medications, no menstrual irregularities, not pregnant or lactating, no unusual dietary patterns); 37 passed the screening examination and started the study; and 31 completed the study. The subjects were paired based on age and relative weight and randomized to one of two dietary groups, P:S = 0.3 (15 subjects) or P:S = 1.0 (16 subjects), which were maintained throughout both the high- and low-fat regimens. Periodic caloric adjustments were made to maintain initial body weight. Initial base-line data were collected during a prestudy period of one menstrual cycle when the subjects consumed self-selected (SS) diets. Composition of the SS diets is given elsewhere (6) and was very similar to the high-fat, low-carbohydrate (HF-LC) diet. After an overnight fast, venous blood samples were collected in EDTA (1.4 mg/mL) and Trasyol® (100 U/mL; FBA Pharmaceuticals, New York, NY) during the midfollicular (proliferative) phase and also during the midluteal (secretory) phase, as determined by the length of the menstrual cycle. The subjects were then placed on a high-fat, low-carbohydrate (HF-LC) diet (39% of energy from fat and 45% from carbohydrate) for four menstrual cycles, followed by a low-fat, high-carbohydrate (LF-HC) diet (19% of energy from fat and 64% from carbohydrate) for an additional four menstrual cycles. Morning fasting blood samples were collected during midfollicular and midluteal phases during the fourth menstrual cycle in each of the two controlled dietary periods.

During the controlled dietary periods all meals were prepared in the Human Study Facility of the Beltsville Human Nutrition Research Center (BHNRC). Breakfast and evening

meals on weekdays were eaten in the BHNRC dining facility and carry-out meals were provided for weekday lunches and all weekend meals. A 14-d menu cycle was used, formulated from commonly available foods. Menus for four caloric intake levels were designed: 1600, 2000, 2400, and 2800 kcal. No vitamin-mineral supplements or alcohol were consumed by subjects during the study.

All hormone analyses were performed by radioimmunoassays. Plasma glucagon was measured by radioimmunoassay with Unger's antibody 04A as previously described (14). Plasma insulin, cortisol, and growth hormone were determined with kits from Immunonuclear Corp, Stillwater, MN (catalog #0600, 9900, and 0700), and DHEA-S was determined with a kit from Radioassay Systems Laboratory Inc, Carson, CA (catalog #1014). The data were analyzed statistically by general linear models and analysis of variance (ANOVA) using a completely randomized split-split plot model (19). A split-split plot design is a design that recognizes three levels of variation (random-error variations: among subjects, within subjects among periods, and within subjects among periods between menses). The design is a nested design in which the nested factors are fixed. Because replications were unequal, least-square means were calculated. Least-square means are means that have been corrected for unequal replication in the study in order to make fair comparisons between all the groups. Means of significant effects were determined with least-significant-difference techniques for unequal replications (19).

Results

Plasma hormone concentrations at the midfollicular and midluteal phases of the menstrual cycle for each dietary regimen are given in Tables 1–5. Statistical significance of the effects of the various experimental parameters on each of the hormone levels is summarized in Table 6. In Tables 1–5 statistical analysis is given only for those parameters that showed significant effects as seen in Table 6. The dietary regimen, ie, variations in the amount of fat and carbohydrate, significantly affected the levels of each hormone except growth hormone. In

TABLE 2
Effect of level and unsaturation of dietary lipids on plasma immunoreactive glucagon levels in premenopausal women*

P:S†	Menstrual-cycle phase	Dietary period‡		
		Self-selected (SS)	High-fat, low-carbohydrate (HF-LC)	Low-fat, high-carbohydrate (LF-HC)
			<i>pmol/L</i>	
0.3	Follicular	42.0 ± 1.3	39.7 ± 1.3	40.1 ± 1.3
0.3	Luteal	44.9 ± 1.4	40.8 ± 1.3	40.6 ± 1.4
1.0	Follicular	36.3 ± 1.3	33.8 ± 1.3	34.7 ± 1.3
1.0	Luteal	37.4 ± 1.3	33.3 ± 1.3	33.6 ± 1.4

* Least-square means ± standard error of least-square means.

† Ratio of polyunsaturated to saturated fatty acids in the experimental diets.

‡ The mean value during the SS dietary period (40.2 ± 0.9 pmol/L) was significantly higher according to least-square means than during the HF-LC and LF-HC periods (36.9 ± 0.9 and 37.2 ± 0.9, respectively); $p < 0.05$.

contrast, the degree of unsaturation of dietary fats (P:S) had no effect on any of the hormones studied. Similarly, no significant interactions between the variables were observed for any of the hormones studied.

Plasma insulin levels (shown in Table 1) were significantly higher during the LF-HC diet compared with the HF-LC or SS diets as well as during the luteal phase of the menstrual cycle compared with the follicular phase. Plasma glucagon levels (Table 2) were not significantly affected by the amount of fat or carbohydrate nor by the level of dietary lipid unsaturation. The higher levels observed during the SS dietary period are surprising because the HF-LC and SS diets were compositionally similar (6) except for the P:S, which was 0.5 for the SS diets.

Plasma cortisol (Table 3) and DHEA-S (Table 5) were significantly lower on the LF-HC compared with the HF-LC diet. The similarities in cortisol and DHEA-S levels between HF-LC and SS diet regimens are reasonable considering the similarities of these diets. Plasma growth hormone levels (Table 4) were not altered by dietary fat

levels but were affected by time of the menstrual cycle, being higher during the midluteal than during the mid-follicular phase.

Discussion

The dietary lipid modifications did result in small but statistically significant changes in plasma lipids of these women as reported earlier (6). The low-fat diet increased plasma triglyceride levels. HDL-cholesterol was higher in subjects fed the diet with more unsaturated fat (P:S = 1.0), though a significant increase was seen only during the LF-HC dietary period. We now report significant effects of the level of dietary fat on plasma insulin, cortisol, and DHEA-S in these premenopausal women. The increased plasma insulin and decreased cortisol and DHEA-S observed on the LF-HC diet would favor a lipogenic response and may at least partly explain the hyperlipidemia observed in these women when fed the LF-HC diet. The inverse relation of dietary fat to plasma insulin

TABLE 3
Effect of level and unsaturation of dietary lipids on plasma immunoreactive cortisol levels in premenopausal women*

P:S†	Menstrual-cycle phase	Dietary period‡		
		Self-selected (SS)	High-fat, low-carbohydrate (HF-LC)	Low-fat, high-carbohydrate (LF-HC)
			<i>nmol/L</i>	
0.3	Follicular	329 ± 23	362 ± 23	314 ± 23
0.3	Luteal	402 ± 25	345 ± 24	317 ± 25
1.0	Follicular	369 ± 23	329 ± 23	316 ± 22
1.0	Luteal	382 ± 22	347 ± 22	289 ± 23

* Least-square means ± standard error of least-square means.

† Ratio of polyunsaturated to saturated fatty acids in the experimental diets.

‡ The mean value during the LF-HC diet (309 ± 12 nmol/L) was significantly lower according to least-square means than during the SS and HF-LC periods (337 ± 12 and 346 ± 12, respectively); $p < 0.05$.

TABLE 4

Effect of level and unsaturation of dietary lipids on plasma immunoreactive growth hormone levels in premenopausal women*

P:S†	Menstrual-cycle phase‡	Dietary period		
		Self-selected (SS)	High-fat, low-carbohydrate (HF-LC)	Low-fat, high-carbohydrate (LF-HC)
			$\mu\text{g/L}$	
0.3	Follicular	1.76 ± 0.47	2.34 ± 0.49	1.50 ± 0.47
0.3	Luteal	2.66 ± 0.61	2.67 ± 0.52	2.59 ± 0.49
1.0	Follicular	1.24 ± 0.52	0.91 ± 0.58	2.59 ± 0.45
1.0	Luteal	2.30 ± 0.47	1.60 ± 0.27	2.57 ± 0.47

* Least-square means ± standard error of least-square means.

† Ratio of polyunsaturated to saturated fatty acids in the experimental diets.

‡ The mean value during the luteal phase ($2.4 \pm 0.21 \mu\text{g/L}$) was significantly higher according to least-square means than during the follicular phase (1.72 ± 0.20); $p < 0.05$.

levels observed here is in agreement with previous reports in which subjects fed a low-fat, high-carbohydrate diet had an increase in plasma insulin (15) whereas those fed a high-fat, low-carbohydrate diet had decreased plasma insulin (20). Increased plasma insulin was also observed when a low-fat diet was given to human subjects intraduodenally (21). Beck-Nielsen et al (22) did not observe any changes in plasma insulin when they fed isocaloric low-fat or low-carbohydrate diets to normal men but hypercaloric diets with high carbohydrate significantly increased plasma insulin level. However, in pregnant women ingestion of pure triglyceride produced an increase in plasma insulin (23). It is important to note that in most instances it is the type of carbohydrate rather than the amount that elicits a greater insulin response. In rats, feeding a high-fat diet was shown to decrease (24) as well as increase (11, 25) plasma insulin levels. However, this difference in response may be due to the use of different strains of rats in these studies because different rat strains show different hormonal responses (26).

In normal men (21) and in pregnant women (24) a

high-fat, low-carbohydrate diet was shown to increase plasma glucagon levels. In the present study we did not observe differences in plasma glucagon when normal premenopausal women were fed high- or low-fat diets. The decrease in plasma glucagon levels during feeding of experimental diets compared with a basal diet could be due to a change in one or more micronutrients.

Hamalainen et al (27) studied the effect of different levels of dietary fat on plasma steroid hormones in normal men. Feeding a low-fat diet with a high P:S lowered serum testosterone and 4-androstenedione in comparison with feeding a high-fat diet with a very low P:S ratio. The decrease in DHEA-S was not significant and estradiol showed no change. In the present study lower levels of DHEA-S and cortisol were observed when women were fed the LF-HC diet than when they were fed the HF-LC diet.

Cortisol and DHEA are derived from the same precursor, pregnenolone (28). In the present study plasma levels of both were lower when the subjects were fed diets with low fat levels. Thus, low dietary fat either decreases

TABLE 5

Effect of level and unsaturation of dietary lipids on plasma immunoreactive DHEA-S levels in premenopausal women*

P:S†	Menstrual-cycle phase	Dietary period‡		
		Self-selected (SS)	High-fat, low-carbohydrate (HF-LC)	Low-fat, high-carbohydrate (LF-HC)
			$\mu\text{mol/L}$	
0.3	Follicular	4.76 ± 0.20	4.24 ± 0.20	3.40 ± 0.20
0.3	Luteal	3.97 ± 0.22	3.91 ± 0.21	3.75 ± 0.22
1.0	Follicular	4.61 ± 0.19	4.29 ± 0.20	3.60 ± 0.19
1.0	Luteal	4.28 ± 0.19	4.39 ± 0.20	3.53 ± 0.22

* Least-square means ± standard error of least-square means.

† Ratio of polyunsaturated to saturated fatty acids in the experimental diets.

‡ The mean value during the LF-HC diet ($3.57 \pm 0.10 \mu\text{mol/L}$) was significantly lower according to least-square means than during the SS and HF-LC diets (4.40 ± 0.10 and $4.19 \pm 0.10 \mu\text{mol/L}$, respectively); $p < 0.05$.

TABLE 6
Significant effects of various parameters by analysis of variance (ANOVA)

	Insulin	Glucagon	Cortisol	Growth hormone	DHEA-S
Dietary period (high- vs low-fat)	0.01	0.02	0.002	NS	0.0001
P:S	NS	NS	NS	NS	NS
Menstrual cycle	0.0003	NS	NS	0.006	NS
Dietary period × P:S	NS	NS	NS	NS	NS
Dietary period × menstrual-cycle phase	NS	NS	NS	NS	NS
P:S × menstrual-cycle phase	NS	NS	NS	NS	NS
Dietary period × P:S × menstrual-cycle phase	NS	NS	NS	NS	NS

pregnenolone level or its conversion to these steroids. Decreases in plasma DHEA-S levels have also been observed with age (29, 30) and in disorders of lipid metabolism such as hypercholesterolemia (31, 32), cardiovascular disease (30, 33), and obesity (30, 34). Similarly, DHEA treatment prevents hyperglycemia, islet atrophy, and severity of diabetes in diabetic mice (28, 35). It also lowers serum insulin levels in obese rats (36). In the present study with normal female subjects, we observed the expected negative correlation between plasma DHEA-S and insulin levels.

In addition to dietary lipids, the menstrual cycle itself can alter plasma lipid composition in women (37-40). In women total cholesterol and triglyceride levels were higher and the HDL-cholesterol level was lower in the follicular phase than in the luteal phase (37). We now report that hormones involved in lipid metabolism are also altered during different phases of the cycle. Significantly higher levels of plasma insulin and growth hormone were observed during the luteal phase than during the follicular phase. It is interesting to note that the caloric requirements of women are higher during the luteal phase (41, 42) of the menstrual cycle. It is, however, not known whether this is a consequence of the increased insulin and growth hormone levels that we observed during the luteal phase.

We did not observe any effect of the level of dietary fat on plasma growth hormone in premenopausal women but Johannessen et al (20) reported higher plasma growth hormone in male subjects fed a fat-enriched diet than when fed a carbohydrate-enriched diet. High-fat diets have also been reported to increase plasma prolactin (43-45), somatostatin (21), and gastric inhibitory polypeptide (46) and to decrease T_3 (20). Similarly, an intraduodenal load of high fat in humans increased plasma gastrin and vasoactive intestinal polypeptide whereas a high carbohydrate load increased plasma gastric inhibitory polypeptide (47).

It is thus clear that in humans the level of fat in the diet alters the concentration of several hormones in plasma, especially pancreatic, gut, and adrenal hormones, that are involved in lipid metabolism, which in turn control plasma lipid levels. In addition, phases of the menstrual cycle per se affect plasma insulin and growth hormone. However, the nature of dietary lipids, viz polyunsaturated vs saturated fat, does not appear to have any major

effect on plasma hormone levels. Thus, diets with varying concentrations of fat and carbohydrate lead to adaptive changes in hormonal balance in normal human subjects.

The results from this study appear to indicate that the relative contribution of dietary fat is an important determinant of circulating hormonal levels of insulin, cortisol, and DHEA-S. The long-term effects of moderate changes in hormonal levels induced by diet on chronic metabolic disorders is still vigorously debated. □

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References

- Hill R, Linazasoro JM, Chevallier F, Chaikoff IL. Regulation of hepatic lipogenesis: the influence of dietary fats. *J Biol Chem* 1958;233:305-10.
- Weisweiler P, Janetschek P, Schwandt P. Influence of polyunsaturated fats and fat restriction on serum lipoproteins in humans. *Metabolism* 1985;34:83-7.
- Snook JT, DeLany JP, Vivian VM. Effect of moderate to very low fat defined formula diets on serum lipids in healthy subjects. *Lipids* 1985;20:808-16.
- Brussaard JH, Katan MB, Groot PHE, Havekes LM, Hautvast JGAJ. Serum lipoproteins of healthy persons fed a low-fat diet or a polyunsaturated fat diet for three months. *Atherosclerosis* 1982;42:205-19.
- Brussaard JH, Dallinga-Thie G, Groot PHE, Katan MB. Effects of amount and type of dietary fat on serum lipids, lipoproteins and apolipoproteins in man. *Atherosclerosis* 1980;36:515-27.
- Jones DY, Judd JT, Taylor PR, Campbell WS, Nair PP. Influence of caloric contribution and saturation of dietary fat on plasma lipids in premenopausal women. *Am J Clin Nutr* 1987;45:1451-6.
- Eaton RP, Schade DS. Hormonal antagonism of insulin. In: Brodoff BN, Bleicher SJ, eds. *Diabetes and obesity*. Baltimore, MD: Williams and Wilkins, 1982:27-34.
- Hodges RE, Krehl WA. The role of carbohydrates in lipid metabolism. *Am J Clin Nutr* 1965;17:334-46.
- Dumaswala UJ, Dumaswala RU, Venkataraman A. The relative effect of dietary fats and carbohydrates on lipid metabolism in the albino rat. *Ital J Biochem* 1976;25:289-303.
- Deshais J. Plasma lipoprotein cholesterol and triglycerides and lipoprotein lipase activity in epididymal white adipose tissue of rats

- fed high sucrose or high corn oil diets. *Can J Physiol Pharmacol* 1986;64:885-91.
11. Gardner LB, Reiser S. Effect of dietary carbohydrate on fasting levels of human growth hormone and cortisol. *Proc Soc Exp Biol Med* 1982;169:36-40.
 12. Ellwood KC, Michaelis OE IV, Emberland JJ, Bhatena SJ. Hormonal and lipogenic and gluconeogenic enzymatic responses in LA/N-corpulent rats. *Proc Soc Exp Biol Med* 1985;129:163-7.
 13. Hallfrisch J, Cohen L, Reiser S. Effect of feeding rats sucrose in a high fat diet. *J Nutr* 1981;111:531-6.
 14. Bhatena SJ, Aparicio P, Revett K, Voyles N, Recant L. Effect of dietary carbohydrates on glucagon and insulin receptors in genetically obese female Zucker rats. *J Nutr* 1987;117:1291-7.
 15. Gutniak M, Grill V, Effendic S. Effect of composition of mixed meals—low- versus high-carbohydrate content—on insulin, glucagon, and somatostatin release in healthy humans and in patients with NIDDM. *Diabetes Care* 1986;3:244-9.
 16. Hill PB, Wynder EL. Effect of a vegetarian diet and dexamethasone on plasma prolactin, testosterone and dehydroepiandrosterone in men and women. *Cancer Lett* 1979;7:273-82.
 17. Marks PH, Banks J. Inhibition of mammalian glucose-6-phosphate dehydrogenase by steroids. *Proc Natl Acad Sci USA* 1960;46:447-52.
 18. Oertel GW, Benes P. The effects of steroids on glucose-6-phosphate dehydrogenase. *J Steroid Biochem* 1972;3:493-6.
 19. Statistical Analysis System Institute. SAS user's guide: statistics, version 5. Cary, NC: SAS Institute, Inc, 1982.
 20. Johannessen A, Hagen C, Galbo H. Prolactin, growth hormone, thyrotropin, 3,5,3'-triiodothyronine, and thyroxine responses to exercise after fat- and carbohydrate-enriched diet. *J Clin Endocrinol Metab* 1981;52:56-61.
 21. Lucey MR, Fairclough PD, Wass JA, et al. Response of circulating somatostatin, insulin, gastrin and GIP to intraduodenal infusion of nutrients in normal man. *Clin Endocrinol* 1984;21:209-17.
 22. Beck-Nielsen H, Pedersen O, Sorensen NS. Effect of diet on the cellular insulin binding and the insulin sensitivity in young healthy subjects. *Diabetologia* 1978;15:289-96.
 23. Hornnes PJ, Kuhl C, Krarup T. Gastroentero-pancreatic hormones in normal and gestational-diabetic pregnancy: response to oral lipid. *Metabolism* 1984;33:304-8.
 24. Ip C, Tepperman HM, Holohan P, Tepperman J. Insulin binding and insulin response of adipocytes from rats adapted to fat feeding. *J Lipid Res* 1976;17:588-99.
 25. Grundleger ML, Thenen SW. Decreased insulin binding, glucose transport, and glucose metabolism in soleus muscle of rats fed a high fat diet. *Diabetes* 1982;31:232-7.
 26. Gardner LB, Reiser S. Differences in hormonal regulation of carbohydrate metabolism between strains of rats. *Comp Biochem Physiol* 1979;64:589-92.
 27. Hamalainen E, Adlercreutz H, Puska P, Pietinen P. Diet and serum sex hormones in healthy men. *J Steroid Biochem* 1984;20:459-64.
 28. Coleman DL, Leiter EH, Appleweig N. Therapeutic effects of dehydroepiandrosterone metabolites in diabetes mutant mice (C57BL/KSJ-db/db). *Endocrinology* 1984;115:239-43.
 29. Migeon CJ, Keller AR, Lawrence B, Shepard TH. Dehydroepiandrosterone and androsterone levels in human plasma. Effect of age and sex, day to day and diurnal variations. *J Clin Endocrinol Metab* 1957;17:1051-62.
 30. Barrett-Conner E, Kahn K-T, Yen SSC. A prospective study of dehydroepiandrosterone sulfate, mortality and cardiovascular disease. *N Engl J Med* 1986;315:1519-24.
 31. Sonka J, Fassati M, Fassati P, Gregorova I, Picek K. Serum lipids and dehydroepiandrosterone excretion in normal subjects. *J Lipid Res* 1968;9:769-72.
 32. Lopez-S A, Wingo C, Hebert JA. Total serum cholesterol and urinary dehydroepiandrosterone in humans. *Atherosclerosis* 1976;24:471-81.
 33. Lopez-S A. Metabolic and endocrine factors in aging. In: Rothschild H, Chapman CF, eds. Risk factors for senility. New York: Oxford University Press, 1984:205-19.
 34. Yen TT, Allan JA, Pearson DV, Acton JM, Greenberg MM. Prevention of obesity in A^{y/a} mice by dehydroepiandrosterone. *Lipids* 1977;12:409-13.
 35. Coleman DL, Leiter EH, Schwizer RW. Therapeutic effects of dehydroepiandrosterone (DHEA) in diabetic mice. *Diabetes* 1982;31:830-3.
 36. Gansler TS, Muller S, Cleary MP. Chronic administration of dehydroepiandrosterone reduces pancreatic B-cell hyperplasia and hyperinsulinemia in genetically obese Zucker rats. *Proc Soc Exp Biol Med* 1985;180:155-62.
 37. Jones DY, Judd JT, Taylor PR, Campbell WS, Nair PP. Menstrual cycle effect on plasma lipids. *Metabolism* 1988;37:1-2.
 38. Oliver MF, Boyd GS. Changes in the plasma lipids during the menstrual cycle. *Clin Sci* 1953;12:217-22.
 39. Low-Beer TS, Wicks ACB, Heaton KW, Durrington P, Yeates J. Fluctuations of serum and bile lipid concentrations during the menstrual cycle. *Br Med J* 1977;1:1568-70.
 40. Kim H-J, Kalkhoff RK. Changes in lipoprotein composition during the menstrual cycle. *Metabolism* 1979;28:663-8.
 41. Dalvit SP. The effect of menstrual cycle on patterns of food intake. *Am J Clin Nutr* 1981;34:1811-5.
 42. Webb P. 24-hour energy expenditure and the menstrual cycle. *Am J Clin Nutr* 1986;44:614-9.
 43. Ishizuka B, Quigley ME, Yen SS. Pituitary hormone release in response to food ingestion: evidence for neuroendocrine signals from gut to brain. *J Clin Endocrinol Metab* 1983;57:1111-6.
 44. Hill P, Wynder ER. Diet and prolactin release. *Lancet* 1976;2:806-7.
 45. Cohen LA, Didato F, Chan PC. Effects of altered dietary fat intake on serum prolactin titer. *Fed Proc* 1974;33:601-12.
 46. Ohneda A, Kobayashi T, Nihei J. Response of gastric inhibitory polypeptide to fat ingestion in normal dogs. *Regul Pept* 1984;8:123-30.
 47. Miazza B, Palma R, Lachance JR, Chayvialle JA, Jonard PP, Modigliani R. Jejunal secretory effect of intraduodenal food in humans. A comparison of mixed nutrients, proteins, lipids, and carbohydrates. *Gastroenterology* 1985;88:1215-22.