ARTICLE

Diabetes, scleroderma, oils and hormones

HOME
ARTICLES
ABOUT RAY PEAT
ART GALLERY
LINKS

Loading

www.RayPeat.com
©2006-16 Ray Peat
All Rights Reserved

The basic argument: Stress and aging make cells less responsive in many ways by damaging their ability to produce energy and to adapt. The polyunsaturated fats are universally toxic to the energy producing system, and act as a "misleading signal" channeling cellular adaptation down certain self-defeating pathways. Diabetes is just one of the "terminal" diseases that can be caused by the polyunsaturated vegetable oils. Coconut oil, in diabetes as in other degenerative diseases, is highly protective.

When the oral contraceptive pill was new (Enovid), it was found to produce signs of diabetes, including decreased glucose tolerance. Spellacy and Carlson (1966) suggested that an elevation of circulating free fatty acids might be responsible, and remarked that "Free fatty acids can block the Krebs cycle, with relative insulin action resistance resulting." "The potential danger of the oral contraceptives is one of prolonged pancreatic stimulation." Recent papers are reporting that the estrogen used to "treat menopause" causes an increase in free fatty acids. Spellacy and Carlson suggested that estrogen's effect was mediated by growth hormone, and that is now the consensus. Women are much more likely than men to develop diabetes.

Ephraim Racker observed that free unsaturated fatty acids inhibit mitochondrial respiration, and recent studies are finding that free linoleic and linolenic acids act as intracellular regulators, stimulating the protein kinase C (PKC) system, which is also stimulated by estrogen and the (cancer promoting) phorbol esters. They stimulate the cell while blocking the energy it needs to respond.

Scleroderma, or systemic sclerosis, is a supposedly mysterious condition in which tissues harden, with an excessive deposition of fibrous material. Besides hardening the skin, it can involve fibrosis of the heart and other organs, and can cause changes in blood vessels of the kidneys like those seen in some types of hypertension, and often involves Raynaud's phenomenon and osteoporosis of the fingers. (Silicone functions as an adjuvant, making exposure to irritants, solvents or infections more harmful. This seems to be the reason for the association between breast implants and scleroderma.) Another type of disease that involves hardening of the skin is scleredema, in which the skin thickens with an accumulation of "mucin" between collagen bundles, and in which fibroblasts are overactive in producing collagen. (Varga, et al.) This condition is believed to often follow a "febrile illness" and is associated with diabetes. My interest in these conditions comes from my awareness that estrogen promotes collagen formation, and that changes in the connective tissue are deeply associated with the processes of stress and aging, following the ideas of Metchnikov and Selye.

Many people are still committed to the various old theories of diabetes, though a few are showing ways in which multiple causes can lead to diabetes. Increasingly, old age itself is seen to be "like diabetes (Meneilly, et al.; Smith, et al.), and the situation is ripe for a recentering of our understanding of diabetes around some of the general facts about aging and stress.

Diabetes mellitus, as named, refers to excessive urination and sugary urine, but it is now often diagnosed in people who neither urinate excessively nor pass glucose in the urine, on the basis of a high level of glucose in the blood. Many other signs (abnormal mucopolysaccharide metabolism with thickening of basement membranes, leakage of albumin through capillary walls and into the urine, a high level of free fatty acids in the blood, insensitivity of

tissues to insulin, or reduced sensitivity of the beta cells to glucose) are considered diagnostic by some people, who believe that the worst aspects of the disease can be prevented if they can diagnose early and take preventive measures. This attitude derives largely from the genetic theory of causation, though it incorporates a belief that (environmental) intervention can ameliorate the course of the disease. When I wrote Nutrition for Women, I mentioned that the sudden appearance of diabetes in non-European Jews when they moved to Isreal made the genetic theory of diabetes untenable, and since then other studies have made the similar point that environmental factors seem crucial. (Shaltout, et al.) Many people are arguing for the racial/genetic theory of diabetes, but they are failing to consider some simple dietary factors, especially the high consumption of unsaturated seed oils and the combination of nutritional deficiencies and environmental stress.

I have known adults and children who were diagnosed as diabetic, and given insulin (and indoctrinated with the idea that they had a terminal degenerative disease) on the strength of a single test showing excessive glucose. When I taught at the naturopathic medical school in Portland, I tried to make it clear that "diabetes" (a term referring to excessive urination) is a function, and that a high level of glucose in the blood or urine is also a function, and that the use of insulin should require a greater diagnostic justification than the use of aspirin for a headache does, because insulin use itself constitutes a serious health problem. (And we seldom hear the idea that "diabetes" might have a positive side [Robinson and Johnston], for example that it reduces the symptoms of asthma [Vianna and Garcialeme], which get worse when insulin is given. Normal pregnancy can be considered "diabetic" by some definitions based on blood sugar. I got interested in this when I talked to a healthy "diabetic" woman who had a two year old child whose IQ must have been over 200, judging by his spontaneous precocious hobbies. Old gynecologists told me that it was common knowledge that "diabetic" women had intellectually precocious children.)

When non-diabetic apes were given insulin treatments, they developed some of the same "complications of diabetes" that are seen in humans, and antibodies to insulin were found in their retinas, suggesting that some "complications of diabetes" were complications of insulin treatment. Patients were seldom well informed of the arguments against the use of insulin, but the justification for the new genetically engineered human insulin is precisely that it avoids immunological damage.

Insulin was introduced into medicine in the 1920s. According to the Britannica Book of the Year for 1947, page 265, "Mortality from diabetes in 1920 in the United States was 16.0 per 100,000, 14,062 deaths, but in 1944, it was 26.4 per 100,000, 34,948 deaths."

One of the theories of the cause of diabetes is that a virus damages the beta cells in the pancreas, and the main argument for that in the 1970s was that the onset of diabetes in children can often be dated to a time shortly after a severe viral infection. It is true that intense sickness and a high fever (and high doses of drugs given to treat the sickness) can cause very high levels of glucose in the blood, and even glucose in the urine, but this is a fairly well recognized consequence of stress. High doses of cortisone (prednisone, etc.) typically cause elevated glucose levels. Cushing's syndrome usually involves hyperglycemia. Normally, this is just a functional response to an excess of glucocorticoids, but studies in dogs suggested that intense and/or prolonged stress can damage the insulin-secreting cells in the pancreas. Dogs had half of their pancreas removed, to increase the burden put on the remaining tissue, and after a large dose of cortisone the dogs became (and remained) diabetic.

One of the problems associated with diabetes is the calcification of blood vessels, though now there is more emphasis on fatty degeneration. Other blood vessel problems include hypertension, and poor circulation in general, leading to gangrene of the feet, impotence, and degeneration of the retina. In muscles, and probably in other tissues of diabetics, capillaries are more widely spaced, as if the basal oxidative requirement were lower than normal. However, mitochondria contain more respiratory enzymes, as if to partly compensate for the poor delivery of oxygen to the cells.

Osteoporosis or osteopenia is a common complication of diabetes, and seems to be associated with the calcification of soft tissues.

F. Z. Meerson's description of the stress-injured heart is very similar to the general changes that occur in chronic diabetes. He found that the stressed heart becomes rigid and unable to contract completely, or to relax completely. Excess calcium enters cells, and fatty acids are mobilized both locally and systemically, and both of these tend to damage the mitochondria. In diabetes, fatty acids are mobilized and oxidized instead of glucose, and calcium enters cells, increasing their rigidity and preventing relaxation of muscles in blood vessels. (I'm not sure whether it is relevant to cell physiology, but the presence of an excess of free unsaturated fatty acids, and of calcium, in cells makes me think of the insoluble soap that these substances form in other situations, including the intestine. It seems that this could form a harmful deposit in cells, blocking many metabolic processes.)

For many years, histologists have observed that calcium and iron tend to be deposited together in "devitalized" tissues. Now we know that cell death from a great variety of causes involves the cell's absorption of increased amounts of calcium. Simply the lack of energy increases the amount of calcium in a cell, and stimulation or excitation does the same, creating or exaggerating a deficiency of energy. In low thyroid people, many (if not all) tissues are very easily damaged. Since glucose is needed by liver cells to produce the active (T3) form of thyroid, diabetes almost by definition will produce hypothyroidism, since in diabetes glucose can't be absorbed efficiently by cells.

In the form of cell damage caused by the "excitotoxins," glutamic and aspartic acids, the damage seems to require both stimulation, and difficulty in maintaining adequate energy production. This combination leads to both calcium uptake and lipid peroxidation. When cells are de-energized, they tend to activate iron by chemical reduction, producing lipid peroxidation. This could explain the presence of chemically active iron, but an actual increase in the iron concentration suggests that there has been prolonged injury (oxidative stress) to the cell, with increased production of the heme group, which binds iron.

Hans Selye found that he could produce scleroderma (hardening and calcification of the skin) in rats by giving them a toxic dose of a heavy metal, and then irritating the skin a little by plucking hair. Iron is now tending to be recognized as a factor in inflammation. Vitamin E was able to prevent the development of scleroderma under Selye's experimental conditions, suggesting that the irritation allowed the heavy metal to cause oxidative damage to the skin. Selye found other ways to cause calcification of tissues, including the walls of arteries, but he directed most of his attention to the role of "pro-inflammatory" hormones. A decreased blood supply was often used to predispose an organ to calcification. In diabetes, a characteristic feature is that the blood supply is relatively remote from cells in muscle and skin, so the oxygen and nutrients have to diffuse farther than in normal individuals, and the ATP level of cells is characteristically lower than normal. In blood cells, both red (Garnier, et al.) and white cells are probably more rigid in diabetes, because of lower ATP production, and higher intracellular calcium and sodium.

Magnesium in the cell is largely associated with ATP, as the complex Mg-ATP. When ATP is "used" or converted to ADP, this lower-energy substance associates with calcium, as Ca-ADP. In a hypothyroid state, the energy charge can be depleted by stress, causing cells to lose magnesium. ATP is less stable when it isn't complexed with magnesium, so the stress-induced loss of magnesium makes the cell more susceptible to stress, by acting as a chronic background stimulation, forcing the cell to replace the ATP which is lost because of its instability. In this state, the cell takes up an excess of calcium.

The picture that I think explains many of the features of diabetes is that an energy deficit produces an alarm state, causing increased production of adrenalin and cortisol. Adrenalin mobilizes fat from storage, and the free fatty acids create a chronic problem involving 1) blocked ATP production, 2) activation of the protein kinase C

system (increasing tension in blood vessels), 3) inhibition of thyroid function with its energetic, hormonal, and tissue-structure consequences, 4) availability of fats for prostaglandin synthesis, and 5) possibly a direct effect on clot dissolving, besides the PAI-1 (plasminogen activator inhibitor) effect seen in diabetes (Ceriello, et al., Udvardy, et al., Vague, et al.). (Estrogen has many pro-clotting effects, and one of them is a decreased activity of vascular plasminogen activator. K. E. Miller and S. V. Pizzo, "Venous and arterial thromboembolic disease in women using oral contraceptives," Am. J. Obst. Gyn. 144, 824, 1982. In 1968, D. G. Daniel et al., reported that estrogen promotes thromboembolism by increasing clotting factor IX in the blood.)

Increased entry of calcium into cells is complexly related to increased exposure to unsaturated fatty acids, decreased energy, and lipid peroxidation. Osteoporosis, calcification of soft tissues and high blood pressure are promoted by multiple stresses, hypothyroidism, and magnesium deficiency. The particular direction a disease takes--diabetes, scleroderma, lupus, Alzheimer's, stroke, etc.--probably results from the balance between resources and demands within a particular organ or system. Calcium overload of cells can't be avoided by avoiding dietary calcium, because the bones provide a reservoir from which calcium is easily drawn during stress. (In fact, the reason calcium can temporarily help prevent muscle cramps seems to be that it makes magnesium more available to the muscles.)

If we want to stop a disease that involves abnormal calcification or contraction of muscle (see Zenere, et al.), we can increase our consumption of magnesium, and to cause cells to absorb and retain the magnesium, we can increase our thyroid function. The use of coconut oil provides energy to stabilize blood sugar while protecting mitochondria and the thyroid system from the harmful effects of unsaturated fats.

In 1947, B. A. Houssay found that a diet based on sugar as a source of energy was more protective against diabetes than a diet based on lard, while the most protective diet was based on coconut oil. Lard reflects the pigs' diet, and is usually extremely unsaturated, especially since it became standard to fatten them on soybeans and corn. Essentially, his study seems to show that unsaturated (pork) fat permits diabetes to develop, sugar is slightly protective, and coconut oil is very protective against the form of diabetes caused by a poison.

At the same time, A. Lazarow was demonstrating that a low protein diet made animals more sensitive to diabetes, and that cysteine, glutathione, and thioglycolic acid (antioxidants) are protective against diabetes. The chelator of metals, BAL (British anti-lewisite), was also found to protect against diabetes.

Taken together, those studies suggest that the oxidizable unsaturated fats are involved in the process of producing diabetes. At the same time, other studies were showing that the unsaturated oils suppress the thyroid, and that coconut oil increases the metabolic rate, apparently by normalizing thyroid function. Hypothyroidism is known to include deposition of mucopolysaccharides in tissues, increased permeability of capillaries with leakage of albumin out of the blood, elevated adrenalin which can lead to increased production of cortisol, decreased testosterone production, high risk of heart and circulatory disease, including a tendency to ulceration of the extremities, and osteoporosis, all of which are recognized "complications of diabetes." Broda Barnes gave all of his diabetic patients a thyroid supplement, and found that none of them developed the expected complications of diabetes.

Recently, a high safflower oil diet was found to cause diabetes (Ikemoto, et al.), and obesity itself is thought to be a factor in developing diabetes. The hormone patterns associated with obesity can be seen as either cause or effect of the obesity (or both cause and effect), since, for example, low thyroid can increase both estrogen and cortisol, which support the formation of fat, and the fat cells can become a chronic source of estrogen synthesis.

On a diet lacking the "essential" unsaturated fatty acids, Benhamou

(1995) found that nonobese diabetic mice didn't develop diabetes, that is, the unsaturated fats themselves, without obesity, are sufficient to cause diabetes. (Also see Girard; Golay, et al., and Kusunoki, et al.)

Estrogen and the polyunsaturated fatty acids (PUFA), linoleic and linolenic acid, alike activate the protein kinase C (PKC) system of cellular activation. Many of the functions of PUFA are similar to the functions of estrogen (e.g., antagonism to thyroid function, promotion of age pigment/lipofuscin), so this information showing that they both act similarly on the same basic regulatory pathway is important. Estrogen increases secretion of growth hormone (GH; it's closely associated with prolactin, also increased by estrogen), and GH causes an increase in free fatty acids in the blood. Estrogen promotes iron retention, so it sets the stage for oxidative stress. At least in some systems, both estrogen and PUFA promote the entry of calcium into the cell.

In diabetes, there is a generalized excess activation of the PKC system. The starch-based diet, emphasizing grains, beans, nuts, and vegetables, has been promoted with a variety of justifications. When people are urged to reduce their fat and sugar consumption, they are told to eat more starch. Starch stimulates the appetite, promotes fat synthesis by stimulating insulin secretion, and sometimes increases the growth of bacteria that produce toxins. It is often associated with allergens, and according to Gerhard Volkheimer, whole starch grains can be "persorbed" from the intestine directly into the blood stream where they may block arterioles, causing widely distributed nests of cell-death. I have heard dietitians urge the use of "complex carbohydrates" (starch) instead of sugar. In the first physiology lab I took, we fed rats a large blob of moist cornstarch with a stomach tube, and then after waiting a few minutes, were told to dissect the rat to find out "how far the starch had gone." In such a short time, we were surprised to find that not a trace of the starch could be found. The professor's purpose was to impress us with the rapidity with which starch is digested and absorbed. Various studies have demonstrated that starch (composed of pure glucose) raises blood glucose more quickly than sucrose (half fructose, half glucose) does. The sudden increase of blood glucose is sometimes thought to contribute to the development of diabetes, but if it does, it is probably mediated by fat metabolism and the hormones other than just insulin.

Brewer's yeast has been used successfully to treat diabetes. In the l930s, my father had severe diabetes, but after a few weeks of living on brewer's yeast, he recovered and never had any further evidence of diabetes. Besides its high B-vitamin and protein content, yeast is an unusual food that should be sparingly used, because of its high phosphorous/calcium ratio, high potassium to sodium ratio, and high estrogen content. The insulin-producing beta cells of the pancreas have estrogen receptors, but I don't know of any new research investigating this aspect of yeast therapy. In rabbit studies, diabetes produced by alloxan poisoning, which kills the beta cells, was cured by DHEA treatment, and beta cells were found to have regenerated in the pancreatic islets.

I think the basic anti-aging diet is also the best diet for prevention and treatment of diabetes, scleroderma, and the various "connective tissue diseases." This would emphasize high protein, low unsaturated fats, low iron, and high antioxidant consumption, with a moderate or low starch consumption. In practice, this means that a major part of the diet should be milk, cheese, eggs, shellfish, fruits and coconut oil, with vitamin E and salt as the safest supplements. It should be remembered that amino acids, especially in eggs, stimulate insulin secretion, and that this can cause hypoglycemia, which in turn causes cortisol secretion. Eating fruit (or other carbohydrate), coconut oil, and salt at the same meal will decrease this effect of the protein. Magnesium carbonate and epsom salts can also be useful and safe supplements, except when the synthetic material causes an allergic bowel reaction..

Although I started this newsletter with the thought of discussing the Mead acids--the unsaturated (n-9) fats that are formed under certain conditions, especially when the dietary polyunsaturated fatty acids are "deficient"--and their prostaglandin derivatives as a

distinct anti-stress, anti-aging system, the loss of which makes us highly susceptible to injury, I will save that argument for a future time, leaving this newsletter as an addition to the view that an excess of the polyunsaturated fats is central to the development of degenerative diseases: Cancer, heart disease, arthritis, immunodeficiency, diabetes, hypertension, osteoporosis, connective tissue disease, and calcification.

REFERENCES WITH EXCERPTS AND COMMENTS

A. A. Alzaid, et al., "Effects of insulin on plasma magnesium in noninsulin-dependent diabetes mellitus: Evidence for insulin resistance," J. of Clin. Endocr. and Metab. 80(4), 1376-1381, 1995. "...insulin resistance in subjects with NIDDM impairs the ability of insulin to stimulate magnesium as well as glucose uptake."

A. B. Akella, et al., "Diminished Ca++ sensitivity of skinned cardiac muscle contractility coincident with troponin T-band shifts in the diabetic rat," Circulation Research 76(4), 600-606, 1995.D. A. Antonetti, et al., "Increased expression of mitochondrial-encoded genes in skeletal muscle of humans with diabetes mellitus--Rapid publication," J. of Clinical Investigation 95(3), 1383-1388, 1995. "The increased mitochondrial gene expression may contribute to the increase in mitochondrial respiration observed in uncontrolled diabetes." (Low ATP with high respiration would suggest uncoupling; unsaturated fatty acids are known uncouplers of respiration from energy production.)

S. Asakuma, et al., "The effects of antianginal drugs on energy expernditure during exercise in normal subjects," Japanese Circulation Journal--English Edition 59(3), 137-145, 1995. "RQ (carbohydrate consumption relative to fat consumption) during exercise was significantly increased and VO2 was decreased after propranolol, metoprolol and amosulalol." "These data suggest that propranolol, metoprolol and amosulalol [beta-blockers] increase the efficiency of energy expenditure during ordinary physical activity by increasing the utilization of carbohydrate and by decreasing the utilization of fat."

M. Bardicef, et al., "Extracellular and intracellular magnesium depletion in pregnancy and gestational diabetes," Amer. J. of Obst. and Gyn. 172(3), 1009-1013, 1995.

P. E. Beales, et al., "Baclofen, a gamma-aminobutyric acid-b receptor agonist, delays diabetes onset in the non-obese diabetic mouse," Acta Diabetologica 32(1), 53-56, 1995.

P. Y. Benhamou, et al., :"Essential fatty acid deficiency prevents autoimmune diabetes in nonobese diabetic mice through a positive impact on antigen-presenting cells and Th2 lymphocytes," Pancreas 11(1), 26-37, 1995.

C. D. Berdanier, "Diet, autoimmunity, and insulin-dependent diabetes mellitus: A controversy," Proc. Soc. Exp. Biol. Med. 209(3), 223-230, 1995. "The majority of the genetic mutations that result in the phenotypic expression of the insulin-dependent diabetes mellitus genotype are in the immune system." Antibodies to milk protein can be found in the patient, but these probably represent antigen mimicry, resulting from the loss of antibody specificity which is a feature of autoimmune disease.

G. Bianchi, et al., "Thyroid volume in type 1 diabetes patients without overt thyroid disease," Acta Diabetologica 32(1), 49-52, 1995. "An association between insulin-dependent diabetes mellitus (type 1) and thyroid diseases has long been reported...."

P. Bjorntorp, "Insulin resistance: The consequence of a neuroendocrine disturbance?" Int. J. Obes. 19(Suppl. 1), S6-S10, 1995. "The decreased capillary density may...be of importance for the apparent insulin resistance."

R. Bouillon, et al., "Influence of age, sex, and insulin on osteoblast function: Osteoblast dysfunction in diabetes mellitus," J. of Clin. Endocr. and Metab. 80(4), 1194-1202, 1995. "...the osteoblast function is significantly decreased in diabetic patients...."

A. Ceriello, et al., "The defence against free radicals protects endothelial cells from hyperglycaemia-induced plasminogen activator inhibitor 1 over-production," Blood Coagulation & Fibrinolysis 6(2), 133-137, 1995. "The hypothesis that oxidative stress may play an important role in the pathogenesis of diabetic complications is ... supported by this study." [GSH reduced PAI-1.]

V. Coiro, et al., "Low-dose ovine corticotropin-releasing hormone stimulation test in diabetes mellitus with or without neuropathy," Metabolism--Clinical and Experimental 44(4), 538-542, 1995. "...basal and CRH-induced cortisol levels were significantly higher in diabetics than in normal controls." "...even uncomplicated diabetes mellitus is associated with adrenal hyperfunction."

S. R. Colberg, et al., "Skeletal muscle utilization of free fatty acids in women with visceral obesity," J. Clin. Invest. 95(4), 1846-1853, 1995. "Visceral obesity is strongly associated with insulin resistance." "...visceral adiposity is clearly associated with skeletal muscle insulin resistance but this is not due to glucose-FFA [free fatty acid] substrate competition. Instead, women with visceral obesity have reduced postabsorptive FFA utilization by muscle."

G. A. Colditz, et al., "Weight gain as a risk factor for clinical diabetes mellitus in women," Annals of Internal Medicine 122(7), 481-486, 1995.

C. Douillet and M. Ciavatti, "Effect of vitamin E treatment on tissue fatty acids and cholesterol content in experimental diabetes," J. Nutr. Biochem. 6(6), 319-326, 1995. "Diabetes induced a decrease of monounsaturated fatty acids and particularly palmitoleic acid in all studied tissues: liver, aorta, plasma." C18:3 n-6 and C20:4 n-6 were increased by diabetes.

M. Garnier, et al., "Red blood cell sodium conent in NID diabetic patients with hemorheological abnormalities," Clinical Hemorheology 15(3), 325-333, 1995.

K. D. Gerbitz, et al., "Mitochondrial diabetes mellitus: A review," BBA--Mol. Basis Dis. 1271(1), 253-260, 1995. This particular kind of diabetes, which is combined with deafness in 60% of the patients, involves a variant mitochondrial gene and occurs in about 1.5% of diabetics. "The underlying pathomechanism is probably a delayed insulin secretion due to an impaired mitochondrial ATP production in consequence of the mtDNA defect." To know the "causal" value of this gene we have to know how often it occurs in people who never develop diabetes. It is interesting that it is suggested to operate by way of impaired ATP production, which can be the result of so many factors, such as excess unsaturated fats, low thyroid, low magnesium, low copper, etc. Pages 141-151 of the same journal as an article by D. C. Wallace, et al., "Mitochondrial DNA mutations in human degenerative diseases and aging," which makes the point that "Generally, individuals inheriting these mitochondrial diseases are relatively normal in early life, develop symptoms during childhood, mid-life, or old age depending on the severity of the ... mutation; and then undergo a progressive decline." Their energy-producing systems are supposedly more susceptible to the effects of aging.

J. Girard, "Role of free fatty acids in insulin resistance of subjects with non-insulin-dependent diabetes," Diabetes Metab. 21(2), 79-88, 1995. "Studies performed in the rat suggest that impaired glucose-induced insulin secretion could also be related to chronic exposure of pancreatic beta cells to elevated plasma free fatty acid levels." [This direct effect of free fatty acids on the beta cells is extremely important. Estrogen--probably via GH--increases free fatty acids, and adrenalin--which is elevated in hypothyroidism--increases the release of free fatty acids from storage. Free fatty acids impair mitochondrail energy production.]

A. Golay, et al., "Effect of lipid oxidation on the regulation of glucose utilization in obese patients," Acta Diabetologica 32(1), 44-48, 1995. [Free fatty acids strongly and quickly depress the ability to oxidize or store glucose.]

A. Gomes, et al., "Anti-hyperglycemic effect of black tea (Camellia sinensis) in rat," J. of Ethnopharmacology 45(3), 223-226, 1995. It

"was found to possess both preventive and curative effects on experimentally produced diabetes in rats."

Y. Hattori, et al., "Phorbol esters elicit Ca++-dependent delayed contractions in diabetic rat aorta," Eur. J. Pharmacol. 279(1), 51-58, 1995. [Diabetic tissue is more responsive to activation of protein kinase C by phorbol esters.]

B. A. Houssay and C. Martinez, "Experimental diabetes and diet," Science 105, 548-549, 1947. [Mortality was zero on the high coconut oil diet, 100% on the high lard diet. It was 90% on the low protein diet, and 33% on the high protein diet. With a combination of coconut oil and lard, 20%.]

B. A. Houssay, et al., "Accion de la administracion prolongada de glucosa sobre la diabetes de la rata," Rev. Soc. argent. de biol. 23, 288-293, 1947.

S. Ikemoto, et al., "High fat diet-induced hyperglycemia: Prevention by low level expression of a glucose transporter (GLUT4) minigene in transgenic mice," Proc. Nat. Acad. Sci. USA 92(8), 3096-3099, 1995. "...mice fed a high-fat (safflower oil) diet develop defective glycemic control, hyperglycemia, and obesity."

M. Inaba, et al., "Influence of high glucose on 1,25-dihydroxyvitamin D-3-induced effect on human osteoblast-like MG-63 cells," J. Bone Miner. Res. 10(7), 1050-1056, 1995.

J. S. Jensen, et al., "Microalbuminuria reflects a generalized transvascular albumin leakiness in clinically healthy subjects," Clin. Sci. 88(6), 629-633, 1995.

G. Jorneskog, et al., "Skin capillary circulation severely impaired in toes of patients with IDDM, with and without late diabetic complications," Diabetologia 38(4), 474-480, 1995.

A. M. Kahn and T. Song, "Insulin inhibits dog vascular smooth muscle contraction and lowers Ca++[i] by inhibiting Ca++ influx," J. of Nutrition 125(6 Suppl.), S1732-S1737, 1995.

F. Kuhlencordt, et al., "Examination of the skeleton in diabetic patients up to age 45," Deutsche med. Wchnschr. 91, 1913-1917, 1966. "Some patients have a generalized osteoporosis-like process, and some have localized bone lesions...."

M. Kusunoki, et al., "Amelioration of high fat feeding-induced insulin resistance in skeletal muscle with the antiglucocorticoid RU486," Diabetes 44(6), 718-720, 1995. "These results suggest that glucocorticoids play, in a tissue-specific manner, a role in the maintenance and/or production of insulin resistance produced by high-fat feeding."

A. Lazarow, "Protection against alloxan diabetes," Anat. Rec. 97, 353, 1947.

A. Lazarow, "Protective effect of glutathione and cysteine against alloxan diabetes in the rat," Proc. Soc. Exp. Biol. & Med. 61, 441-447, 1946. [While certain doses of cysteine, glutathione, and thioglycolic acid completely prevented alloxan diabetes, it was interesting that all of the rats receiving ascorbic acid became diabetic. To me, this argues for the free radical cause of diabetes, rather than just the sulfhydryl oxidation. Lazarow suggested that succinic dehydrogenase, and various other sulfhydryl enzymes, including those involved in fatty acid oxidation, might be involved.]

R. B. Lipton and J. A. Fivecoate, "High risk of IDDM in African-American and Hispanic children in Chicago, 1985-1990," Diabetes Care 18(4), 476-482, 1995. "The relatively early age at onset may point to an environmental factor associated with this high incidence of the disease."

G. S. Meneilly, et al., "Insulin-mediated increase in blood flow is impaired in the elderly," J. Clin. Endocrinol. Metab. 80(6), 1899-1903, 1995. "Normal aging is characterized by resistance to insulin-mediated glucose uptake."

J. Ma, et al., "Associations of serum and dietary magnesium with

cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: The ARIC study," J. Clin. Epidemiol. 48(7), 927-940, 1995. [Carotid wall thickness increased in women as serum Mg level decreased.]

Y. Matsumoto, et al., "Creatine kinase kinetics in diabetic cardiomyopathy," Amer. J. Physiol.-Endocrinol. Met. 31(5), E1070-E1076, 1995.

F. Mercure and G. Vanderkraak, "Inhibition of gonadotropin-stimulated ovarian steroid production by polyunsaturated fatty acids in teleost fish," Lipids 30(6), 547-554, 1995. "The inhibitory actions by PUFAs were not restricted to long-chain PUFAs, as linoleic and linolenic acids had similar actions in the goldfish. The inhibitory action of EPA on testosterone production was reversible upon removal of the PUFA from medium." "[Stimulated] ...testosterone production ... was attenuated by PUFAs...."

H. Mulder, et al., "Non-parallelism of islet amyloid polypeptide (amylin) and insulin gene expression in rat islets following dexamethasone treatment," Diabetologia 38(4), 395-402, 1995.

S. Nagasaka, et al., "Effect of glycemic control on calcium and phosphorus handling and parathyroid hormone level in patients with non-insulin-dependent diabetes mellitus," Endocr. J. 42(3), 377-383, 1995. "...hyperglycemia causes excess urinary calcium and phosphorus excretion in patients with NIDDM. In response to urinary calcium loss, PTH secretion is mildly stimulated. Bone formation seems to be suppressed in the hyperglycemic state in spite of increased PTH secretion." [These are the changes I would expect to see in hypothyroid people with high cortisol.]

B. Oztas and M. Kucuk, "Influence of acute arterial hypertension on blood-brain barrier permeability in streptozocin-induced diabetic rats," Neuroscience Letters 188(1), 53-56, 1995.

S. Phillips, et al., "Neuropathic arthropathy of the spine in diabetes," Diabetes Care 18(6), 876-869, 1995.

J. F. Pouliot and R. Beliveau, "Palmitoylation of the glucose transporter in blood-brain barrier capillaries," Bioch. et Bioph. Acta--Biomembranes 1234(2), 191-196, 1995. "Palmitoylation may be involved in the regulation of glucose transport activity in hyperglycemia."

R. Ramakrishnan and A. Namasivayam, "Norepinephrine and epinephrine levels in the brain of alloxan diabetic rats," Neuroscience Letters 186(2-3), 200-202, 1995. [Epinephrine increased in striatum, hippocampus and hypothalamus, Norepinephrine increased in hypothalamus and decreased in pons and medulla.]

J. G. Regensteiner, et al., "Effects of non-insulin-dependent diabetes on oxygen consumption during treadmill exercise," Med. Sci. Sports Exerc. 27(6), 874-881, 1995. "The reduced rate of increase in oxygen consumption during increasing submaximal work loads in NIDDM suggests that limitations in oxygen delivery may impair exercise performance in otherwise healthy persons with diabetes."

A. A. Shaltout, et al., "High incidence of childhood-onset IDDM in Kuwait," Diabetes Care 18(7), 923-927, 1995. The incidence of IDDM in children is high in the region and has apparently increased nearly fourfold in the last decade. This is especially significant, since diabetes that appears in childhood is especially important for the theory of genetic causation. This study should give the gene people real trouble. They might have to call in the "gene for bed-wetting" people to help with their case.

M. A. Smith, et al., "Radical AGEing in Alzheimer's disease," Trends in Neurosciences 18(4), 172-176, 1995.

A. Tchernof, et al., "Relation of steroid hormones to glucose tolerance and plasma insulin levels in men: Importance of visceral adipose tissue," Diabetes Care 28(3), 292-299, 1995.

A. Tchernof, et al., "Reduced testosterone and adrenal C-19 steroid levels in obese men," Metabolism--Clin. and Exp. 44(4), 513-519,

1995. "...reduced concentrations of testosterone and adrenal C-19 steroid precursors are associated with increased body fatness rather than with excess visceral fat accumulation." [These results] "...emphasize the importance of adrenal steroids as correlates of body composition in men."

B. G. Trumper, et al., "Circadian variation of insulin requirement in insulin dependent diabetes mellitus--The relationship between circadian change in insulin demand and diurnal patterns of growth hormone, cortisol and glucagon during euglycemia," Hormone and Metabolic Research 27(3), 141-147, 1995. "The results of the study showed that the early morning rise in the insulin demand is related to the increased early morning cortisol secretion and to the nocturnal peaks of growth hormone concentration."

M. Udvardy, et al., "Altered lysis resistance of platelet-rich clots in patients with insulin-dependent diabetes mellitus," Thromb. Res. 79(1), 57-63, 1995. Suppression of clot-dissolving "...was remarkably stronger in IDDM, along with the highest PAI-1 activity concentration ratio of the platelet lysates, compared to plasmatic levels."

P. Vague, et al., "Hypofibrinolysis and the insulin resistance syndrome," Int. J. Obes. 19(Suppl. 1), S11-S15, 1995. Hypofibrinolysis is observed among obese subjects and it has been shown that an excess of plasminogen activator inhibitor 1 (PAI 1) the main regulator of the fibrinolytic system, is closely associated to other components of the insulin resistance syndrome, namely, excessive body weight, high waist to hip ratio, elevated blood pressure, hyperinsulinemia and hypertriglyceridemia."

E. O. Vianna and J. Garcialeme, "Allergen-induced airway inflammation in rats: Role of insulin," American J. of Respiratory and Critical Care Med. 151(3), 809-814, 1995. "Clinical asthma appears to be less severe when diabetes mellitus is superimposed."

A. Warley, et al., "Capillary surface area is reduced and tissue thickness from capillaries to myocytes is increased in the left ventricle of streptozotocin-diabetic rats," Diabetologia 38(4), 413-421, 1995.

G. C. Weir, "Which comes first in non-insulin-dependent diabetes mellitus: Insulin resistance or beta-cell failure? Both come first," JAMA 273(23), 1878-1879, 1995.

N. R. Williams, et al., "Plasma, granulocyte and mononuclear cell copper and zinc in patients with diabetes mellitus," Analyst 120(3), 887-890, 1995. "...the copper and zinc status of these diabetic patients was reduced, providing further evidence of a role for these antioxidant" trace elements in this disease.

T. Yamakawa, et al., "Augmented production of tumor necrosis factor-alpha in obese mice," Clinical Immunology and Immunopathology 75(1), 51-56, 1995. "...the TNF-alpha derived from adipose tissues might be involved in the induction of peripheral insulin resistance..."

T. Yamashita, et al., "Increased transendothelial permeation of albumin by high glucose concentration," Metabolism 44(6), 739-744, 1995.

M. B. Zemel, "Insulin resistance vs. hyperinsulinemia in hypertension: Insulin regulation of Ca++ transport and Ca++-regulation of insulin sensitivity," Journal of Nutrition 125(6 Suppl.), S1738-S1743, 1995.

B. M. Zenere, et al., "Noninvasive detection of functional alterations of the arterial wall in IDDM patients with and without microalbuminuria," Diabetes Care 18(7), 975-982, 1995. [There is a reduced vasodilatory capacity in diabetes, and especially in patients who are leaking albumin.]

D. B. Zilvermit, et al., "Oxidation of glucose labelled with radioactive carbon by normal and alloxandiabetic rats," J. Biol. Chem. 176, 389-400, 1948. [Diabetic rats had the same rate of glucose oxidation as normal rats, in this experiment. This is an

artificial form of diabetes that doesn't immediately involve an excess of unsaturated fatty acids, as occurs during stress, estrogen excess, hypothyroidism, or diets high in polyunsaturated fats which can cause a more "natural" kind of diabetes. The artificial alloxandiabetes forces the animal to oxidize an excess of fatty acids, and eventually should lead to the same kind of mitochondrial damage seen in natural diabetes.]

© Ray Peat 2006. All Rights Reserved. www.RayPeat.com

^^^ Top ^^^