

Unrecognized Pandemic Subclinical Diabetes of the Affluent Nations: Causes, Cost and Prevention

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Abstract

Regarding populations on the industrialized "western affluent" diet, arguments are made that: (1) plasma glucose values commonly seen and accepted as normal are abnormal; (2) their glucose tolerance is innately unstable; (3) most of their morbidity and mortality is produced by hyperglycemia far below glycosuria and or arteriosclerosis which can occur independently or together; (4) simple low cost methods for preventing and treating both have been in the literature for decades (correction of the sugar, fat and protein excesses; and controlled supplementation of pyridoxine (vitamin B₆), Mg, Cr and coenzyme Q10); and (5) these lessons were missed by mainstream medicine because of the vast size of the literature, enforcement of "treatment of choice", and lack of computer aided diagnosis. Cited as striking evidence of this tragic situation is the failure of mainstream clinical medicine to understand the cause of the remarkable decline in CVD in the 1960s and 1970s that followed U.S. enrichment of cereals with pyridoxine (vitamin B₆). Recommendations are made for correction of unnecessary costly delays between publication and implementation of such research findings.

Brief Overview of the Pathology Ascribed to Low Ratio of B₆ to Protein Intakes

Over 40 years ago Kotake et al reported¹ they had confirmed that xanthurenic acid (XA) appeared copiously in urine of B₆ deficient animals when fed high protein (i.e., high tryptophan) diets and disappeared quickly when B₆ was given; and they had discovered that: (1) adding fatty acids to the diet greatly increased the excretion of XA and the amount of B₆ needed to eliminate it; (2) both natural and synthetic XA damaged pancreatic beta cells

and produced diabetes in the animals; and (3) XA was found in the urine of each of the eight diabetic humans tested. They pointed out that diabetes incidence is much higher in countries where much fat and tryptophan (from animal protein) is consumed. Because of this simply testable response of XA rapidly disappearing from urine of diabetics or heart patients (or anyone given a high dietary ratio of fat or tryptophan to B₆), awareness of this striking and important effect should have spread rapidly like an information avalanche through clinical medicine world wide.

A second important discovery was announced 27 years ago when McCully published his theory² that made a number of predictions including: (1) a low ratio of B₆ to protein causes a toxic metabolite called homocysteine (HO) to be formed (from the amino acid methionine); and (2) HO would collect in the blood and result in lesions of the intimal surface. In the following year (1970), he reported a study on rabbits supporting his theory (this and essentially all work on HO up to 1983 are described in his review³ with 201 references). In 1974, more support came from extensive studies on baboons.⁴ In the 1970s, all of the theory's predictions were borne out. HO appears to be more toxic than XA in the sense that vascular damage occurs rapidly when blood HO is below the level that can be detected in urine; but XA can be detectable for years while pancreatic damage slowly accumulates. Yet, paradoxically, only 10 mg of B₆ per day is believed to provide ample margin of protection against HO formation whereas over 100 mg of B₆ appeared necessary to eliminate XA in many subjects. It was found that normal humans on a B₆ deficient diet for only three weeks (or anyone

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deficient in B₆) would excrete HO in the urine when fed methionine; this has extremely important implications because virtually all Americans above age 60 are reported to be B₆ deficient. In addition, compared to controls, women using the oral contraceptive formulations in the 1970s: (1) had lower blood B₆; (2) would excrete urinary HO after methionine challenge; (3) had ten times the death rate due to vascular disease.³

Karl Folkers at Merck was a leading figure in determining the molecular structure of both B₆ in 1939 and CoQ10 in 1958, two molecules that will revolutionize all medicine (if we can get medicine's attention), not only cardiovascular disease. He is still a driving force in the endless applications of CoQ10 that include cancer, AIDS and aging itself.⁵

John M. Ellis, a giant in his own right, was well aware of the work of these people including the 1953 findings of Kotake. As a result, Ellis⁶ had already done extensive clinical trials with B₆ in the 100 mg per day range by the time Mc Cully's theory had (quite rapidly) deduced that HO might be lethal to 40,000 times more people in North America than die of genetic homocystinuria (i.e., ~50% vs 0.001%). So, it was essentially known in the early 1970s that CVD and diabetes were preventable by a diet low in fat, sugar, and animal protein but high in complex carbohydrate and vegetable protein (when supplemented as necessary daily to absorb: B₆, ca 100 mg with half in B complex; Mg 400 mg; 200 mcg tri-valent chromium (as in certain yeasts); CoQ10 at doses not yet known but empirically adjusted for age and severity of CVD⁵). Space does not permit coverage of the important 1960s work on chromium by Mertz, Schwarz and Henry A. Schroeder who, prior to 1973 had written "B₆ is necessary for the smooth integrity of arterial walls" and performed cadaver analyses world-wide related to the role of Cr in diabetes and atherosclerosis. Some reviews with extensive reference lists cover various aspects of the pathology and the successful research.³⁻⁹

The Literature Problem (again)

According to the easily testable findings cited above, vascular disease and diabetes, the principle causes of morbidity and mortality and ruinous health care costs, are both preventable by extremely simple and very low cost measures that were demonstrated 30 to 40 years ago. In a recent mini-survey of 20 diabetics including three Type 1, not one was found whose physician had ever prescribed or even discussed B₆ or magnesium. One wonders how this can be possible. The vast size and growth rate of the medical science literature (over 4 million new pages per year of indexed journals)¹⁰ is the major physically insurmountable problem. What else can solve this except Computer Aided Diagnosis (with monthly updates as is done now for Medline) from the National Library of Medicine. Related to the literature size problem, is the understandable tendency for the pressured clinician to seize upon a convenient and fashionable dictum, especially if it bears the authority of the journal with the largest circulation. In the case of B₆, exactly this occurred. In the August 25, 1983, NEJM, two featured articles focused on the important problems of neuropathy from B₆ abuse. The articles correctly commented on specific cases of abuse, but included the application of B₆ in carpal tunnel syndrome, along with obvious abuses, in a manner that (in this author's opinion) could only impugn in the reader's mind that application and all of the B₆ findings cited here. Both papers failed to point out the dosing methods, the size of the Texas trials and the types of benefit that have been demonstrated.¹¹

Gross Glycemic Abnormality of Western Society

During the Calcutta Diabetes Study, the 2-hour postprandial blood glucose values for non-diabetic humans aged 40 to 70 in India were reported to range from 50 to 90 mg/dl.¹² However, in a long term investigation of 1400 people in the U.S.A., decadal age group medians for the same 2-hour values were reported to range from 105

to 122 mg/dl in nondiabetic 40 to 70 year olds;¹³ this distribution is completely disjoint from the Indian median values (which clearly must fall inside the 50 to 90 range reported above). In addition, the 2-hour GTT values are observed to rise circa 10% per decade of age in the U.S.A.¹⁴ With regard to the U.S.A. and similarly fed nations, we argue from data published in leading journals that: (1) these results have a dietary basis; and (2) these populations should be recognized as hyperglycemic, and are in subclinical diabetes (i.e., have depressed insulin sensitivity) the leading contributor to U.S.A. morbidity, mortality, and health care costs.¹⁵ We cite the findings that arteriosclerosis is prevented and treated by the same simple corrections that apply to most cases of hyperglycemia.

The Affluent Diet: Toxic Factors

Several long known but ignored factors elucidate both the causes and cures of this human and fiscal tragedy. These factors are the following listed departures of the 20th century affluent diet from that prevalent in 19th century agrarian cultures: (1) high glycemic index meals due to greatly increased content of sugars and rapidly hydrolyzable carbohydrate in general; (2 and 3) excesses of protein and fat with respect to intakes of pyridoxine (vitamin B₆) and magnesium; (4) insufficient “glucose-tolerance factor” (widely believed to be some form of tri-valent chromium); and (5) insufficient nutrient content to support synthesis of endogenous ubiquinone (CoQ10). The physical injuries reported to be associated with hyperglycemia occur even at “modest” levels below 150 mg% that do not produce glycosuria or elicit a diagnosis of diabetes. These include: (1) accelerated aging; (2) birth defects; (3) cancer; (4) diabetes; (5) infectious diseases; (6) neurological and psychiatric disorders (due to micromercurialism) and (7) vascular disease producing damage in all organs.^{10,16-21} Various mechanisms include low intracellular ascorbate which slows mitosis,¹⁹ and reduces

phagocytic clearance of thrombi by neutrophils.¹⁸

In essence, we impugn four characteristics of the affluent diet as outweighing all other factors in producing a progressive hyperglycemia that is widely regarded as normal. This clinical oversight persists even though it has been known for some decades that the relatively mild symptomless hyperglycemia discussed here is accompanied by increased risks of all vascular diseases,^{12,13} cancer,^{10,21} and birth defects.^{16,17,20} The relevant dietary defects associated with affluence are: (1) a major increase in sugar (the U.S.A./India ratio of per capita sugar consumptions circa 1975 was over ten fold, 65 kg vs 5 kg) [WHO data]; (2 and 3) an excessive intake of fat and (cooked) protein compared to that of pyridoxine (vitamin B₆) and magnesium,^{1,3} and (4) low intake of an insulin cofactor called “glucose tolerance factor” or GTF (believed to be tri-valent Cr that is low in the soil of some areas such as North America and removed in much food processing).²² Another factor is age dependent and may become dominant in many people as they grow older; this is CoQ10 for which human synthesis falls off after age 20 although its continuous replacement is always needed in all cells.⁵

Innate Instability of Hyperglycemia and Other Features of Sugar and Fat

Because the natural or primitive diet had very low sugar content and persisted to this century, there was not time for evolutionary pressure to select for uniformity in human pancreatic response to sugar load. Thus many people who would do well on the 19th century or agrarian (unrefined) diet become reactive hypoglycemics and or simply hyper-glycemic on the affluent fare. Foods that are high in both sugar and fat are predicted to accelerate atherosclerosis since fat agonizes platelet aggregation and sugar impairs phagocytic removal of the thrombi.¹⁸ Numerous papers prior to 1960²³ established the basis for the following model

(Ely unpub.): The first of the affluent dietary insults above refers to habitual postprandial hyperglycemia initially due to "high glycemic index" meals. Hyperglycemia rapidly induces a persistent (but easily reversible) insulin resistance (simple and convenient for studies in mice) by causing internalization of insulin receptors (to protect the cellular cytoplasm from glucose excess). Hyperglycemia demands more insulin which forces more receptor internalization. This further increases insulin resistance, raising blood glucose and insulin further, eventually exhausting beta cells.

Early success suggested that most cases of diabetes, both types 1 and 2, can be reversed by using exogenous insulin to carefully lower blood glucose to the range circa 70 mg % for a few months until the dose becomes zero (due to reductions necessary to prevent hypoglycemia); this regimen which allowed the beta cells and insulin sensitivity to recover would seem vastly more assured of success now (by B₆, Mg Cr, and CoQ10). The arginine test can be used to test insulin secretion (in cases of paradoxical suppression). Was most of the vast human and financial cost of diabetes in recent decades avoidable?

A Closing Overview

The primate line, as evolving omnivores, up to the present day adapted to a diet that included much plant bulk and little animal protein. Hence the ratio of pyridoxine (vitamin B₆) to protein intakes has been much larger than that found in the diets of affluent peoples today. In particular, the ratios of B₆ to the essential amino acids tryptophan and methionine are greatly reduced in those with high meat consumption, more so if the meat is cooked. As serious consequences, the toxic metabolite xanthurenic acid (XA) is produced from tryptophan, and HO is produced from methionine. The role of HO in vascular lesions even in the young and normoglycemic has been discussed in this and other journals over the last two dec-

ades. A decline in vascular disease and related deaths became clearly evident in the 1970s among populations with moderate methionine intake and was attributed to an increase in average B₆ intake due to large increases in imported synthetic B₆ used to fortify cereals. Here we have concerned ourselves more with certain aspects of XA and diabetes because: (1) the B₆ requirement to protect against HO is so much smaller than that needed for XA; and (2) in spite of much attention from the medical sciences, diabetes has not been placed in proper perspective or given adequate attention by clinicians. As a result, it appears that diabetes which should be preventable in most cases is so pandemic that a major fraction of the developed nations' populations is in subclinical diabetes and progressing to clinical. This is especially tragic in view of long reported findings that modest supplementation of B₆ and Mg has been shown decades ago in both human and animals to prevent the formation of XA and the related pancreatic lesions.

In addition to the costly and terrible morbidity and mortality of diabetes itself, it has long been known^{24,25} that the incidences of the same vascular injuries and of numerous other diseases are increased by the effects of "modest" hyperglycemia. Yet such hyperglycemia is accepted by most clinicians as normal among those patients who have not yet developed clinical diabetes in any of its forms (by present definitions).

Conclusion

Researchers appear to have efficiently produced solutions for our most costly health problems. But these seem ignored by the clinical community. Although clinicians appear to be (innately) much more efficient people, even they cannot cope with the literature due both to its size (Problem 1) and to their time burdens that result in large part from the very inefficient and ineffectual modalities that are enforced as "treatment of choice" (Problem 2).

It is concluded that even a relatively

primitive and low cost Computer Aided Diagnostic system (CAD) should be evaluated. [Such a scheme might use simple algorithms such as linking manuscripts (that might discuss either a disorder or a therapy) via symptom key words that are provided by the authors (or NLM data processing technician) at the source and the real symptoms provided by the patient to the diagnostician at the user end.] Before the present clinicians would feel free to use such a system, it might be necessary that the orientation of medical disciplinary boards must be reversed to require use of published knowledge (rather than essentially forbid it, as at present). This could best be done by changing the composition of boards to include a major fraction of medical science researchers. It is concluded that the billions that could be saved on the diseases considered here might dwarf the tens of millions necessary for the CAD.

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