

DIABETES MELLITUS THE TRACE ELEMENT CONNECTION

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Diabetes mellitus was known to the ancient Greeks who more or less correctly assumed that the victim was literally urinating (Greek ο υ ρ ο υ, urine) himself away. Since 1674, when Sir Thomas Willis suggested that diabetics should have gummy and starchy food, a lot has been written. Satisfactory adequately controlled studies have yet to be done to establish the role of trace elements in the pathogenesis of diabetes mellitus and many studies have lead to contradictory findings and controversial conclusions. In some cases the disease is associated with metal abnormalities and in some of these, correction of the abnormality would affect a cure. Much work, however, remains to be done to pin—point these cases.

ZINC

Insulin is stored in complexes with varying ratios of zinc in pancreatic B —cells¹. It has been found that zinc deficiency in animals leads to decreased insulin secretion and increased insulin resistance², that zinc enhances the binding of insulin to hepatocyte membranes³ and that the antigenic properties of insulin vary on altering the zinc to insulin ratio⁴. However, others found that in rats zinc deficiency had no effect on oral glucose tolerance⁵, the development of diabetes in mice may lead to zinc deficiency⁶ and an acute administration of zinc produced a transient elevation of blood glucose in rats with a decrease in circulating insulin⁷. Major causes of morbidity and mortality in older diabetics relate to impaired immune function which leads to increased infections, foot ulcers, osteomyellitis, etc. Zinc plays an important role in wound healing and zinc supplements were shown to accelerate the healing of leg ulcers in elderly patients⁸. Although zinc deficiency and poor taste acuity, zinc supplementation in zinc deficient diabetics failed to improve their taste perception⁹.

CHROMIUM

Deficiency of chromium or its biologically active form, the glucose tolerance factor (GTE) has been implicated in some forms of glucose intolerance. The GTF appears to be a complex of nicotinic acid, amino acids (mainly glycine, cysteine and glutamic acid) and chromium. Its molecular weight is about 400—600¹⁰. Richest sources of GTE are brewer's yeast, liver and kidney. The exact mechanism of the action of GTE is not known. It appears that either GTE converts insulin into some other active form or it transports insulin to specific intracellular sites¹¹. Numerous trials have been carried out on diabetic patients. In some, administration of either inorganic chromium (as chromic chloride) or of GTE have had beneficial effects¹² on blood glucose levels but in others, none¹³. In yet another study, brewer's yeast extract has resulted in a 17% decrease in glycosylated haemoglobin and a 36% increase in HDL but no change in fasting blood glucose levels¹⁴. In humans, it does not seem to matter whether inorganic chromium is administered or GTF, and those whose glucose tolerance is affected are presumably those with low storage levels of chromium — which are not necessarily reflected in fasting plasma or blood levels of chromium. Plasma chromium in a group of womçn with abnormal oral glucose tolerance decreased in response to an oral glucose load. After supplementation with brewer's

yeast, glucose ingestion gave rise to an increase in plasma chromium levels¹². Presumably these women were originally chromium deficient, but the picture is more complicated than this. Chromium also: appears to have an important role in lipid metabolism. Clinical trials have shown that in some cases chromium supplementation may decrease serum total cholesterol and HDL-cholesterol levels but has no effect on triglycerides¹². Hence, chromium deficiency may be a factor in the pathogenesis of atherosclerosis in certain cases and supplementation may have beneficial effects in some of these.

MAGNESIUM

Magnesium, a cofactor in the glucose transport system of plasma membranes, a cofactor of many enzymes involved in glucose oxidation, plays a role in insulin release and is bound to ATP. Diabetes mellitus, when poorly controlled, is associated with increased urinary loss of magnesium¹⁵ and is the most frequent chronic disease associated with hypomagnesaemia¹⁶. Although conflicting results have been obtained, significantly lower plasma levels were found in diabetics than in normals¹⁷. Conversely, one group of insulin dependent diabetics had a 30% decrease in the trabecular bone magnesium content of iliac crest biopsies but the magnesium levels in erythrocytes, leukocytes and muscle were normal suggesting that the effect of diabetes or of insulin treatment on different tissue pools of magnesium can be variable¹⁸. Ketoacidosis, results in large urinary losses of magnesium and the resulting hypomagnesaemia is implicated in insulin resistance, in the life-threatening effects on myocardium and skeletal muscle¹⁹. in diabetic retinopathy²⁰, and perhaps in the accelerated atherosclerosis of diabetes.

COPPER

The role of copper in glucose haemostasis is not well defined. Experimental data suggest that impairment of glucose tolerance can be secondary to copper deficiency²¹ whereas serum copper and ceruloplasmin were found elevated in some Type II diabetics²². Russian diabetics were found to have low blood copper levels but those with gangrene had high levels²³. The results in the latter case are presumably because ceruloplasmin is an acute phase protein and blood copper levels rise with those of ceruloplasmin.

MANGANESE

Experimental evidence suggests that manganese deficiency, in guinea pigs can cause impaired glucose tolerance which is reversed by manganese supplements²⁴. Conversely, the hepatic manganese content in rats with streptozotocin-induced diabetes was elevated²⁵. One molecule of arginase contains four atoms of manganese and it is possible that increased rates of amino acid metabolism and urea synthesis, which characterise insulin deficiency, are related to increased arginase activity. Manganese status in human diabetics is controversial. It has been reported that diabetics in one group had about half the normal blood level²⁶ and in another, 62% had raised serum manganese levels²⁷. Elevated serum levels have been reported in cases of myocardial infarction and in atherosclerosis²⁸. Whether diabetic patients with elevated blood manganese levels are at risk for cardiovascular diseases remains to be seen²⁸.

SELENIUM

Selenium, being an integral part of glutathione peroxidase, has a protective role against tissue damage

caused by peroxides produced in lipid metabolism. Selenium deficiency causes reduced glutathione peroxidase activity and cardiomyopathy²⁸. In rats selenium deficiency produced glucose intolerance²⁹ but in a study on 27 children with insulin-dependent diabetes, the mean serum selenium level was higher than that of normals³⁰. Although serum levels may not necessarily reflect tissue levels, it appears that diabetic children do not have selenium deficiency contributing to the known problems of diabetes mellitus. Although evidence is incomplete and contradictory, some diabetics undoubtedly owe their state to a bodily deficiency of one or more metals. Trace element analysis on a large scale requires flameless atomic absorption spectroscopy. One analysis takes about one minute at negligible cost, apart from technologist's time. However, the initial outlay is high. Some governmental institutions have this, technique, but no medical institution in Karachi has. Even in healthy populations, metal deficiency is surprisingly common, for example, in U.S. in a group of 37,000 healthy individuals, 75% had a magnesium intake of less than the recommended daily allowance³¹. Hence, early detection may solve many later problems.

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