SAMPLE

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Steroids

By Raymond Peat, Ph.D.

This type of molecule might be the most common carbon compound in the universe. It is made by single celled organisms, by plants, and by animals, and has many kinds of function. The steroid hormones are involved in all aspects of animal physiology, and overlap with control functions of the nervous system, peptide hormones, metabolites, prostaglandins, cyclic nucleotides, etc. Sometimes people speak of "steroids" when they mean glucocorticoids such as cortisol or a synthetic like dexamethasone, or, among athletes, when they mean anabolic steroids or synthetic androgens; and so it is common to associate "steroids" with harmful side effects. All foods contain steroids and sterols (a major type, containing an alcohol group and a side-chain) some of which are beneficial and some of which are toxic or allergenic.

In animals, cholesterol is the basic sterol molecule, which is massively converted into other substances, including the steroid hormones. Thyroid hormone and vitamin A are required for this conversion. The first step occurs in the energy-producing mitochondrion, where cholesterol loses its side-chain and is slightly oxidized, producing pregnenolone. Being less fat soluble than cholesterol, pregnenolone leaves the mitochondrion, so it can't inhibit its own synthesis. Rather, it seems to stimulate its own synthesis, though this isn't as clearly established as in the case of progesterone.

Depending on the tissue, pregnenolone will be converted by enzymes in the cytoplasm into either progesterone or DHEA (Also called DHA, dehydroepiandrosterone). The fact that progesterone (and probably pregnenolone) stimulates its own synthesis means that taking it does not suppress the body's ability to synthesize it, as happens with cortisol. Sometimes, one dose or a few doses can restore the body's ability to produce enough of its own.

Progesterone also allows the thyroid gland to secrete its hormones, especially when the thyroid function has been inhibited by estrogen. Since the thyroid hormone is needed to produce progesterone, a supplement of either tends to normalize both thyroid and progesterone production.

Progesterone and DHEA are the precursors for the other more specialized steroid hormones, including cortisol, aldosterone (sodium-retaining hormone), estrogen, and testosterone. The formation of these other hormones is tightly regulated, so that taking the precursor will correct a deficiency of a specialized hormone, but will not create an excess. At least in the case of progesterone, an excess tends to balance or neutralize an excess of the specialized hormone, so it has been described as having anti-androgenic, anti-estrogen, ant-aldosterone, and anti-cortisol functions.

Many steroids have a protective ("catatoxic") action against a wide variety of poisons. Some of the quick effects (e.g., within 10 minutes) of progesterone and pregnenolone probably represent a catatoxic action, as well as a neutralizing or balancing of excessive estrogen or cortisol. Improved metabolic efficiency, sparing oxygen and glucose, will have a quick effect in reducing edema.

> **"All foods contain steroids and sterols... some of which are beneficial and some of which are toxic..."**

During pregnancy, very large amounts of progesterone are made. It protects and stabilizes practically all functions of both the mother and the fetus. Progesterone, glucose and the thyroid hormones powerfully influence the brain development and intelligence of the baby, probably by influencing both the number and the size of brain cells, and the quality of their functioning.

Part of progesterone's protective effect is a result of its quieting effect on cells. For example, it tends to prevent seizure activity in brain cells. During childbirth, its normal function is to act as an anesthetic. When the level of estrogen is too high, progesterone can't achieve this effect. In a non-pregnant person, it is important to determine the minimum effective dose by taking only a few drops at a

time, and repeating this small dose about every 20 minutes until symptoms have been controlled. Otherwise, serious "drunkenness" can be produced, with loss of coordination, and even unconsciousness.

The only solvent for progesterone which isn't toxic and which will dissolve an effective quantity, is vitamin E. In this form, it can be absorbed through the skin or other membranes, or can be taken orally. Taken orally, it is absorbed as chylomicrons, going into the general circulation (as vitamin E does), instead of to the liver where it would be prepared for excretion. In this form, therefore, it is fully and quickly available to all tissues. It is approximately 20 times more powerful in its action than other preparations, so it is important to use it in physiological quantities, rather than in the huge doses commonly given rectally or by injection. Ten or 20 mg. is often an effective dose, though people with low thyroid or high estrogen sometimes use 50 to 100 mg. per day. In the customary 10% solution, one drop contains about 3 mg. progesterone, and 1 ml. (1/4 tsp.) contains 100 mg. The first dose should never be more than 15 mg. (An ounce of 10% progesterone in vitamin E is $15; a dozen one-ounce bottles is $144.)

Pregnenolone, taken orally, does nothing noticeable to a healthy animal or person, but if the stress-related hormones are elevated, they return to normal when pregnenolone is taken. The brain contains much more pregnenolone, DHEA, and progesterone than do other organs or the blood, and these levels decrease progressively with age. Older people are more likely to feel an effect from pregnenolone, than are young people. (A ten gram bottle of pregnenolone is $20; 1/4 kg. is $250. A tenth of a gram is a reasonable first dose, though some people seem to need as much as 1 gram per day.)

Thyroid

By Raymond Peat, Ph.D.

Measuring the amount of thyroid in the blood isn't a good way to evaluate adequacy of thyroid function, since the response of tissues to the hormone can be suppressed (for example, by unsaturated fats).

In the 1930's accurate diagnosis was made by evaluating a variety of indications, including basal oxygen consumption, serum cholesterol level, pulse rate, temperature, carotenemia, bowel function, and quality of hair and skin. A good estimate can be made using only the temperature and pulse rate.

Oral or armpit temperature, in the morning before getting out of bed, should be around 98° F, and it should rise to 98.6° by mid-morning. This is not valid of you sleep under an electric blanket, or if the weather is hot and humid. A person who is hypothyroid produces heat at a low rate, but doesn't lose it at the normal rate, since there is less sweating, and the skin is relatively cool. Many hypothyroid people compensate with high adrenalin production (sometimes 40 times higher than normal), and this tends to keep the skin cool, especially on the hands, feet, and nose. The high adrenalin is the consequence of low blood glucose, so a feeding of carbohydrate, such as a glass of orange juice, will sometimes lower the pulse rate momentarily. Healthy populations have an average resting pulse rate of about 85 per minute. Especially in hot weather it is useful to consider both temperature and pulse rate.

The Achilles tendon reflex is another quick way to estimate thyroid function. This reflex is used because of the insignificant weight of the toes in relation to contraction of the gastrocnemius muscle. The T (repolarization) wave on the electrocardiogram is a similar indicator of the rate of energy production. Thumping the Achilles tendon causes the muscle to contract (unless it is already in a semi-contracted state, which isn't uncommon). The contraction consumes energy, and the muscle can't relax until enough energy has been produced to restore the threshold and the readiness for a new contraction.

"Healthy populations have an average pulse rate of about 85 per minute."

If energy production is efficient, relaxation is faster than the passive return motion of the foot, so the foot swings freely back to its original position, and over shoots slightly, causing a slight swinging action. In hypothyroidism, the foot returns as if controlled by a pneumatic door-closer, and settles slowly and precisely into its relaxed position, sometimes with a hesitating, intermittent motion. This slow replenishment of energy, and slow relaxation, can cause muscles to cramp easily. The aching leg muscles of children at the end of an active day are often a sign of hypothyroidism, and sometimes the gastrocnemius muscle becomes very swollen and hypertrophied in hypothyroid children. The same process, of slow energy regeneration, can cause rhythm disturbance in the heart, and often causes insomnia and restless sleep.

The thyroid gland secretes about 3 parts of thyroxin to one part of triiodothyronine, and this allows the liver to regulate thyroid function, by converting more of the T4 to the active T3 when there is an abundance of energy. Glucose is essential for the conversion, so during fasting there is a sharp decrease in metabolic rate, and in experiments, 200 or 300 calories of carbohydrates can be added to the diet without causing fat storage.

When the liver is the main cause of hypothyroidism, your temperature (and especially the temperature of your nose, hands and feet) will fall when you are hungry, and will rise when you eat carbohydrates. If a hypothyroid person has a very slow pulse, and feels lethargic, it seems that there is little adrenalin; in this case, a feeding of carbohydrate is likely to increase both the pulse rate and the temperature, as the liver is permitted to form the active T3 hormone.

Women often have above-average thyroxin, with symptoms of hypothyroidism. This is apparently because it isn't being converted to the active form (T3). Before using a Cytomel (T3) supplement, it might be possible to solve the problem with diet alone. A piece of fruit or a glass of juice or milk between meals, and adequate animal protein (or potato protein) in the diet is sometimes enough to allow the liver to produce the hormone. If Cytomel is used, it is efficient to approximate the physiological rate of T3 formation, by nibbling one (10 or 25 mcg.) tablet during the day. When a large amount is taken at one time, the liver is likely to convert much of it to the inactive reverse-T3 form, in a normal defensive response.

Women normally have less active livers than men do. Estrogen can have a directly toxic effect on the liver, but the normal reason for the difference is probably that temperature and thyroid function strongly influence the liver, and are generally lower in women than in men. Estrogen inhibits the secretion of hormone by the thyroid gland itself, probably by inhibiting the proteolytic enzyme which dissolves the colloid. Progesterone has the opposite effect, promoting the release of the hormones from the gland. At puberty, in pregnancy, and at menopause, the thyroid gland often enlarges, probably as a result of estrogen dominance.

Thyroid function stimulates the liver to inactivate estrogen for secretion, so estrogen dominance can create a vicious circle, in which excess estrogen (or deficient progesterone) blocks thyroid secretion, causing the liver to allow estrogen to accumulate to even higher levels. Progesterone (even one dose, in some causes) can break the cycle. However, if the gland is very big, the person can experience a few months of hyperthyroidism, as the gland returns to normal. It is better to allow the enlarged gland to shrink more slowly by using a thyroid supplement. If an enlarged gland does begin to secrete too much thyroid hormone, it can be controlled with tablets of propylthiouracil, or even with raw cabbage or cabbage juice, and cysteine-rich meats, including liver.

Besides fasting, or chronic protein deficiency, the common causes of hypothyroidism are excessive stress or "aerobic" (i.e., anaerobic) exercise, and diets containing beans, lentils, nuts, unsaturated fats (including carotene), and undercooked broccoli, cauliflower, cabbage, or mustard greens. Many health conscious people become hypothyroid with a synergistic program of undercooked vegetables, legumes instead of animal proteins, oils instead of butter, carotene instead of vitamin A, and breathless exercise instead of a stimulating life.

3 : 1

T4 : T3

Si Hypo à cause de foie = Temp° ↓ quand Tu as faim (nez, main, pied) et ↑ si tu manges

Si Hyp à Fréble FC et ressent léthargique ça veut dire pas assez adrénaline. Si prend carbs ça ↑ Temp et FC. Car le foie recommence à faire du T3

Du lait entre 2 repas, lactose & patate, va stimuler le foie à produire T3

THYRO stimule le foie à inactiver les T3 par élimination Sauf que lactose inhibe la THYRO qui elle est nécessaire pour stimuler le foie.

Propylthiouracil ou chou cru, sur le chou + cystéine + du foie inhibe thyroïde

of oestroprogestins due to their effects on metabolic parameters. As shown by prescription for contraceptive use, **replacement therapy with oral synthetic oestrogens induces a diabetogenic tendency as well as hypertensive, dyslipidaemic and thrombogenic risks,** especially when associated with progestins issued from nortestosterone. Reducing the oestrogen doses, using equine sulfoconjugates and selecting non-androgenic progestins has already minimized these deleterious effects. The present availability of oral or percutaneous natural 17 beta oestradiol and of norpregnanes calls for reconsideration of the glucidic risk due to oestroprogestin prescription. A few studies have already shown that in fact they can improve glucose tolerance. The recommended substitution of menopause to prevent atherosclerosis must lead to a better characterization of its glycaemic and insulinaemic effects.

"Effects of oral contraceptives on carbohydrate and lipid metabolisms in a healthy population: the Telecom study," Simon D; Senan C; Garnier P; Saint-Paul M; Garat E; Thibult N; Papoz L, Am J Obstet Gynecol, 1990 Jul, 163:1 Pt 2, 382-7. "In a cross-sectional study that aimed to identify risk factors for diabetes, 1290 consecutive, healthy, nonpregnant women of child-bearing age were examined in a center for preventive medicine. An in-depth interview about menses, use of oral contraceptives, and menopause was performed. Plasma glucose at fasting and 2 hours after a 75 gm glucose load, glycated hemoglobin A1c, fasting plasma insulin, total plasma cholesterol, and triglycerides were measured. Compared with nonusers taking no progestogens, oral contraceptive users (n = 431; 33.4%) were younger (p less than 0.001) and leaner (p less than 0.001). After adjustment for age and body mass index, oral contraceptive users had higher 2-hour plasma glucose (p less than 0.001), higher fasting plasma insulin (p less than 0.01), and higher triglycerides levels (p less than 0.01). Fasting plasma glucose, glycated hemoglobin A1c, and total cholesterol did not significantly differ between the two groups. In relation to dosage and types of steroid components, few differences have been found between high-dose and low-dose oral contraceptives or according to the estrogen-progestogen balance of the preparations. Use of oral contraceptives **appears to induce an increase of insulin-resistance markers, which have recently been cited as risk factors for ischemic vascular diseases.** These markers should be carefully monitored in oral contraceptive users.

"Effect of estrogen on hyperprolactinemia-induced glucose intolerance in SHN mice," Matsuda M; Mori T, *Proc Soc Exp Biol Med,* 1996 Jul, 212:3, 243-7. "The effects of prolactin (PRL) on circulating levels of glucose and insulin, and of estradiol on hyperprolactinemia-indu ced glucose intolerance of tissues were studied in pituitary-grafted SHN mice (PG mice) and sham-operated controls. Pituitary grafting (PG) decreased blood glucose levels in male mice at 1 and 3 months after the operation but did not alter those in females. PG had little effect on serum insulin levels in males, but increased those in females. In female mice at 2 months after PG, blood glucose levels were significantly higher at 1, 2, and 4 hr after glucose load when compared with those in controls. In contrast, there was no significant difference in blood glucose levels after glucose load between male PG and control mice. The rate at which blood glucose levels decreased was slower in female PG mice than in controls during the 30 min after insulin injection, whereas there was no difference in the rate after insulin injection between male PG and control mice. In ovariectomized (Ovx) mice, no significant difference was found in the blood glucose levels after a glucose load between PG and control groups at 2 months after PG. In Ovx mice treated daily with estrogen, however, a PG-dependent high level of blood glucose was observed after glucose load. These results **suggest that hyperprolactinemia decreases glucose tolerance via an increase in insulin resistance in female SHN mice and that estrogen is essential to the expression of the PRL effect."**

NOTICE THE PROPAGANDISTIC USE OF SAFFLOWER OIL AS THE CONTROL DIET: "Dietary fish oil delays puberty in female rats," Zhang Z; Benson B; Logan JL, *Biol Reprod,* 1992 Dec, 47:6, 998-1003. "Marine oils contain eicosapentaenoic acid, a fatty acid that competes for cyclooxygenase and reduces the synthesis of dienoic prostanoids including prostaglandin E2 (PGE2). Since PGE2 plays an important role in the estrogen-stimulated release of hypothalamic GnRH on proestrus, it was postulated that a diet containing fish oil would delay first ovulation through inhibitory effects on GnRH release. Thirty, 22-day-old female Sprague-Dawley rats were fed a diet containing fish oil ad libitum. **Controls were pair-fed an identical diet with the substitution of safflower oil as the dietary fat.** All rats were killed on the morning of first metestrus after vaginal opening and the display of an estrous smear(s). Fish oil feeding did not affect growth as indicated by the lack of an observed effect on body weights or femur lengths. On the other hand, pituitary, ovarian, and uterine weights were significantly lower in the rats fed fish oil ($p < 0.001$). The age at first estrus of the rats fed fish oil was significantly increased compared with the controls (42.9 +/- 1.0 vs. 36.1 +/- 0.3 days; $p < 0.001$), whereas the number of rats with corpora lutea (CL), as well as the number of CL per ovary (2.3 +/- 0.4 vs 4.8 +/- 0.6 for controls; $p < 0.001$) was significantly reduced by fish oil feeding. GnRH concentration in the preoptic area/hypothalamus was significantly increased in the fish oil-fed rats (21.4 +/- 4.0 pg/mg vs. 7.6 +/- 2.2 pg/mg for controls; $p < 0.01$); radioimmunoassable hypothalamic PGE2 was concomitantly reduced ...."

"Effects of androgens on haemostasis," Winkler UH, Maturitas, 1996 Jul, 24:3, 147-55. **"Androgen deficiency is associated with an increased incidence of cardiovascular disease. There is evidence that thromboembolic disease as well as myocardial infarction in hypogonadic males are mediated by low baseline fibrinolytic activity.**

Hypogonadism in males is associated with an enhancement of fibrinolytic inhibition via increased synthesis of the plasminogen activator inhibitor PAI 1."

"Progesterone production from granulosa cells of individual human follicles derived from diabetic and nondiabetic subjects," Diamond MP; Lavy G; Polan ML, *Int J Fertil,* 1989 May-Jun, 34:3, 204-8. "Insulin and insulin-like growth factors have been implicated in the stimulation of ovarian steroidogenesis. To assess the effect of diabetes mellitus on this process, a comparison was made of progesterone production by cultured granulosa cells (50,000 cells/well) from 11 **individual follicles of nondiabetic and 6 individual follicles of diabetic women.** Diabetic metabolic control was fair [HbA1C 6.8, 8.7 (nl 5.0-7.5)]. Cells were collected by laparoscopic follicular aspiration after ovulation induction and isolated by Percoll gradient centrifugation. Progesterone production was measured after culture with hCG (10 IU/mL) or insulin (100 microU/mL). In both nondiabetic and diabetic groups on day 4, hCG significantly stimulated progesterone production (1,686 +/- 1,268 ng/mL to 4,123 +/- 2,825 ng/mL and 1,059 +/- 249 ng/mL to 1,506 +/- 245 ng/mL, respectively). **In nondiabetic follicles, insulin also stimulated progesterone production on days 4 (2366 +/- 1032 ng/mL to 3699 +/- 1582 ng/mL; P less than .05) and 7 (987 +/- 475 ng/mL to 1858 +/- 929 ng/mL; P less than .05); this response was not noted in diabetic granulosa cells. We suggest that insulin-stimulated progesterone production by granulosa cells isolated in the presence of fair diabetic metabolic control is impaired."**

"Breast cancer risk in rats fed a diet high in n-6 polyunsaturated fatty acids during pregnancy," Hilakivi-Clarke L; Onojafe I; Raygada M; Cho E; Clarke R; Lippman ME, *J Natl Cancer Inst,* 1996 Dec 18, 88:24, 1821-7. **"...Since a high-fat diet may increase circulating estrogen levels** and possibly breast cancer risk, dietary factors during pregnancy could influence the risk of developing this disease." "Pregnant or virgin female Sprague-Dawley rats that had been previously treated with 10 mg 7, 12-dimethylbenz[a]anthracene (DMBA) by oral gavage when 55 days old were assigned to one of two isocaloric diets containing either 16% calories from fat (low-fat) or 43% calories from fat (high-fat) for the length of pregnancy or for the equivalent time of approximately 21 days. There were 20 pregnant and 10 nonpregnant DMBA-treated rats per group. Ten additional pregnant animals (not previously treated with DMBA) per group were used for hormone analysis. **The fat source used was corn oil, which is high in n-6 polyunsaturated fatty acids, primarily linoleic acid.** The animals were checked for tumors at least once per week by palpation. The tumor size, number, and latency to appearance after carcinogen exposure were recorded. The statistical significance of observed differences was tested by use of appropriate two-sided tests. RESULTS: Female rats on different diets had virtually identical food intakes and weight gains during pregnancy. **On gestation day 19, serum estradiol levels were approximately twofold higher in rats fed a high-fat diet than in rats fed a low-fat diet (P < .02).** The serum insulin levels and insulin/glucose ratios (an index of insulin resistance) in rats fed the high-fat diet were approximately twofold lower than in rats fed the low-fat diet, but the differences did not reach statistical significance (P < .09 and P < .09, respectively). On week 18 following DMBA administration, the number of rats developing mammary tumors was significantly higher in the group exposed to a high-fat diet (40% of animals) than in the group exposed to a low-fat diet (10% of animals) during pregnancy (P < .05). Tumor multiplicity, latency to tumor appearance, and size of tumors upon first detection were similar among the dietary groups. No intergroup differences in the mammary tumor incidence were noted in virgin animals that were exposed to the high- or low-fat diets for an equivalent period of time. CONCLUSIONS: **Our findings indicate that consumption of a diet high in fat (primarily in the form of n-6 polyunsaturated fatty acids) during pregnancy increases the risk of developing carcinogen-induced mammary tumors, possibly by increasing the pregnancy levels of circulating estrogens.** IMPLICATIONS: If further studies find that the results from animal model studies are applicable to humans, some human breast cancers may be preventable by dietary manipulations during pregnancy."

Metabolism of glomerular basement membrane in normal, hypophysectomized, and growth-hormone-treated diabetic rats," Reddi AS, *Exp Mol Pathol,* 1985 Oct, 43:2, 196-208. "The in vivo synthesis of the renal **glomerular basement membrane (GBM)** collagen was studied in **normal, hypophysectomized (hypox), diabetic, and growth-hormone (GH)-treated diabetic rats....**" "A significant decrease in both proline and hydroxyproline specific activities were observed in GBM of hypox rats at all periods of study. Administration of GH to hypox rats returned the GBM collagen synthesis to normal. Diabetic GBM had higher proline and hydroxyproline specific activities when compared to normal rats. **Treatment of diabetic rats with GH for 10 days further increased both proline and hydroxyproline specific activities when compared either to diabetic or normal rats treated with GH.** The activity of glucosyltransferase, an enzyme involved in the biosynthesis of the disaccharide unit of GBM collagen was found to be decreased in glomeruli of hypox rats. In contrast, the activity of N-acetyl-beta-glucosaminidase, a glycoprotein-degrading enzyme, was found to be significantly increased in hypox rats. GH treatment restored both enzyme activities to normal. The results of the present study show that **GBM collagen synthesis is decreased in hypox rats and increased in diabetic rats.** not only normalized GBM collagen synthesis in hypox rats but also caused significant increase in diabetic rats. This suggests that the renal GBM metabolism is influenced by GH, and this may be of particular significance in view of GH involvement in diabetic microvascular complications."