

AS WE SEE IT

What You Don't Know About Blood Sugar

The most cherished benefit of Foundation membership is discovering something new in every Life Extension publication. Unlike typical health journals, we inform members about what they don't know concerning medical findings that are overlooked by conventional and alternative doctors.

In our relentless review of the scientific literature, we have uncovered data that calls into question what the safe range of blood sugar really is. Current guidelines state that a person is diabetic if fasting blood glucose levels exceed 126 mg/dL on two consecutive occasions. Fasting glucose levels over 109 are flagged as potential prediabetic (glucose intolerant) states. Life Extension has long argued that optimal glucose ranges are less than 100.



William Faloon

In a new hypothesis that shakes the pillars of conventional wisdom, it now appears that optimal fasting blood glucose levels should probably be under 86 mg/dL. This means that those with high "normal" glucose (86-109) are at an increased risk of premature death. While the medical establishment clearly understands the lethal dangers of hyperglycemia (blood sugar over 126), they have yet to recognize that even high normal glucose levels pose a serious threat to one's health.

Why "Normal" Glucose Levels Are Dangerous

To support our hypothesis that higher "normal" ranges of blood glucose represent a health risk, we first investigated the multifaceted toxic effects that sugar inflicts throughout the body. We found many studies showing that sugar damages cells via multiple mechanisms and is a causative factor in common diseases of aging.¹⁻³⁷ It thus appears desirable to maintain the lowest level of blood glucose needed to sustain healthy metabolic function.

We then looked at the effects of caloric restriction, and noted one study in which fasting glucose declined from an average of 92 to 74 mg/dL in a group of adults who reduced their food intake.³⁸ This corresponded to animal studies in which caloric restriction induced significant reductions in blood glucose levels.³⁹⁻⁴¹ It is well established that cutting calorie intake reduces one's risk of age-related diseases and probably slows aging itself.⁴²⁻⁵⁰ One reason for this may be the reduction in blood glucose levels that occurs in response to ingesting fewer calories.

As people age, their fasting glucose levels normally increase as their health declines. Standard laboratory reference ranges show an aging person having a "normal" fasting glucose level of up to 109 mg/dL. Yet the most effective anti-aging therapy—caloric restriction—lowers glucose levels to the low 70s (mg/dL).

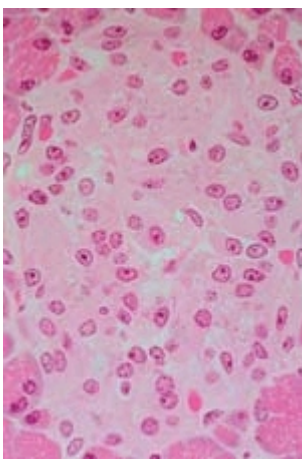
Many theories of aging focus on the deleterious effects of glucose itself. Only a few studies have evaluated disease risk in people whose fasting blood glucose levels are in normal ranges. One study of nearly 2,000 men looked at fasting blood glucose levels over a 22-year period. Its startling results showed that men with fasting glucose levels over 85 mg/dL had a 40% increased risk of death from cardiovascular disease. The researchers concluded, "fasting blood glucose values in the upper normal range (appear) to be an important independent predictor of cardiovascular death in nondiabetic apparently healthy middle-aged men."⁵¹

Conventional Medicine's Interpretation Of Fasting Glucose Blood Tests

70-109 mg/dL Normal glucose tolerance
 110-125 mg/dL Impaired fasting glucose (prediabetes)
 126+ mg/dL Probable diabetes

Life Extension's Fasting Glucose Guidelines

70-85 mg/dL Optimal (no glucose intolerance)
 86-99 mg/dL Borderline impaired fasting glucose
 100+ mg/dL Probable prediabetes



A light micrograph of a human pancreas.

The pancreas is a digestive gland, but also controls blood sugar levels by secreting insulin.

Foundation members often have their blood tested through our discounted mail-order blood-testing service. In addition to using the results of these blood tests to improve members' health, Life Extension is able to use this information to evaluate trends that can lead to better recommendations for extending longevity. We compiled data from all fasting glucose tests conducted over the past 12 months. The average reading was 94 mg/dL. While physicians would consider this "normal" result to be excellent, our new hypothesis indicates that optimal glucose levels should be below 86 mg/dL (and ideally as low as 74 mg/dL).

Where Your Pancreas Thinks Glucose Levels Should Be

The pancreas plays a major role in regulating blood glucose levels by secreting insulin to transport sugar out of the blood and into cells for energy production or storage.

Insulin also drives fat into cells, prevents fat from being released from cells, and makes people hungry. High insulin levels contribute to obesity and the disease states associated with being overweight, such as type II diabetes, cardiovascular disease, kidney failure, and certain types of cancers.

In normal health, the pancreas stops secreting insulin when glucose levels drop below 83 mg/dL.⁵²⁻⁵⁴ As I noted earlier, healthy aging people typically have fasting glucose levels over 90 mg/dL, and even competent doctors wait until fasting glucose is over 109 before suspecting a pre-diabetic (glucose-intolerant) condition.

But insulin continues to be secreted when blood glucose levels are over 83 mg/dL, which indicates that the pancreas is striving to drive glucose levels down to a range safer than what aging people typically are able to achieve.

An in-depth discussion about the lethal dangers of excess insulin can be found in the chapter on obesity in our Disease Prevention and Treatment reference book (4th edition). In the obesity protocol, we present evidence that excess insulin is a causative factor for body fat accumulation.

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Dr. Roy Walford is a pioneering scientist who demonstrated that maximum life span could be extended when calorie intake is reduced. Dr. Walford's research showed that caloric restriction lowers fasting glucose by 21% (from 92 to 74 mg/dL) in humans. Even more significant was Dr. Walford's finding that these calorie-restricted people had a 42% reduction in fasting insulin!

Overweight and obese people have very high insulin levels.⁵⁵⁻⁵⁶ Chronically elevated insulin contributes to a host of degenerative diseases.⁵⁷⁻⁶³ Our new hypothesis suggests that lowering fasting glucose levels results in an even greater reduction in fasting insulin. By secreting insulin when blood sugar levels exceed 83 mg/dL, the pancreas is telling us to keep blood glucose far below the high "normal" reference ranges used by blood test labs. While today's standard fasting glucose reference range extends to 109 mg/dL before flagging a problem, our new hypothesis suggests that fasting glucose over 85 mg/dL is cause for concern.

As you will read in this month's cover story, "Pathways of Aging," excess blood glucose induces enormous damage to tissues throughout the body. The question is, what to do about it?

How to Assess Your Fasting Glucose Status

In order to assess your fasting blood glucose status, a standard blood chemistry test provides this information at a modest cost.

New Glucose Guidelines Issued by American Diabetes Foundation

On October 24, 2003, a scientific committee of the American Diabetes Association issued a new definition of "impaired glucose tolerance," also known as a "prediabetic" state.

Under the new definition, the cut-off point for normal fasting blood glucose levels was reduced from 109 to 100 mg/dL, meaning that a value of 100 mg/dL or above would lead to a diagnosis of impaired fasting glucose (or prediabetes). Studies show that many people who fall in the prediabetic range will develop diabetes within 10 years.

A member of the Association's scientific committee stated that lowering the fasting glucose threshold to 100 mg/dL should help doctors identify more people at risk for developing type II diabetes. These people could then be prescribed an intensive diabetes-prevention program, such as diet and exercise therapy. The objective in intervening early, according to the American Diabetes Association representative, is to reduce the risk of diabetic complications such as heart disease.

Now that the American Diabetes Association has joined the Life Extension Foundation in recommending optimal fasting glucose levels below 100 mg/dL, blood testing laboratories may change their "standard reference range" to alert more people who are in a prediabetic state.

The problem is that the Life Extension Foundation's new hypothesis indicates that fasting glucose levels above 85 mg/dL are cause for concern. So even if blood labs lower their upper limit range to 100 mg/dL, many people will not be warned that their blood sugar levels are too high.



Ways to Lower Blood Glucose

The safest, most effective way to lower blood glucose levels is caloric restriction. Few people, however, are able to consistently under-eat. Consuming a lower glycemic index/load diet reduces blood glucose levels somewhat.⁶⁴⁻⁶⁹ (For more information about the "glycemic index/load," see pages 1151-4 of Disease Prevention and Treatment.)

Chromium supplements have been shown to reduce blood glucose significantly.⁷⁰⁻⁷⁴ The dose used in human studies ranges from 200 to 1000 mcg of elemental chromium a day, with best results occurring when 400 mcg or more of chromium is taken daily.

Of interest is an animal study showing that chromium extended mean and maximum life span.⁷⁵ This study surprised gerontologists, as chromium had not been considered a particularly promising antiaging nutrient. It may have been chromium's effect in lowering glucose levels that resulted in the significant prolonging of life span demonstrated in this study.

Magnesium, carnitine, alpha lipoic acid, and biotin also can help maintain glycemic control.⁷⁶⁻¹⁰⁸ A prescription drug for diabetes called metformin significantly lowers glucose levels in most people, but not everyone can take this medication.¹⁰⁹⁻¹¹⁹

**Nutrients That Have
Been Shown to Reduce
Fasting Blood
Glucose Levels
(primarily in diabetic
patients)**

Alpha Lipoic acid⁸¹⁻⁹⁴
Biotin⁹⁸⁻¹⁰⁸
Carnitine⁹⁵⁻⁶
Chromium⁷⁰⁻⁴
Magnesium⁷⁶⁻⁸⁰
Vanadium¹⁴⁶⁻⁵⁰
Zinc¹³⁸⁻⁴⁵

Regrettably, many aging people will not be able to maintain optimal blood glucose levels of less than 86 mg/dL. In this situation, protecting the body from the toxic effects of glucose becomes paramount. Glycation is a pathological process that occurs when glucose binds to protein molecules, resulting in the formation of non-functioning structures in the body. Higher blood glucose levels mean more-damaging glycation reactions.

Glycation advances slowly and accompanies every fundamental process of cellular metabolism. Glycation accelerates aging and neurodegenerative disorders such as Alzheimer's disease. Fortunately, a nutrient called carnosine confers significant protection against glycation processes.¹²⁰⁻¹²¹

Higher blood glucose also causes increased oxidative stress. Consumption of antioxidants has shown beneficial results in type II diabetics.¹²²⁻¹⁵⁰ Based on our hypothetical definition that blood sugar over 85 mg/dL is too high, antioxidants may be more important to healthy people than previously thought.

A new fat-soluble form of vitamin B1 has demonstrated significant protection against sugar toxicity at the cellular level. In Europe, this vitamin B1 derivative called benfotiamine is prescribed for those suffering from disorders related to sugar toxicity, such as peripheral neuropathy. The good news is that this nutrient has been added to popular supplements already being taken by most Life Extension members. Consumers can thus help protect themselves against the lethal dangers of excess sugar (glucose) without having to swallow more capsules or spend more money.

Why Our Hypothesis May Revolutionize Antiaging Medicine

Despite their efforts to lead healthier lifestyles, many people are dying prematurely of age-related diseases. Heart attack remains the number-one killer. Kidney failure is a major problem in those fortunate enough to make it past 85 years of age.¹⁵¹ The diseases of aging can be related to an impaired glucose state that we hypothesize may be defined as fasting glucose levels chronically greater than 85 mg/dL.

Sugar levels higher than what cells require to sustain energy metabolism inflict greater damage than lower sugar levels. If moderate to high "normal" fasting glucose levels increase cardiovascular mortality by 40% (as was shown in one large human study), then high normal glucose (and the corresponding excess insulin secretion it provokes) could be one of the leading preventable risk factors for heart attack and stroke.

Because blood sugar levels over 126 mg/dL substantially increase the risk of disease, it might be logical to assume that levels somewhere below 126 also represent an unacceptable danger.

Our new hypothesis indicates that fasting blood glucose of greater than 85 mg/dL is a signal of a metabolic disturbance that may lead to the development of degenerative disease. Most aging people have glucose levels above 85, and this age group also suffers from a plethora of disease states.

We know that type II diabetes markedly accelerates the rate at which humans contract age-related diseases. Type II diabetes is initially characterized by high levels of glucose and insulin in the blood. Today's reference range for diabetes (fasting glucose of 126 mg/dL or greater on two consecutive occasions) does not adequately reflect the "prediabetic" quandary (fasting glucose over 85 mg/dL) faced by most aging people.



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The diseases associated with diabetes include heart attack, stroke, blindness, kidney failure, circulatory deficits, and more. Non-diabetic aged people, however, also suffer from these same disorders, albeit at an older average age. Our hypothesis asserts that diabetic-related diseases manifest as humans grow older, and these age-related diseases may be related to fasting glucose levels chronically above 85 mg/dL. In other words, while diabetics contract these diseases at an earlier age, if non-diabetics live long enough with fasting glucose levels above 85 mg/dL, they could develop similar illnesses.

The fact that most aging humans have higher than optimal fasting glucose levels (above 85 mg/dL) should not lull us into accepting this as an inevitable consequence of growing older. To the contrary, specific nutrient, drug, and dietary alterations can reduce glucose levels in virtually everyone. The impact of people maintaining fasting glucose blood levels of 85 mg/dL or lower could be a significant reduction in the crippling, lethal diseases that have overwhelmed our health care system.

Avoiding Hypoglycemia (Low Blood Sugar)

While most adults have blood glucose levels that are higher than that required to sustain metabolic processes, over 20 million Americans suffer from some form of hypoglycemia—i.e., blood glucose levels that are lower than desirable. Of the several different types of hypoglycemia, one of the most common is reactive hypoglycemia, which is caused by the excess release of insulin in response to ingestion of too many refined carbohydrates or sugars.

Conventional medical textbooks define hypoglycemia as blood sugar below 60 mg/dL. These textbooks acknowledge that hypoglycemic symptoms vary widely in individuals, meaning that some people experience hypoglycemic symptoms with fasting glucose levels above 60 mg/dL while others do not develop symptoms until fasting glucose levels are lower than 60mg/dL. A conservative principle of hypoglycemia diagnosis is a blood glucose level of less than 70 mg/dL at the time of symptom onset and relief after eating.



The body tries to maintain a nearly constant blood sugar level. This is especially important for the brain and nervous system. If blood sugar is depressed below normal, the brain is unable to function appropriately. This can lead to a wide variety of physical and psychological symptoms associated with abnormal nervous-system function, such as fatigue, mood swings, premenstrual syndrome, sugar craving, headaches, difficulty focusing the eyes, tremors, temperamental outbursts, depression, excessive sweating, palpitations, and feeling "spaced-out." Hypoglycemia must be treated when blood glucose falls below 60 mg/dL, with or without symptoms.

It is unlikely that any of the natural approaches to reducing blood glucose levels would induce a hypoglycemic state. These nutrients typically stabilize glycemic control in the body. Some caution should be employed, however, when using antidiabetic drugs such as metformin. Nondiabetics using metformin may start off at 500 mg a day and gradually build up to 1000-1500 mg a day. The objective is not to take so much metformin as to induce a hypoglycemic state. Healthy people have used metformin as an antiaging drug over a decade. For complete safety information about metformin, log on to www.glucophage.com.

Our Commitment to Your Longevity

Health-conscious people join the Life Extension Foundation for a variety of reasons. Some members are grateful for our pioneering scientific research, while others appreciate our war against FDA malfeasance. Many members value having personal access to knowledgeable health advisors, while others appreciate being able to obtain state-of-the-art supplements at discount prices.

The Life Extension Foundation is committed to helping members achieve and maintain the best possible state of health. We have been identifying new compounds to guard against age-related disorders at a record pace. Whenever possible, these nutrients are added to popular products so that members automatically receive the added benefits.

Whenever you purchase a Life Extension product, you support a revolutionary program to correct today's broken health care system. We have exposed flawed FDA policies to the extent that our logic has prevailed in Congress, the courts, and the law itself. The pioneering research we fund has enabled us to identify specific genes responsible for making us age. Our meticulous review of the published scientific literature has resulted in the discovery of novel methods for preventing and treating disease.

At the end of each year, Life Extension discounts the prices of all our supplements. Members take advantage of these "Super Sale" prices to stock up on the pharmaceutical-quality nutrients they use every day.

I want to thank Foundation members for their support this year, which has allowed us to expand our scientific research programs while simultaneously battling FDA tyranny. Every time you purchase a product from us, you support the most comprehensive program on the planet aimed at abolishing infirmity, disease, and death.

For longer life,



William Faloon.

Rebel Against the Reference Ranges

Commercial testing laboratories develop "standard reference ranges" based on typical blood level averages for particular indicators. If you and your doctor rely on these "average" reference ranges, you can expect your health and longevity also to be "average."

If your intention, however, is to live in an excellent state of health beyond an average life span, then you may have to rebel against the average reference ranges. This mandates taking action to bring your blood indicators into "optimal" ranges. Achieving these optimal ranges may involve changes in diet or the use of certain drugs, hormones, or nutrients.

The current reference range for fasting glucose is between 65 and 109 mg/dL of blood. Our new hypothesis indicates that optimal glucose levels are between 70 and 85 mg/dL.



The Life Extension Foundation has a track record of being many years ahead of conventional medicine in determining optimal reference ranges. For instance, when we first alerted members to the dangers of high homocysteine levels, standard reference ranges indicated that blood levels of up to 15 mmol/L were acceptable. Blood lab reports now show that higher levels of homocysteine statistically increase the risk of vascular disease. For many years, we advised that both LDL cholesterol and triglyceride levels be kept below 100 mg/dL. Only recently has conventional medicine recommended as "optimal" these very same lower levels for LDL and triglycerides.

While we do not know when conventional medicine will recognize fasting glucose above 85 mg/dL as too high, Life Extension members can request a low-cost blood chemistry test and ascertain their own fasting glucose levels. If fasting glucose is elevated, members can speak with our licensed medical doctors or take the blood-test results to their own physicians to discuss safe ways of bringing blood glucose levels into the optimal range.

Life Extension members can order a Chemistry Panel/CBC (complete blood count) test for just \$35. This test measures glucose, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, iron, liver enzymes, and many other important health indicators. To order, call 1-800-208-3444.

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References

1. Kikuchi S, Shinpo K, Takeuchi M, et al. Glycation—a sweet tempter for neuronal death. *Brain Res Brain Res Rev.* 2003 Mar;41(2-3):306-23.
2. Hudson BI, Bucciarelli LG, Wendt T, et al. Blockade of receptor for advanced glycation endproducts: a new target for therapeutic intervention in diabetic complications and inflammatory disorders. *Arch Biochem Biophys.* 2003 Nov 1;419(1):80-8.
3. Haffner SM. Insulin resistance, inflammation, and the prediabetic state, *Am J Cardiol.* 2003 Aug 18;92(4A):18J-26J.
4. Manduteanu I, Voinea M, Antohe F, et al. Effect of enoxaparin on high glucose-induced activation of endothelial cells. *Eur J Pharmacol.* 2003 Sep 23;477(3):269-276.
5. Nakanishi S, Yamane K, Kamei N, Okubo M, Kohno N. Elevated C-reactive protein is a risk factor for the development of type 2 diabetes in Japanese Americans. *Diabetes Care.* 2003 Oct;26(10):2754-7.
6. Jakus V. The role of nonenzymatic glycation and glyco-oxidation in the development of diabetic vascular complications. *Cesk Fysiol.* 2003 May;52(2):51-65.
7. Tauer A, Zhang X, Schaub TP, et al. Formation of advanced glycation end products during CAPD. *Am J Kidney Dis.* 2003 Mar;41(3 Suppl 1):S57-60.
8. El-Assaad W, Buteau J, Peyot ML, et al. Saturated fatty acids synergize with elevated glucose to cause pancreatic beta-cell death. *Endocrinology.* 2003 Sep;144(9):4154-63.
9. Lin RY, Reis ED, Dore AT, et al. Lowering of dietary advanced glycation endproducts (AGE) reduces neointimal formation after arterial injury in genetically hypercholesterolemic mice. *Atherosclerosis.* 2002 Aug;163(2):303-11.
10. Chia-Lin Li, Shih-Tzer Tsai, Pesus Chou. Comparison of metabolic risk profiles between subjects with fasting and 2-hour plasma glucose impairment. The Kinmen Study. *Journal of Clinical Epidemiology* 55 (1) (2002) pp. 19-24.
11. Kalousova M, Skrha J, Zima T. Advanced glycation end-products and advanced oxidation protein products in patients with diabetes mellitus. *Physiol Res.* 2002;51(6):597-604.
12. Bonnefont-Rousselot D. Glucose and reactive oxygen species. *Curr Opin Clin Nutr Metab Care.* 2002 Sep;5(5):561-8.
13. Gregg EW, Engelgau M, Narayan, V. Complications of diabetes in elderly people. *BMJ* October 26, 2002, Volume 325, Number 7370, pp. 916-917.
14. Maedler K, Spinas GA, Lehmann R, et al. Glucose induces beta-cell apoptosis via upregulation of the Fas receptor in human islets. *Diabetes* 2001 Aug; 50(8): 1683-90.
15. Ha H, Lee HB. Oxidative stress in diabetic nephropathy: basic and clinical information. *Curr Diab Rep.* 2001 Dec;1(3):282-7.
16. Vlassara H. The AGE-receptor in the pathogenesis of diabetic complications. *Diabetes Metab Res Rev.* 2001 Nov-Dec;17(6):436-43. 17. Kimura C, Oike M, Koyama T, Ito Y. Impairment of endothelial nitric oxide production by acute glucose overload. *Am J Physiol Endocrinol Metab.* 2001 Jan;280(1):E171-8.
18. Agardh E, Hultberg B, Agardh C. Effects of inhibition of glycation and oxidative stress on the development of cataract and retinal vessel abnormalities in diabetic rats. *Curr Eye Res.* 2000 Jul;21(1):543-9.
19. Siskova A, Wilhelm J. Role of nonenzymatic glycation and oxidative stress on the development of complicated diabetic cataracts. *Cesk Fysiol.* 2000 Feb;49(1):16-21.

20. Aso Y, Inukai T, Tayama K, Takemura Y. Serum concentrations of advanced glycation endproducts are associated with the development of atherosclerosis as well as diabetic microangiopathy in patients with type 2 diabetes. *Acta Diabetol.* 2000;37(2):87-92.
21. Teixeira AS, Andrade SP. Glucose-induced inhibition of angiogenesis in the rat sponge granuloma is prevented by aminoguanidine. *Life Sci.* 1999;64(8):655-62.
22. Giugliano D, Ceriello A, Paolisso G. Oxidative stress and diabetic vascular complications. *Diabetes Care.* 1998 Feb;21(2):326-7.
23. Levi B, Werman MJ. Long-term fructose consumption accelerates glycation and several age-related variables in male rats. *J Nutr.* 1998 Sep;128(9):1442-9.
24. Ono Y, Aoki S, Ohnishi K, Yasuda T, Kawano K, Tsukada Y. Increased serum levels of advanced glycation end-products and diabetic complications. *Diabetes Res Clin Pract.* 1998 Aug;41(2):131-7.
25. Ren J, Gintant GA, Miller RE, Davidoff AJ. High extracellular glucose impairs cardiac E-C coupling in a glycosylation-dependent manner. *Am J Physiol.* 1997 Dec;273(6 Pt 2):H2876-83.
26. Larkins RG, Dunlop ME, Johnson EI. The pathogenesis of diabetic retinopathy. *Aust N Z J Ophthalmol.* 1996 May;24(2):97-104.
27. Vlassara H. Advanced glycation end-products and atherosclerosis. *Ann Med.* 1996 Oct;28(5):419-26. 28. Howard EW, Benton R, Ahern-Moore J, Tomasek JJ. Cellular contraction of collagen lattices is inhibited by nonenzymatic glycation. *Exp Cell Res.* 1996 Oct 10;228(1):132-7.
29. Sugiyama S, Miyata T, Horie K, et al. Advanced glycation end-products in diabetic nephropathy. *Nephrol Dial Transplant.* 1996;11 Suppl 5:91-4. 30. Emekli, N. Nonenzymatic glycosylation of tissue and blood proteins. *J. Marmara Univ. Dent. Fac.* 1996 Sep; 2(2-3): 530-4.
31. Yarat A, Uguz Z, Ustunel A, Emekli N. Lens glutathione, lens protein glycation and electrophoretic patterns of lens proteins in STZ induced diabetic rats. *Glycoconj J.* 1995 Oct;12(5):622-6.
32. Morohoshi M, Fujisawa K, Uchimura I, Numano F. The effect of glucose and advanced glycosylation end products on IL-6 production by human monocytes. *Ann N Y Acad Sci.* 1995 Jan 17;748:562-70.
33. Ziyadeh FN. Mediators of hyperglycemia and the pathogenesis of matrix accumulation in diabetic renal disease. *Miner Electrolyte Metab.* 1995;21(4-5):292-302.
34. Kaneto H, Fujii J, Suzuki K, et al. DNA cleavage induced by glycation of Cu,Zn-superoxide dismutase. *Biochem J.* 1994 Nov 15;304 (Pt 1):219-25. 35. Makino H, Shikata K, Kushihiro M, et al. Roles of advanced glycation end-products in the progression of diabetic Nephropathy. *Nephrol Dial Transplant.* 1996;11 Suppl 5:76-80.
36. Winocour PD. Decreased platelet membrane fluidity due to glycation or acetylation of membrane proteins. *Thromb Haemost.* 1992 Nov 10;68(5):577-82.
37. Brownlee M, Vlassara H, Cerami A. Nonenzymatic glycation and the pathogenesis of diabetic complications. *Ann. Intern. Med.* 1984; 101: 527-37.
38. Walford RL, Harris SB, Gunion MW. The calorically restricted low-fat nutrient-dense diet in Biosphere 2 significantly lowers blood glucose, total leukocyte count, cholesterol, and blood pressure in humans. *Proc Natl Acad Sci U S A.* 1992 Dec 1;89(23):11533-7.
39. Bluher M, Kahn BB, Kahn CR. Extended longevity in mice lacking the insulin receptor in adipose tissue. *Science* 2003 Jan 24; 299(5606): 572-4.
40. Lane MA, Ingram DK, Roth GS. Calorie restriction in nonhuman primates: effects on diabetes and cardiovascular risk. *Toxicol. Sci.* 1999 Dec; 52(2 Suppl.): 41-8.

41. Kemnitz JW, Roecker EB, Weindruch R, Elson DF, Baum ST, Bergman RN. Dietary restriction increases insulin sensitivity and lowers blood glucose in rhesus monkeys. *Am. J. Physiol.* 1994 Apr; 266(4, Pt. 1): E540-7.
42. Kent, S. BioMarker pharmaceuticals develops anti-aging therapy. *Life Extension magazine* 2003 Jun; 9(6): 56–67. Ft. Lauderdale, FL: Life Extension Foundation (http://www.lef.org/magazine/mag2003/2003_preprint_bio_01.html?GO.X=9&GO.Y=7).
43. Suh Y, Lee KA, Kim WH, Han BG, Vijg J, Park SC. Aging alters the apoptotic response to genotoxic stress. *Nat. Med.* 2002 Jan; 8(1):3-4.
44. Mukherjee P, El-Abbadi MM, Kasperzyk JL, Ranes MK, Seyfried TN. Dietary restriction reduces angiogenesis and growth in an ortho- topic mouse brain tumour model. *Br. J. Cancer* 2002 May 20; 86(10): 1615-21.
45. Kritchevsky D. Caloric restriction and cancer. *J. Nutr. Sci. Vitaminol.* 2001 Feb; 47(1): 13-9.
46. Moreschi C. The connection between nutri- tion and tumor promotion. *Z. Immunitaetsforsch.* 1909; 2: 651.
47. Spindler SR. Reversing aging rapidly with short-term calorie restriction. *Life Extension magazine* 2001a; 7(12): 40–61. Ft. Lauderdale, FL: Life Extension Foundation (www.lef.org/magazine/mag2001/dec2001_cover_spindler_04.html).
48. Yoshida K, Inoue T, Hirabayashi Y, Nojima K, Sado T. Calorie restriction and sponta- neous hepatic tumors in C3H/He mice. *J. Nutr. Health Aging* 1999; 3(2): 121-6.
49. Wickner S, Mauriz M, Gottesmann S. Posttranslational quality control: folding, refolding, and degrading proteins. *Science* 1999 Dec 3; 286(5446): 1888-93.
50. Kritchevsky D. The effect of over- and under- nutrition on cancer. *Eur. J. Cancer Prev.* 1995 Dec; 4(6): 445-51.
51. Bjornholt JV, Erikssen G, Aaser E, et al. Fasting blood glucose: an underestimated risk factor for cardiovascular death. Results from a 22-year follow-up of healthy nondiabetic men. *Diabetes Care* 1999;22:45-49.
52. HARRISON'S PRINCIPLES OF INTER- NAL MEDICINE, Thirteenth Edition, McGraw-Hill, 1994.p. 2001 "In one study in normal persons (arte- rialized venous samples), insulin secretion ceased at a 4.6 nmol/L glucose (83mg/dl)..."
53. IBID., p.2004 "Plasma insulin concentration generally reaches background levels for the assay when plasma glucose falls below 4.6 nmol/L (83mg./dl). . ."
54. IBID. Table 328-4 Mean plasma glucose and insulin during fasting. [Zero values obtained after overnight fast. Results are mean values for 20 normal men and 60 normal women]
55. Heller RF. Hyperinsulinemic obesity and car- bohydrate addiction: the missing link is the carbohydrate frequency factor. *Med Hypotheses* 1994 May;42(5):307-12.
56. Goodpaster BH, Katsiaras A, Kelley DE. Enhanced fat oxidation through physical activity is associated with improvements in insulin sensitivity in obesity. *Diabetes.* 2003 Sep;52(9):2191-7.
57. Bahceci M, Tuzcu A, Bahceci S, Tuzcu S. Is hyperprolactinemia associated with insulin resistance in non-obese patients with polycys- tic ovary syndrome? *J Endocrinol Invest.* 2003 Jul;26(7):655-9.
58. Fujiwara S, Emoto M, Komatsu M, et al. Arterial wall thickness is associated with insulin resistance in type 2 diabetic patients. *J Atheroscler Thromb.* 2003;10(4):246-52.
59. Taniguchi A, Fukushima M, Seino Y, et al. Platelet count is independently associated with insulin resistance in non-obese Japanese type 2 diabetic patients. *Metabolism.* 2003 Oct;52(10):1246-9.
60. Welin L, Bresater LE, Eriksson H, Hansson PO, Welin C, Rosengren A. Insulin resistance and other risk factors for coronary heart dis- ease in elderly men. The Study of Men Born in 1913 and 1923. *J Cardiovasc Risk.* 2003 Aug;10(4):283-8.
61. Hitsumoto T, Iizuka T, Takahashi M, et al. Relationship between insulin resistance and oxidative stress in vivo. *J Cardiol.* 2003 Sep;42(3):119-27.

62. Festa A, Hanley AJ, Tracy RP, D'Agostino R Jr, Haffner SM. Inflammation in the prediabetic state is related to increased insulin resistance rather than decreased insulin secretion. *Circulation*. 2003 Oct 14;108(15):1822-30. Epub 2003 Sep 29.
63. Wiernsperger NF, Bouskela E. Microcirculation in insulin resistance and diabetes: more than just a complication. *Diabetes Metab*. 2003 Sep;29(4 Pt 2):6S77-87.
64. Brand-Miller JC. Glycemic load and chronic disease. *Nutr Rev*. 2003 May;61(5 Pt 2):S49-55.
65. Wolever TM, Mehling C. Long-term effect of varying the source or amount of dietary carbohydrate on postprandial plasma glucose, insulin, triacylglycerol, and free fatty acid concentrations in subjects with impaired glucose tolerance. *Am J Clin Nutr*. 2003 Mar;77(3):612-21.
66. Li J, Kaneko T, Qin LQ, Wang J, Wang Y, Sato A. Long-term effects of high dietary fiber intake on glucose tolerance and lipid metabolism in GK rats: comparison among barley, rice, and cornstarch. *Metabolism*. 2003 Sep;52(9):1206-10.
67. Li J, Kaneko T, Wang Y, Qin LQ, Sato A. Effects of dietary fiber on the glucose tolerance in spontaneously diabetic rats—comparison among barley, rice, and corn starch. *Nippon Eiseigaku Zasshi*. 2003 May;58(2):281-6.
68. Liu S, Willett WC. Dietary glycemic load and atherothrombotic risk. *Curr Atheroscler Rep*. 2002;4(6):454-61.
69. Willett W, Manson J, Liu S. Glycemic index, glycemic load, and risk of type 2 diabetes. *Am J Clin Nutr*. 2002 Jul;76(1):274S-80S.
70. Preuss HG, Jarrell ST, Scheckenbach R, Lieberman S, Anderson RA. Comparative effects of chromium, vanadium and gymnema sylvestre on sugar-induced blood pressure elevations in SHR. *J Am Coll Nutr*. 1998 Apr;17(2):116-23.
71. Anderson RA, Cheng N, Bryden NA, et al. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes*. 1997 Nov;46(11):1786-91.
72. Baker B. Chromium supplements tied to glucose control. *Family Practice News*, 7/15/1996, pg 5.
73. Mirsky N. Glucose tolerance factor reduces blood glucose and free fatty acids levels in diabetic rats. *J Inorg Biochem*. 1993 Feb 1;49(2):123-8.
74. J.A. Vinson, K-H. Hsiao. Comparative Effect Of Various Forms Of Chromium On Serum Glucose: An Assay For Biologically Active Chromium. *Nutritional Reports International*, 32, (1), 1985.
75. Evans GW, Meyer L. Chromium picolinate increases longevity, *Age (Chester)* 15(4):p 135 1992. Twenty-second Annual Meeting of the American Aging Association and the Seventh Annual Meeting of the American College of Clinical Gerontology - San Francisco, California, USA October 16-20, 1992; 19921016.
76. Rosolova H, Mayer O Jr, Reaven G. Effect of variations in plasma magnesium concentrations on resistance to insulin-mediated glucose disposal in non-diabetic subjects. *J. Clin. Endocrinol. Metab*. 1997; 82: 3783-5.
77. Tosiello L. Hypomagnesemia and diabetes mellitus. A review of clinical implications. *Arch Intern Med* 1996 Jun 10;156(11):1143-8.
78. Paolisso G, Sgambato S, Gambardella A, et al. Daily magnesium supplements improve glucose handling in elderly subjects. *Am. J. Clin.Nutr*. 1992 Jun; 55(6): 1161-7.
79. Paolisso G, Scheen A, D'Onofrio F, Lefebvre P. Magnesium and glucose homeostasis. *Diabetologia* 1990;33:511-4.
80. Paolisso G, Passariello N, Pizza G, et al. Dietary magnesium supplements improve B-cell response to glucose and arginine in elderly non-insulin dependent diabetic subjects. *Acta Endocrinol. Copenh*. 1989 Jul; 121(1): 16-20.
81. Borenshtein D, Ofri R, Werman M, et al. Cataract development in diabetic sand rats treated with alpha-lipoic acid and its gamma-linolenic acid conjugate. *Diabetes Metab Res Rev*. 2001 Jan-Feb;17(1):44-50.
82. Midaoui AE, Elimadi A, Wu L, Haddad PS, de Champlain J. Lipoic acid prevents hypertension, hyperglycemia, and the increase in heart mitochondrial superoxide production. *Am J Hypertens*. 2003 Mar;16(3):173-9.
83. Ametov AS, Barinov A, Dyck PJ, et al. The sensory symptoms of diabetic polyneuropathy are improved with alpha-lipoic acid: the SYDNEY trial. *Diabetes Care*. 2003 Mar;26(3):770-6.
84. Dicter N, Madar Z, Tirosh O. Alpha-lipoic acid inhibits glycogen synthesis in rat soleus muscle via its oxidative activity and

the uncou-pling of mitochondria. *J Nutr.* 2002 Oct;132(10):3001-6.

85. Yilmaz O, Ozkan Y, Yildirim M, Ozturk AI, Ersan Y. Effects of alpha lipoic acid, ascorbic acid-6-palmitate, and fish oil on the glu- tathione, malonaldehyde, and fatty acids lev- els in erythrocytes of streptozotocin induced diabetic male rats. *J Cell Biochem.* 2002;86(3):530-9.

86. Evans JL, Heymann CJ, Goldfine ID, Gavin LA. Pharmacokinetics, tolerability, and fruc- tosamine-lowering effect of a novel, con- trolled-release formulation of alpha-lipoic acid, *Endocr Pract.* 2002 Jan-Feb;8(1):29-35.

87. Packer L, Kraemer K, Rimbach G. Molecular aspects of lipoic acid in the prevention of dia- betes complications. *Nutrition.* 2001 Oct;17(10):888-95.

88. Evans JL, Goldfine ID. Alpha-lipoic acid: a multifunctional antioxidant that improves insulin sensitivity in patients with type 2 dia- betes. *Diabetes Technol Ther.* 2000 Autumn;2(3):401-13.

89. Melhem MF, Craven PA, Derubertis FR. Effects of dietary supplementation of alpha- lipoic acid on early glomerular injury in dia- betes mellitus. *J Am Soc Nephrol.* 2001 Jan; 12(1): 124-33.

90. Jain SK, Lim G. Lipoic acid decreases lipid peroxidation and protein glycosylation and increases (Na⁺ + K⁺)- and Ca⁺⁺-ATPase activities in high glucose-treated red blood cells (RBC). *Free Radical Biol. Med.* 1998; 25: S94 (Abstr. 268); see also *Free Radical Biol. Med.* 2000; 29(11): 1122-8.

91. Khamaisi M, Rudich A, Potashnik R, Tritschler HJ, Gutman A, Bashan N. Lipoic acid acutely induces hypoglycemia in fasting nondiabetics and diabetic rats. *Metabolism* 1999 Apr; 48(4): 504-10.

92. Jacob S, Henriksen EJ, Ruus P, et al. The radical scavenger a-lipoic acid enhances insulin sensitivity in patients with NIDDM; a placebo controlled trial. Presented at Oxidants and Antioxidants in Biology, Santa Barbara, California, February 27- March 1, 1997.

93. Jacob S, Streeper RS, Fogt DL, et al. The antioxidant a-lipoic acid enhances insulin- stimulated glucose metabolism in insulin- resistant rat skeletal muscle. *Diabetes* 1996 Aug; 45:1024-9.

94. Jacob S, Henriksen EJ, Schiemann AL, et al. Enhancement of glucose disposal in patients with type 2 diabetes by alpha- lipoic acid. *Arzneimittelforschung* 1995 Aug; 45(8): 872-4.

95. Derosa G, Cicero AF, Gaddi A, Mugellini A, Ciccarelli L, Fogari R. The effect of L-carni- tine on plasma lipoprotein(a) levels in hyper-

cholesterolemic patients with type 2 diabetes mellitus. *Clin Ther.* 2003 May;25(5):1429-39. 96. Mingrone G, Greco AV, Capristo E, et al. L- carnitine improves glucose disposal in type 2 diabetic patients. *J Am Coll Nutr.* 1999; 18(1): 77-82.

97. Pessotto P, Liberati R, Petrella O, Romanelli L, Calvani M, Peluso G. In experimental dia- betes the decrease in the eye of lens carnitine levels is an early important and selective event. *Exp. Eye Res.* Feb 1997; 64: 195-201.

98. Yoshikawa H, Tajiri Y, Sako Y, Hashimoto T, Umeda F, Nawata H. Effects of biotin on glu- cotoxicity or lipotoxicity in rat pancreatic islets. *Metabolism.* 2002 Feb;51(2):163-8.99. Furukawa Y. Enhancement of glucose- induced insulin secretion and modification of glucose metabolism by biotin. *Nippon Rinsho.* 1999 Oct;57(10):2261-9.100. Romero-Navarro G, Cabrera- Valladares G, German MS, et al. Biotin regulation of pan- creatic glucokinase and insulin in primary cul- tured rat islets and in biotin-deficient rats. *Endocrinology.* 1999 Oct;140(10):4595-600.

101. McCarty MF. High-dose biotin, an inducer of glucokinase expression, may synergize with chromium picolinate to enable a definitive nutritional therapy for type II diabetes. *Med Hypotheses.* 1999 May;52(5):401-6.102. Tsunoda K, Osada K, Komai M, et al. Effects of dietary biotin on enhanced sucrose intake and enhanced gustatory nerve responses to sucrose seen in diabetic OLETF rat. *J Nutr Sci Vitaminol (Tokyo).* 1998 Apr;44(2):207-16.103. Zhang H, Osada K, Maebashi M, Ito M, Komai M, Furukawa Y. A high biotin diet improves the impaired glucose tolerance of long-term spontaneously hyperglycemic rats with non- insulin-dependent diabetes mellitus. *J Nutr Sci Vitaminol (Tokyo).* 1996 Dec;42(6):517-26.104. Borboni P, Magnaterra R, Rabini RA, et al. Effect of biotin on glucokinase activity, mRNA expression and insulin release in cul- tured beta-cells. *Acta Diabetol.* 1996 Jul;33(2):154-8.105. Koutsikos D, Fourtounas C, Kapetanaki A, et al. Oral glucose tolerance test after high-dose i.v. biotin administration in normoglycemic hemodialysis patients. *Ren Fail.* 1996 Jan;18(1):131-7.106. Koutsikos D, Agroyannis B, Tzanatos- Exarchou H. Biotin for diabetic peripheral neuropathy. *Biomed. Pharmacother.* 1990; 44: 511-4.

107. Reddi A, DeAngelis B, Frank O, Lasker N, Baker H. Biotin supplementation improves glucose and insulin tolerances in genetically diabetic KK mice. *Life Sci.* 1988;42(13):1323-30.108. Zhang H, Osada K, Sone H, Furukawa Y. Biotin administration improves the impaired glucose tolerance to streptozotocin-induced diabetic Wistar rats. *J Nutr Sci Vitaminol.* 1997; 43: 271-80.
109. Jones P, Yate P. Contraindications to the use of metformin, *BMJ* 2003;326:4-5 (4 January).
110. Wulfele MG, Kooy A, Lehert P, et al. Combination of Insulin and Metformin in the Treatment of Type 2 Diabetes. *Diabetes Care* 25:2133-2140, 2002.
111. Diabetes Prevention Research Group, Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Eng. J Med*, 2002, vol 346, pp. 393-403.
112. Freemark M, Bursey D. The effects of metformin on body mass index and glucose tolerance in obese adolescents with fasting hyperinsulinemia and a family history of type 2 diabetes. *Pediatrics* (online) 2001;107:e55.
113. Klow NE, Draganov B, Os I. Metformin and contrast media-increased risk of lactic acidosis. *Tidsskr. Nor. Laegeforen.* 2001 Jun 10; 121(15):1829 (in Norwegian).
114. Charles MA, Eschwege E. Prevention of type 2 diabetes: role of metformin. *Drugs* 1999; 58(Suppl. 1): 71-3; discussion, 75-82.
115. Brown JB, Pedula K, Barzilay J, Herson MK, Latare P. Lactic acidosis rates in type 2 diabetes, *Diabetes Care.* 1998 Oct;21(10):1659-63.
116. Abbasi F, Kamath V, Rizvi AA, Carantoni M, Chen YD, Reaven GM. Results of a placebo-controlled study of the metabolic effects of the addition of metformin to sulfonylurea-treated patients. Evidence for a central role of adipose tissue. *Diabetes Care.* 1997 Dec;20(12):1863-9.
117. Scheen AJ. Clinical pharmacokinetics of metformin. *Clin Pharmacokinet.* 1996 May;30(5):359-71.
118. DiGiugliano, N De Rosa, G Di Maro, et al. Metformin improves glucose, lipid metabolism, and reduces blood pressure in hypertensive, obese women. *Diabetes Care* 1993, Vol 16, Issue 10 1387-90.
119. Hollenbeck CB, Johnston P, Varasteh BB, Chen YD, Reaven GM. Effects of metformin on glucose, insulin and lipid metabolism in patients with mild hypertriglyceridaemia and non-insulin dependent diabetes by glucose tolerance test criteria. *Diabete Metab.* 1991 Sep-Oct;17(5):483-9. 120. Jakus V. The role of nonenzymatic glycation and glyco-oxidation in the development of diabetic vascular complications. *Cesk Fysiol.* 2003 May;52(2):51-65. 121. Hipkiss AR, Brownson C. A possible new role for the anti-ageing peptide carnosine. *Cell. Mol. Life Sci.* 2000; 57(5): 747-53.
122. Palanduz S, Ademoglu E, Gokkusu C, Tamer S. Plasma antioxidants and type 2 diabetes mellitus. *Res Commun Mol Pathol Pharmacol.* 2001;109(5-6):309-18.
123. Kaneto H, Kajimoto Y, Miyagawa J, et al. Beneficial effects of antioxidants in diabetes: possible protection of pancreatic beta-cells against glucose toxicity. *Diabetes* 1999 Dec; 48(12): 2398-2406.
124. Ruhe RC, McDonald RB. Use of antioxidant nutrients in the prevention and treatment of type 2 diabetes. *J Am Coll Nutr.* 2001 Oct;20(5 Suppl):363S-369S; discussion 381S-383S.
125. Rauscher FM, Sanders RA, Watkins JB 3rd. Effects of coenzyme Q10 treatment on antioxidant pathways in normal and streptozotocin-induced diabetic rats. *J. Biochem. Mol. Toxicol.* 2001; 15(1): 41-6.
126. McCarty MF. Can correction of sub-optimal coenzyme Q status improve beta-cell function in type II diabetics. *Med. Hypotheses* 1999 May; 52(5): 397-400.
127. Brignardello E, Gallo M, Aragno M, et al. Dehydroepiandrosterone prevents lipid peroxidation and cell growth inhibition induced by high glucose concentration in cultured rat mesangial cells. *J. Endocrinol.* 2000 Aug; 166(2): 401-6.
128. Yamaguchi Y, Tanaka S, Yamakawa T, et al. Reduced serum dehydroepiandrosterone levels in diabetic patients with hyperinsulinemia. *Clin. Endocrinol.* 1998 Sep; 49(3): 377-83.

129. Houseknecht KL, Vanden Heuvel JP, Moya-Camarena SY, et al. Dietary conjugated linoleic acid normalizes impaired glucose tolerance in the Zucker diabetic fatty fa/fa rat. *Biochem. Biophys. Res. Commun.* 1998 Mar 27; 244(3): 678-82. <http://generous.net/health/purdue/shtml> or contact Purdue News Service at (765) 494-2096).
130. Wenzel S, Stolte H, Soose M. Effects of silybin and antioxidants on high glucose-induced alterations of fibronectin turnover in human mesangial cell cultures. *J. Pharmacol. Exp. Ther.* 1996; 279: 1520-6.
131. Du Y, Smith MA, Miller CM, Kern TS. Diabetes-induced oxidative stress in the retina, and correction by aminoguanidine. *J Neurochem.* 2002 Mar; 80(5): 771-9.
132. Friedman EA, Distant DA, Fleishhacker JF, Boyd TA, Cartwright K. Aminoguanidine prolongs survival in azotemic-induced diabetic rats. *Am J Kidney Dis.* 1997; 30(2): 253-9.
133. Paolisso G, Di Maro G, Galzerano D. Pharmacological doses of vitamin E improve insulin action in healthy subjects and non-insulin dependent diabetic patients. *Am J Clin Nutr.* 1993; 57: 650-6.
134. Pariza M. First human studies promising for popular nutritional supplement: CLA could help control weight, fat, diabetes, and muscle loss. Presented at the American Chemical Society Meeting, Washington, D.C., August 20, 2000 (www.acs.org/portal/Chemistry-PID=acsdisplay.html&DOC=daily\sunday\weight.html).
135. Sargeant LA, Wareham NJ, Bingham S, et al. Vitamin C and hyperglycemia in the European Prospective Investigation in Cancer-Norfolk (EPIC-Norfolk) study; a population-based study. *Diabetes Care* 2000 Jun; 23(6): 726-32.
136. Schwille PO, Schmiedl A, Herrmann U, Wipplinger J. Postprandial hyperinsulinaemia, insulin resistance and inappropriately high phosphaturia are features of younger males with idiopathic calcium urolithiasis: attenuation by ascorbic acid supplementation of a test meal. *Urol. Res.* 1997; 25: 49-58.
137. Obrenovich ME, Monnier VM. Vitamin B1 blocks damage caused by hyperglycemia. *Sci SAGE KE.* 2003 Mar 12;2003(10):PE6.
138. Anetor JI, Senjobi A, Ajose OA, Agbedana EO. Decreased serum magnesium and zinc levels: atherogenic implications in type-2 diabetes mellitus in Nigerians. *Nutr Health.* 2002;16(4):291-300.
139. Ho E, Quan N, Tsai YH, Lai W, Bray TM. Dietary zinc supplementation inhibits NFkappaB activation and protects against chemically induced diabetes in CD1 mice. *Exp Biol Med (Maywood)* 2001 Feb;226(2):103-11.
140. Raz I, Karsai D, Katz M. The influence of zinc supplementation on glucose homeostasis in NIDDM. *Diabetes Res.* 1989; 11: 73-9.
141. Gupta R, Garg VK, Mathur DK, Goyal RK. Oral zinc therapy in diabetic neuropathy. *J Assoc Physicians India.* 1998 Nov;46(11):939-42.
142. Lukasiak J, Cajzer D, Dabrowska E, et al. Low zinc levels in metabolic X syndrome (mzX) patients measured by hair zinc composition analysis. *Rocz Panstw Zakl Hig.* 1998;49(2):241-4.
143. Wang P, Yang Z. Influence of insufficient zinc on immune functions in NIDDM patients. *Hunan Yi Ke Da Xue Xue Bao.* 1998;23(6):599-601.
144. Cunningham JJ, Fu A, Mearkle PL, Brown RG. Hyperzincuria in individuals with insulin-dependent diabetes mellitus: concurrent zinc status and the effect of high-dose zinc supplementation. *Metabolism* 1994 Dec;43(12):1558-62.
145. Faure P, Roussel A, Coudray C, et al. Zinc and insulin sensitivity. *Biol Trace Elem Res* 1992 Jan-Mar;32:305-10.
146. Sakurai H. A new concept: the use of vanadium complexes in the treatment of diabetes mellitus. *Chem Rec.* 2002;2(4):237-48.
147. Beliaeva NF, Gorodetskii VK, Tochilkin AI, Golubev MA, Semenova NV, Kovel'man IR. Vanadium compounds—a new class of therapeutic agents for the treatment of diabetes mellitus. *Vopr Med Khim.* 2000 Jul-Aug;46(4):344-60.
148. Sun Q, Sekar N, Goldwaser I, Gershonov E, Fridkin M, Shechter Y. Vanadate restores glucose 6-phosphate in diabetic rats: a mechanism to enhance glucose metabolism. *Am J Physiol Endocrinol Metab.* 2000 Aug;279(2):E403-10.
149. Thompson KH. Vanadium and diabetes. *Biofactors.* 1999;10(1):43-51.
150. Badmaev V, Prakash S, Majeed M. Vanadium: a review of its potential role in the fight against diabetes. *J Altern Complement Med.* 1999 Jun;5(3):273-91.

151. Guyer B, Freedman MA, Strobino DM, Sondik EJ. Annual summary of vital statistics: trends in the health of Americans during the 20th century. *Pediatrics*. 2000 Dec;106(6):1307-17.

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