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Relationship of Environmental Chromium and Zinc Levels to Tissue Chromium and Zinc Levels from Individuals with Maturity Onset Diabetes Mellitus in Selected Watershed Areas of Utah

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RELATIONSHIP OF ENVIRONMENTAL CHROMIUM AND ZINC LEVELS TO TISSUE CHROMIUM AND ZINC LEVELS FROM INDIVIDUALS WITH MATURITY ONSET DIABETES MELLITUS IN SELECTED WATERSHED AREAS OF UTAH

by

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Carol H. Williams

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ABSTRACT

Relationship of Environmental Chromium and Zinc Levels to Tissue Chromium and Zinc Levels From Individuals with Maturity Onset Diabetes Mellitus in Selected Watershed Areas of Utah

by

Carol H. Williams, Master of Science

Utah State University, 1979

Major Professor: Dr. Deloy G. Hendricks
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This study was conducted to determine whether a functional relationship exists between human tissue and environmental levels of chromium and/or zinc and in individuals with maturity onset diabetes.

Three counties of Utah were selected as sites:

1. Wayne County, where a State Health Department screening had shown a 12.7 percent incidence of diabetes, and, where there is very little industry, and an assumed low level of environmental chromium and zinc.

2. Utah County, where the diabetic screening had shown an 0.75 percent incidence of diabetes and where there is nearby large industry and an assumed higher level of zinc and chromium.

3. Cache County, in which the incidence of diabetes was 3.79 percent and where there is an assumed low level of environmental zinc and chromium and very little industry.

A full three hour glucose tolerance test was carried out on 76 subjects for classification as diabetic or non-diabetic. Chromium and zinc concentrations in serum, hair, urine and tap water were determined by atomic absorption. Serum cholesterol and triglycerides were determined for all subjects. Taste acuity was also determined in each subject.

Wayne County subjects had some characteristics differing from those in Cache and Utah. The weight/height ratio for diabetics and nondiabetics was the same. The weight/height ratio for diabetics and nondiabetics was significantly different in Utah and Cache Counties. There was no significant difference between diabetics and nondiabetics in Wayne County in the fasted glucose levels. This was not true in Cache and Utah. The blood glucose levels in diabetics was significantly lower at all intervals in Wayne diabetics than in Utah and Cache Counties.

There was a significantly lower concentration of chromium in tap water in Wayne County. Subjects from Wayne County also had the lowest tissue concentration of chromium. Tap water from Utah County had the highest concentration and the subjects from this county had the highest body tissue chromium. Concentration of chromium in body tissues was similar for diabetics and nondiabetics.

It was found that diabetics had higher serum zinc values than nondiabetics. There was no difference in the zinc values in serum in a fasting state and one hour post prandial in either diabetics or nondiabetics. Urine zinc was significantly higher in diabetics than in nondiabetics. Hair zinc concentration was similar in diabetics and nondiabetics.

The recognition of bitter and salty taste were significantly reduced in diabetics, but there were no taste differences among people from different counties.

A different diabetic pattern emerged in Wayne County where water chromium levels were significantly lower and tissue chromium levels tended to be lower. It appears that although the incidence of diabetes is higher in the low chromium area (Wayne County) the severity of diabetes is less. This phenomenon requires further investigation.

(129 pages)

INTRODUCTION

From 1964 to 1969 the Utah State Division of Health conducted a state-wide diabetes screening program in which 15,371 individuals were screened. As a result, 528 previously unknown cases of diabetes were discovered. This represented 3.4 percent of the people who were tested. In Wayne County, 466 people were screened and 59 new cases of diabetes discovered. This represents 12.7 percent of the population screened in that county. Juab County was the only other county to have over a 6 percent incidence of diabetes in the people tested. Of the 581 people screened in Juab, 8.3 percent were found to have diabetes.

Maturity onset diabetes, which is characterized by the delayed release of endogenous insulin in response to a carbohydrate challenge, is a condition commonly found in adults over 40 years of age. It differs from juvenile diabetes, which is characterized by abnormalities relating to absolute insulin deficiency. Symptoms of maturity onset diabetes have responded to control of carbohydrates in the diet, weight reduction, and, more recently, to supplementation of chromium or glucose tolerance factor in the diet. Diabetes is a genetic metabolic disorder, but the manifestations of the genetic character are probably modified by nutritional factors. The effects of nutrition are probably

more evident in maturity onset diabetes than in juvenile diabetes (Boyle, Mondschein, and Dash, 1977).

Mertz (1969) stated that trivalent chromium acts as a cofactor for the peripheral action of insulin. Schwartz and Mertz (1959) showed that impaired glucose tolerance of rats maintained on certain purified and laboratory chows is restored by small doses of chromium III ion.

Schroeder, Balassa and Tipton (1962) found that tissue chromium levels are exceptionally high in the newborn baby and Hambidge (1971) reported a pattern of declining concentration of tissue chromium with age.

Schroeder and Nason (1968) found tissue chromium concentrations were lower in American males than in males from Africa, the Near East and the Far East in the subjects tested, and that it was lower in American children than in children from other countries.

Whole wheat bread contains 0-49 ppm chromium. Bread made from refined white flour contains 0-14 ppm chromium. Highly refined white sugar contains 0-.02 ppm chromium compared to .08-1.21 ppm chromium in less refined sugars and molasses (Schroeder and Nason, 1968). Some researchers believe that a highly refined diet may be causitive in low tissue chromium levels.

A low chromium status may be a factor in diabetes mellitus in humans. Chromium dosing increased the rate of glucose removal in Jordanian infants from 0.6 percent per

minute to 2.9 percent per minute. Jordanian children raised in an area where the water contained 0.5 ppb chromium in the water had a glucose removal rate of 0.7 percent per minute, while those from an area having 1.6 ppb chromium in the water had a glucose removal rate of 3.8 percent per minute (Hopkins, Ransome and Majaj, 1968).

Glinsman, Feldman and Mertz (1966) showed a two-fold increase in the concentration of chromium in plasma in subjects with normal glucose utilization after administration of glucose by mouth.

Glinsman and Mertz (1966) showed an improvement of glucose tolerance in some maturity onset diabetics when supplemented with 1000 µg of chromium per day for 8-20 days. Impaired glucose tolerance returned when supplementation was discontinued.

A form of chromium found in food has been labeled the Glucose Tolerance Factor and has been identified as a true potentiator of the action of insulin (Mertz, 1974).

Zinc also has been linked with carbohydrate metabolism since it was first discovered that crystalline insulin contains considerable amounts of zinc (Kirchgessner, Roth and Weigand, 1976).

Low levels of zinc in plasma and blood cells and high 24 hour urine zinc excretion are characteristics of diagnosed diabetics (Kumar and Rao, 1974).

Studies with zinc depleted animals suggest that zinc deficiency could reduce the physiological potency of insulin and affect free active and bound inactive insulin levels in the circulation. Zinc deficiency was said to have caused a "prediabetic condition" (Kirchgessner, Roth and Weigand, 1976).

Zinc deficiency also has been associated with a syndrome of altered taste, smell and response to food and drink, a condition first described by Henkin, et al. (1971). The condition has been found following surgery, flu, burns and drug-induced zinc deficiency which also are characterized, in many cases, by hyperzincuria (Cohen, Schechter and Henkin, 1973; Catalanotto, 1978; and Henkin, 1977). In many of these same cases the symptoms were relieved by zinc dosing.

Zinc is ordinarily widely distributed in food, drinking water, and the air. Even metalic zinc, which may occur in industrial pollution, can be dissolved by gastric juices and become available for absorption (Fox, 1970).

Wayne County has no industry that would lead to environmental chromium or zinc contamination. A recent water study of the Fremont River Basin showed that all water tested contained less than 10 ppb chromium and 10-50 ppb zinc (Hansen, 1971). It is, therefore, possible that people in Wayne County have an increased incidence of chromium and/or zinc deficiency which is expressed in increased incidence of maturity onset diabetes.

This study was an attempt to determine if there is a relationship between the tissue and environmental levels of chromium and/or zinc and diabetes mellitus in three areas of Utah, selected on the basis of assumed levels of environmental chromium and zinc.

In each of these areas persons suffering from maturity onset diabetes and nondiabetic persons participated in the study.

REVIEW OF LITERATURE

Diabetes

Diabetes Mellitus is a chronic systemic disease characterized by disorders of the metabolism of insulin, carbohydrate, fat and protein and the structure and function of blood vessels. Diabetes Mellitus ordinarily appears as one of two clinical pictures: Juvenile or youth-onset, ketosis prone, or maturity-onset or ketosis resistant (Galloway, et al., 1973).

Juvenile-onset diabetes is characterized by abnormalities relating to absolute insulin deficiency. This results in hyperglycemia and hyperketonemia. Juvenile diabetes may manifest itself by polyuria, polydipsia, and weight loss. There also may be visual disturbances, leg pain, fatigue, sugar spots on clothing, depression, high blood pressure, itching of skin and other symptoms. There is occasionally a history of hypoglycemica symptoms. Juvenile diabetes is usually diagnosed in patients under 20 years of age but is not confined to the young (Keen and Jarrett, 1969).

Maturity onset diabetes is characterized by the delayed release of endogenous insulin in relation to carbohydrate challenge. There is also a delayed hyperinsulinism in which insulin level rises higher than in the nondiabetic (Yalow

and Berson, 1965). A maturity onset diabetic also has been defined as a patient forty years of age or older, with recent onset of the disease, insulin requirement twenty units or less or none at all and without tendency toward ketoacidosis (Balodimos and Marble, 1971).

The criteria for diagnosis of diabetes mellitus or abnormal glucose tolerance have differed from clinic to clinic and author to author. This presented some problems in comparing and pooling information. A report of the Committee on Statistics of the American Diabetes Association (1969) recommends a set of conditions for conducting oral glucose tolerance tests which is now widely used and makes diagnosis more uniform.

A Bureau of Census Survey (Public Health Publication, 1967) estimates that, in the United States, one person in twenty has or is potentially a diabetic. Nearly seven of ten known persons with diabetes had their diabetes discovered at age 45 years or older. Nearly half discovered the disease between 45 years and 64 years. One in five was discovered at 65 years or older. Glucose tolerance diminishes after 45 or 50 years of age and individuals in this age group show a much higher prevalence of diabetes if the same standards for diagnosis are applied (Sharkey, 1971). There was an increase of 95 percent in the number of people with diabetes in the United States between 1950 and 1965 (American Diabetes Association, 1969).

The Utah State Division of Health conducted a diabetes screening in 20 of 29 counties from 1964 to 1969. They found a high incidence of new cases of diabetes among persons screened in Wayne (12.6 percent), Juab (8.3 percent), and Millard (6.3 percent) counties. All other counties reported less than 5 percent of the people screened as being diagnosed as diabetics. This survey raised questions as to the high incidence of diabetes in these particular areas of the State of Utah (Utah State Division of Health, Results of Diabetic Screening, 1969).

Factors related to the prevalence of diabetes

Heredity. An accumulation of high risk factors is present in families in which the onset of diabetes occurs early, where such factors may not be involved in families of late onset diabetes (Galloway, et al., 1973).

It is generally recognized that diabetes begins at the time of conception, and the development of overt diabetes may vary from a few months to many years (Sharkey, 1971). Diabetics who developed the disease before age 20 had an unusually large number of first degree relatives with diabetes as compared with those who developed the disease late in life (Galloway, et al., 1973).

Ethnic groups such as Indians and Blacks show distinct differences in the prevalence of diabetes, both very low and very high, as compared to the general public (Westfall and Rosenbloom, 1971; Mouratoff, Carroll, and Scott, 1969).

Researchers have proposed many modes of genetic transmission for diabetics. Klimt, et al. (1967) reported that diabetes is due to a combination of genetic factors and such environmental factors as the type of diet and eating habits.

Obesity. West and Kalbfleisch (1971) reported that an overweight condition may be the most important single environmental factor in the emergence of diabetes among different races. Other researchers (Jackson, 1972, and Baird, 1973) have supported this concept through population studies. Baird (1973) cites researchers who consider that obesity is an integral part of the diabetic state, the result of, rather than the cause of diabetes while others postulate that genetically poorly endowed beta cells of the pancreas may be unable to meet the stress of obesity and that this may also be true of other environmental stress factors such as diet.

While correlation between obesity or overnutrition and diabetes has been quite consistent, the protective effect of marked leanness or undernutrition has been less consistent. In Latin American studies, the diabetes was only slightly less common among the very lean than among individuals of normal weight (West and Kalbfleisch, 1971).

Age. Blood glucose levels increase with age (Sharkey, 1971). Andrus (1971) pointed out that regardless of the population studied, there is a progressive deterioration of glucose tolerance, decade by decade of life on all the commonly used diagnostic tests for diabetes. West and

Kalbfleisch's (1971) work in ten countries showed that elderly subjects had poor glucose tolerance that was not attributable to greater adiposity in older subjects. In all countries studied, subjects over 34 years of age did not increase in weight, and in all the countries there was a decline in mean body weight of subjects between age 55 and 65. In a long term study in a home for the aged, the findings amply confirmed that diabetes and diminished glucose tolerance are very prevalent among the aged (Grobin, 1970).

Pregnancy and parity. Pregnancy often has a diabetogenic effect which is transitory and clears after delivery. Also the metabolic error of the diabetic is found to increase in the majority of patients with advancing pregnancy (Burt, 1960). Westfall and Rosenbloom (1971) report that eleven mature women with abnormal glucose tolerance had a total parity of 54; and all were over 36 years of age. They were compared with twelve normal women who had a total parity of 50. Apparently parity in itself does not contribute to abnormal glucose tolerance but can be modified by other factors.

Sex. Cohen, Teitelbaum and Saliternik (1972) showed in rats which were genetically disposed to diabetes, that there were significantly more male than female rats with blood glucose levels higher than 181 mg/100 ml at 60 minutes after a glucose load. These results agree with work done by

Houssay, Foglia, and Rodriguez (1954) which showed that a protective action is accorded by estrogens while androgens appeared to enhance the severity of the disease.

Diet. Cohen, Teitelbaum and Saliternik (1972) studied several Jewish ethnic groups as a result of their immigration. In all groups he found an association between increased sucrose consumption and increased diabetes. West and Kalbfleisch (1971) found a correlation between the prevalence of the diabetes and sugar consumption among natives of ten countries. They showed a negative association between the total amount of carbohydrates consumed and the prevalence of diabetes. Their hypothesis was that carbohydrates consumed in the more bulky natural foods may protect a population from developing diabetes. Their work also suggested that neither protein nor fat in themselves produce diabetes.

Cohen, Teitelbaum and Saliternik (1972) showed that the dietetic factor exposed the genetic factor in genetically predisposed rats. The genetic factor alone did not result in diabetes. None of the starch fed rats developed impaired glucose tolerance. In their siblings, fed the sucrose diet, however, the impaired glucose tolerance that developed was accompanied by glycosuria and the rats were labeled as frankly diabetic. Rats that had previously impaired glucose tolerance returned to normal when they were reverted from the high sucrose to the regular starch diet.

Socio economic. The socio-economic standards seem to correlate to diabetes only to the point that they allow calories in the diet to produce obesity. In a study of six ethnic groups, the poorer people had a slightly greater prevalence of diabetes than those with higher economic status (Jackson, 1972).

Plasma cholesterol and triglycerides. Mildly impaired glucose tolerance, hypertriglyceridemia, coronary artery disease, insulin resistance and mild obesity are often associated. Total cholesterol and triglycerides tend to increase with age up to sixty years, with greater frequency in men than in women (Sharkey, 1971). Fredrickson, Levy and Lees (1967) stated that carbohydrate intolerance was found in over 90 percent of Type III hyperlipoproteinemia which manifests itself by hypercholesteremia and hypertriglyceridemia. Glucose tolerance decreased faster with age with this condition than it did in the normal state.

West and Kalbfleisch (1971) found cholesterol levels substantially higher in subjects with impaired glucose tolerance than in normal patients. In males, a statistically significant increase in cholesterol values was observed even in those with minimal impairment of tolerances. In females, no significant change in cholesterol values was observed until two hour post prandial glucose values reached 200 mg/100 ml. There was a positive association between adiposity and cholesterol values. Although cholesterol levels were

greater among diabetics, there were no instances of marked hypercholesterolemia in any subject. The highest value among 2,034 subjects was 360 mg/100 mls.

Chromium

Biochemically, chromium is an active compound that forms many complexes with proteins, stimulates several enzyme systems, may stabilize certain nucleic acid structures, and is found in brain tissue. Low chromium states have been associated with aortic lesions in animals, and, most interpretable, with a diabetic like syndrome (Mayer, 1971).

Diabetes Mellitus is a genetic metabolic disorder, but the manifestations of the genetic character are probably modified by carbohydrate and chromium nutritional factors. The effects of such nutritional factors are more evident in maturity-onset diabetes than in juvenile diabetes. In compensation for a dietary deficiency of chromium, excessive insulin secretion coupled with a subsequent inability to tolerate substantial carbohydrate insults might be an important factor in the cause of diabetes (Boyle, Mondschein, and Dash, 1977).

The Glucose Tolerance Factor

The nutritional history of chromium can be traced to an observation by Mertz and Schwarz (1955) that rats developed an impairment of intravenous glucose tolerance when they

were fed Torula yeast in their diets but not when they were fed brewers yeast. The responsible agent was not yet known, and it was termed the Glucose Tolerance Factor (GTF). Subsequent testing of 47 different elements in GTF deficient rats detected GTF only in chromium complexes which contained the trivalent form (Cr^{+3}) of chromium (Schwarz and Mertz, 1959). In this study most Cr^{+3} complexes improved glucose tolerance overnight with oral doses of 20 µg of chromium/100 g of body weight.

Mertz (1961) showed that in comparing epididymal adipose tissue of chromium sufficient and chromium deficient rats, both tissue groups took up approximately the same amount of glucose. There was a significant difference, however, in the positive response of chromium-sufficient tissue to insulin. Similar work has been done by Doisy (1963).

Evans, Roginski and Mertz (1973) extracted GTF from Brewer's yeast and showed that when GTF was mixed with 125 I-insulin, the insulin produced a significantly greater effect on the glucose uptake of epididymal tissue than that of native insulin. In testing GTF, exclusive of insulin, the fraction which potentiated insulin activity had an elution volume greater than that of insulin. These results demonstrated that GTF binds to insulin. Results of these tests also indicated that GTF is low molecular weight compound which potentiates insulin activity after binding to the insulin molecule.

Mertz (1969) demonstrated that chromium in physiological doses acts by correcting a deficiency and that an optimal dose of an active chromium complex may raise impaired activity to a level found in tissue from sufficient animals, but not beyond.

Recent studies seem to indicate that chromium forms a complex between insulin and tissue insulin receptors facilitating the initial insulin-tissue interaction (Mertz, et al., 1974). Those workers explain that chromium emerges not as an insulin like agent, but as a true potentiator of the action of the hormone.

A complex group of compounds has now been synthesized and partly identified that possess biological activity similar to the naturally occurring chromium compounds found in brewer's yeast. It has a niacin-chromium-niacin as the essential GTF configuration. The preparations extracted from brewer's yeast contained chromium, nicotinic acid, glycine, glutamic acid and cysteine. The definitive identification of glucose tolerance factor in yeast has not been fully accomplished (Toepfer, et al., 1977).

Supplementation

Human subjects respond to trace supplementation of chromium with a normalization of impaired glucose tolerance. Glinnsman and Mertz (1966) demonstrated an improvement of glucose tolerance in three out of six diabetics after dietary supplementation with chromium in the first reported

trial of chromium supplementation. Schroeder and Nason (1968) reported improvement of glucose metabolism in four of twelve diabetic outpatients who were given high chromium doses for six months and one year. Four male patients were studied under strictly controlled conditions. Three of the subjects responded to daily doses of trivalent chromium with significant improvement of oral glucoses tolerance. In supplementation trials with elderly human subjects, glucose removal rate was improved with no change in the level of circulating insulin (Levine, Streetan and Doisy, 1968).

Supplementation in adult humans has always taken from several days to several weeks to be noticeable. This interval could not be shortened by giving higher doses (Mertz, 1975).

Malnourished children show an immediate improved glucose tolerance when given doses of chromium. Hopkins, Ransome and Majaj (1968) found abnormally low glucose levels in the fasted state and abnormally high glucose levels after glucose dosing with low removal rates in Jordanian children from a section of the country with low levels of chromium in the drinking water (5 ppb). More normal levels were restored in both parameters by giving doses of chromium to the children. In Nigerian children, rates of glucose removal from the blood stream were increased after being given similar doses of chromium but the mean fasting level was not affected. Glucose removal rates for children from a Jordan

valley with chromium levels in the drinking water of 1.6 ppb were relatively normal. A similar response was found by Gurson and Saner (1971) among infants from Turkey.

Doisy, et al., (1976) studied the effects of brewer's yeast extract supplementation in children and elderly subjects. In older persons with abnormal glucose tolerance, 50 percent improved to the point of normal response. The authors also observed a reduced endogenous insulin release in both old and young subjects after supplementation.

Underwood (1977) indicated that there are several reports of malnourished infants, diabetics and old persons who have not responded to chromium supplementation. This indicated that the chromium status of the nonresponders is adequate for this function or perhaps the body is not converting inorganic chromium to the physically active substance in these people.

Distribution

The concentration of chromium in human tissues is decreased with age, especially in the United States. Mayer (1971) stated that it seems to be the only mineral to evolve in this way.

Human tissue from the United States contained, on the average, smaller quantities of chromium than did those from several other areas of the world, and the frequency of

occurrence was less. There were some differences in tissues of American adults according to the city of origin. Liver and kidney of some Americans, but of no foreigners, lacked detectable chromium (Schroeder, Balassa, and Tipton, 1962).

Schroeder, Balassa and Tipton (1962) analyzed for chromium in eight human tissues on autopsied specimens ranging in age from 9 days to 80+ years. These were taken from cities in the continental United States. They were compared to human tissue chromium concentrations from Alaska, Hawaii and thirteen other countries. High levels were found at birth, with a rapid decline to low levels in adults. Kidney and liver appeared to maintain neonatal concentrations until the second decade of life. Lung, aorta, heart and spleen lost chromium early. Lung was the only tissue in which concentrations rose later in life. Many samples did not have detectable levels.

Doisy, et al., (1971) also reported lower values in the elderly and have agreed that the elderly suffer a chromium deficiency.

Hepatic chromium content was determined in postmortem tissue from diabetic and control subjects by Morgan (1972). The mean hepatic chromium was 12.7 µg/g of ash for the control group and 8.59 µg/g of ash for the diabetic subjects. This finding supports the theory that chromium deficiency may be a cause of diabetes in elderly subjects.

Chromium is widely distributed throughout the human body in low concentrations of about 0.02 to 0.04 ppm without special concentrations in any known tissue or organ (Underwood, 1977).

Mayer (1971) previously reported that chromium is low in the heart, very high in the various parts of the brain, hair, skin, fat and omentum.

Urine

Urinary chromium excretion is closely related to glucose metabolism and can be a meaningful indicator of the chromium status of population groups. Urine chromium has also been shown to decrease with age (Underwood, 1977).

The major excretory route of chromium is via the kidney. In 1961 (Collins, Fromm and Collings, 1961) suggested that characteristics of this form of chromium are similar to that of GTR chromium. Urine probably contains the more biologically active form of chromium, and can be a meaningful reflection of the chromium status of an individual.

Schroeder and Nason (1968) showed that after a glucose load, urinary chromium rose, indicating that urine is the major excretory route for the chromium that is involved in the metabolism of glucose. In diabetic patients urinary chromium also is increased after a glucose load.

The 24-hour urinary excretion of chromium is partly dependent on urine volume (Punsar, et al., 1977). Mertz (1974) suggested that normal urinary excretion is 5-10 µg/day.

Hambidge (1971) reported the mean urinary chromium excretion of twenty normal young adults as 8.5 ± 5.2 µg/day. Mitman, et al. (1975) studied nine young women who showed normal glucose tolerance, normal height-weight ratios and were all non parous. The mean daily chromium excretion values for all subjects was 7.2 ± 0.4 µg/day. The patients were eating freely chosen diets, but there were no differences in chromium urinary excretion. This probably indicates that any dietary differences in chromium were too small to affect urinary chromium output.

Punsar, et al. (1977) showed that urinary chromium excretion in two populations of male Finnish atherosclerotics was very similar (3.6 µg/24 hours and 3.6 µg.24 hours) and low when compared to the average of 5 to 10 µg/day in other studies. One population came from an area with a low concentration of chromium in the water; the second from an area with a much higher level of water chromium. The low urinary chromium output levels in both of the areas were almost as low as those from a supposedly chromium deficient area in Turkey studied by the same author.

Similar to the effect of glucose loading on the chromium concentration in plasma, there is a question of urinary chromium concentration after glucose loading. Gurson and Saner (1978) compared urinary chromium excretion before and after glucose loading in normal individuals, individuals

from families with chemical or established overt diabetes and in diabetics. The normal subjects showed a significant increase both in terms of chromium excretion per minute and the chromium/creatinine of the subjects from diabetic families. Only five of thirteen subjects increased their chromium excretion and chromium/creatinine ratio. Mean values for the whole group remained statistically unchanged before and after the glucose challenge. Three of the overt diabetics had a moderate increase in chromium excretion and chromium/creatinine ratio, but a decrease occurred in the others, resulting in nearly identical means before and after the glucose loading.

Blood and serum

The reported levels of chromium in blood have declined markedly in recent years and a reliable range still cannot be given with complete confidence. Since blood chromium is not in equilibrium with tissue stores, the level in blood is not a good indicator of body chromium status (Underwood, 1977).

Glinnsman, Feldman and Mertz (1966) reported that an increase in serum insulin concentration caused by injection of insulin or by oral or parenteral administration of glucose, can lead to an acute increase in serum chromium within 30-120 minutes in normal healthy subjects. The mean for 1 hour

was 35 mg/100 ml and 41 mg/100 ml at 2 hours. There has been some controversy concerning the validity of these values (Burt and Davison, 1973; Gurson and Saner, 1978).

Hambidge (1971) found no correlation between serum chromium concentrations and blood sugar levels in diabetic children. He also found this to be true in different age groups, pregnancy, parity in disorders of carbohydrate metabolism, or in association with evidence of chromium deficiency.

Liu and Morris (1978) recently reported a new value by which serum chromium can be measured. The value is termed RCR and is a measurement of the relative chromium response as an index of response to glucose, and as an indicator of chromium nutritional status. Their work was done with normal women subjects and hyperglycemic women who were dosed with brewer's yeast extract. Glucose, insulin and chromium levels were then analyzed. Seventy-three percent of the normal subjects showed an improved RCR Mean:RCR 107 percent before, and 140 percent after. Seventy-five percent of the hyperglycemics showed an improved RCR mean:RCR 81 percent before and 149 percent after supplementation. The increased RCR was associated with decreased serum insulin and glucose levels. Both groups had an improved chromium state. In response to glucose load, serum chromium levels dropped in inadequate chromium storage and that there was a low value of relative chromium response at the one hour point in a

suboptimal nutritional status. This index may become a useful measurement in chromium nutritional status.

Hair

The levels of chromium in hair provide a useful index of the chromium status of groups, although absolute levels indicative of chromium deficiency in the individual remain to be defined (Underwood, 1977).

The chromium concentration in the hair of normal newborn infants is significantly higher than in older children (Hambidge and Baum, 1972). Children who ranged in age from 0-7 days had a hair chromium concentration mean of 910 ppb. Children from 2-3 years of age had a hair chromium concentration mean of 412 ppb.

Schroeder, Balassa and Tipton (1962) reported earlier that the mean tissue chromium concentration of human newborns was seven fold greater than those of the older child or adult. Schroeder and Nason (1969) reported that hair chromium did not decline with age, but they had not included newborn and young children in their study.

Gurson, et al. (1975) examined the hair chromium in a series of subjects of different age groups and of different nutritional background. They were unable to establish significant differences in hair chromium related to age or nutritional state. They attributed these findings to a

slowing in the rate of hair growth in malnourished children and adults. They speculated that chromium may show an accumulation with slow growth.

They did find, however, significantly lower hair chromium concentrations in the Turkish population than in reported USA values. For example, they found 331 ± 124 ng/g in newborn infants and 240 ± 130 ng/g in well nourished adults in the Turkish population.

Saner and Gurson (1976) obtained hair samples from newborn babies and their mothers. The mean hair chromium concentrations were significantly higher in mothers (203 ng/g) compared to their babies (119 ng/g). However, when taken individually, twelve of the babies had slightly higher hair chromium than their mothers. There was a positive correlation between the hair chromium of the babies with slightly higher content and their mothers. In the total group, the hair chromium concentration of the newborn did not show any correlation with the mothers age, birth rank, mothers hair chromium concentration, or birthweight.

Hambidge, Rodgerson and O'brien (1968) studied the chromium levels from children with juvenile diabetes and healthy non-related children living in the same area. The mean hair chromium level for the normal children was 0.85 ng/g; the diabetic children had a mean hair chromium level of 0.56 ng/g. There was no relation of hair chromium to age or sex.

In a study of adult onset diabetics and nondiabetics, the mean hair chromium levels of the diabetics was 94 ppb. This was significantly lower than the mean value of 241 ppb for hair chromium levels in the control subjects (Benjanuvatra and Bennion, 1975).

Hambidge, Franklin and Jacobs (1972) studied hair chromium concentrations with increasing distances from hair roots. Their results indicate that the concentration is not dependent of the time the hair has been exposed to the external environment. Large variations in chromium levels along the hair shaft were similar to newly grown hair of the same individual over a period of many months, and were considered to reflect past fluctuations in the chromium nutritional status of the individual, that closer to the scalp, reflecting more recent nutriture.

Parity and pregnancy

Parity or the number of pregnancies is an important factor which influences chromium levels in humans. Hambidge and Rodgerson (1969) showed that parous women have significantly lower levels of chromium than non parous women. Chromium may be one of the nutrients stored by the fetus at the expense of the mother. The depletion of maternal stores of a number of essential nutrients during pregnancy has been reported frequently.

Hambidge and Rodgerson (1969) found hair chromium concentrations of a group of parous women consistently low (mean 0.22 μg/g) in contrast to the higher range (mean 0.75 μg/g) of concentrations found in a group of similar aged nulliparous women. In family studies, levels for the mother were without exception, lower than those of other family members.

An analysis of hair chromium concentration in nulliparous and parous women who had just given birth to a child was made by Mahalko and Bennion (1976). They found a highly significant difference in the values in the two groups. Hair chromium concentration for parous and nonparous women were 117 ± 10 and 309 ± 23 ppb, respectively. Interestingly, they observed no further decrease in hair chromium in women who had borne more than one child. They also found that concentrations increased significantly with time between pregnancies, especially when at least four years had passed.

Transitory diabetes which clears after delivery is commonly found during pregnancy and the metabolic error of the diabetic patient increases with advancing pregnancy (Burt, 1960). Burt and Davidson (1973) showed that chromium levels in peripheral plasma and hair were significantly lower in pregnant women than in normal nonpregnant women. After insulin administration chromium levels were unaltered in pregnancy in contrast to significant and prolonged decreases in nonpregnant subjects. These authors speculate on the

possibility that altered glucose-insulin homeostasis of pregnancy may be, in part, due to a relative deficiency of chromium or an alteration of chromium physiologically by the pregnant state. They consider it unlikely that the increased tissue volume of pregnancy could be responsible because chromium levels are depressed as early as 8-10 weeks after conception when tissue volume is small.

Lipid metabolism

Disturbances of lipid and glucose metabolism are associated with coronary artery disease. Chromium supplementation, therefore, with other dietary alterations aimed at treating these metabolic disturbances, might prove helpful in treating atheroscerosis and diabetes.

Schroeder (1969) showed that chromium supplementation via the food or drinking water of a previously low chromium diet decreased rat serum cholesterol levels and, in males, restrained the tendency of cholesterol levels to increase with advancing age.

Schroeder (1969) had earlier reported a significant decline in serum cholesterol in some institutionalized patients fed chromium daily for a period of five months. Other patients with similar treatment showed no response.

Schroeder's findings were confirmed by Staub, Reussner, and Thiessner (1969) who found that the addition of chromium to the drinking water of rats on a hypercholesterolemic

diet with either sucrose or starch as the carbohydrate lowered the serum cholesterol levels.

Sintz, Seedman and Graff (1970) showed that rats which were fed brown sugar or white sugar with added chromium had lower serum cholesterol levels than rats consuming white purified sugar alone.

Boyle, Mondschein and Dash (1977) explained that if chromium depletion results in biologically ineffective insulin and seriously deranged glucose metabolism, then the body must rely on lipid metabolism to meet energy requirements. This would result in accumulated cholesterol which is associated with the atherosclerotic process. Chromium deficiency tends to decrease hepatic uptake of cholesterol and fatty acids. This process could favor the deposition and accumulation of lipids in the arteries. Hyperinsulinemia and chromium depletion appear to disrupt lipid metabolism and promote hyperlypidemia, as well as atherogenesis in the arterial wall. They also reported that in several Oriental nations, where characteristically low serum cholesterol levels are found, these same populations have relatively high chromium concentrations in tissues. Chromium depletion in the human aorta and other arteries inhibits lipid oxidation. These observations could help explain why diabetic subjects exhibit high mortality from atherosclerosis.

Source

Chromium intakes in the United States vary from 5 µg to over 100 µg per day (World Health Organization, 1973). Masironi, Wolf and Mertz (1973) reported that the average American diet supplies about 60 (range 30-140) µg of chromium per day.

Mertz (1974) reported that chromium analyses have indicated certain common diets, even though otherwise complete, furnish only 5 µg chromium per day.

Foods containing the greatest concentration of chromium include meats, the bran and germ portions of cereal grains, and certain spices, but the overheating of some foods may form a chromium complex difficult to absorb (Schroeder and Nason, 1968). Natural sugars and grains contain chromium concentrations sufficient to facilitate the metabolism of these high carbohydrate foods but it is removed in refining. For example, there is a high concentration of chromium in molasses, none in white sugar. The processed carbohydrates further deplete chromium reserves since the chromium excretion rate is increased after glucose loading (Schroeder and Nason, 1968; Glinnsman and Mertz, 1966).

Techniques for analyzing food chromium are limited and it is difficult to determine the adequacy of chromium intake in the normal diet (Mitman, et al., 1975).

A number of reports of the chromium content of human foods and dietaries have appeared but many are of little

value nutritionally because past analytical methods and instruments have been inadequate and little is known of chromium forms and their relative absorbability and biological activity (Underwood, 1977). Nevertheless, human dietary chromium intakes are greatly influenced by the amounts and proportions of refined carbohydrates consumed (Underwood, 1977).

Masironi, Wolf and Mertz (1973) analyzed molasses and unrefined, brown and highly refined sugar from several countries for chromium content. The mean levels were 266 µg Cr/g for molasses, 162 µg Cr/g for unrefined sugar, 64 µg Cr/g for brown sugar and 20 µg Cr/g for refined white sugar. There is a greater loss of organically bound chromium than inorganic chromium in refinement. This is significant in nutrition since the glucose tolerance factor is the biologically functional form of chromium and is an organically bound complex (Masironi, Wolf and Mertz, 1973).

Some chromium in food is inorganic and some is organically bound and has biological activity and is available for glucose oxidation. Chromium containing extracts with GTF activity have been obtained from brewer's yeast and have been used in supplementation (Mertz, et al., 1974).

Toepfer, et al. (1973) determined the chromium content and the relative biological activity of selected food items. Their work verifies and supports earlier reports that brewer's yeast, some spices, black pepper in particular,

wheat germ and meat contain the highest level of chromium. Most of the grains and cereal products were in the middle group followed by the fruits and vegetables.

Requirements

Mertz (1974) estimates the daily requirement of chromium to be 10 to 30 µg from good sources such as brewer's yeast.

The minimum human chromium requirements compatible with satisfactory growth and long-term health and fertility cannot yet be given because of inadequate knowledge of the forms and availability of chromium in foods (Underwood, 1977). A daily intake varying from 20 to 500 µg chromium has been suggested, depending on the chemical nature of chromium in individual foods. This would be needed to compensate for a urinary loss of 5 µg chromium/day (World Health Organization, 1973). Many individuals excrete more than 5 µg per day and insulin-dependent diabetics secrete much more (Underwood, 1977). This suggests that chromium intake of man in the United States and perhaps in other countries may be suboptimal.

Metabolism

Inorganic chromium compounds are poorly absorbed in animals and man to the extent of 1-3 percent or less

regardless of dose and dietary chromium status. Natural complexes in the diet are more available than simple chromium salts (Underwood, 1977).

Little is known of the site or mechanism of chromium absorption but Underwood (1977) refers to several studies which indicate that the small intestine appears to be a diffusable segment for chromium and that chromium and zinc may be metabolized by a common pathway.

Physiological amounts of chromium are transported in the blood complexed to siderophilin (transferrin), a component of the β-globulin fraction of plasma protein (Hopkins and Schwarz, 1964).

Water

The concentration of the elements available in the soil for plants and animals will vary, depending on the geochemical environment. They may enter the food chain, be concentrated, passed on or filtered out by portions of the ecosystem. They may be available in one segment or another of the chain, including water or plant or animal which has taken it from the system. Drinking water can be a source of trace elements including chromium. The United States drinking water standards of 1946 set a maximum limit of 0.05 ppm for the hexavalent form, but none for the trivalent form of chromium (Selby, Marienfeld, and Pierce, 1970).

Glucose tolerance in malnourished infants from families who lived in the Jordanian hill area where the drinking water contains 0.4-0.5 ppb of chromium were compared to glucose tolerance in malnourished infants from families who resided in the Jordanian valley area where chromium in the drinking water ranged from 1.2-1.8 ppb. Glucose tolerance was severely impaired in the infants from the hill area and was nearly normal in the infants from the valley. The families of the infants from both areas had received similar food rations from the United Nations and the hill area families enjoyed a slightly better economic situation. Hopkins, Ransome, and Majaj (1968) believed that the important difference in the nutrition intake between the two groups was registered in the different sources of drinking water. The infants with impaired glucose tolerance improved markedly after receiving supplementry chromium.

Punsar, et al. (1977) reported a study of urinary chromium excretion and atherosclerotic manifestations in two Finnish male populations. A 10-year follow-up showed a particularly high mortality from coronary heart disease in the area where the concentrations of chromium in the drinking water were lower than in the area where they were high. However, extensive tests on urinary chromium excretion of the male population from each area suggested that in the diets of these men, water was not important for the supply of chromium.

Lifetime exposure to 5 mg/liter of Cr. III in the drinking water induced no toxic effects in rats and mice (Hutcheson, et al., 1975).

Air

A study of the concentration of chromium in Buffalo, New York, an industrial city, showed concentrations in the air ranging from 0.01 to 0.18 $\mu g/m^3$ with a mean of 0.006 $\mu g/m^3$. Data in tables showing percentages of total human intake of metals from air based on the highest reported atmospheric concentration of metals, showed that the maximum concentration of chromium reported was 0.18 g/m^3; daily intake from food and water was 245µg and the daily intake from air was 3.6 µg (Woolrich, 1973).

Zinc

Carbohydrate metabolism

Since the discovery by Scott in 1934 that crystalline insulin contains considerable amounts of zinc, many studies have investigated the extent to which zinc nutrition influences the zinc content of the pancreas and its production and storage of insulin (Kirchgessner, Roth and Weigand, 1976).

One of the best known functions of insulin is to lower blood glucose levels. Hendricks and Mahoney (1972) found no difference between zinc deficient and zinc supplemented

rats in their ability to metabolize orally administered glucose. However, Quarterman (1966) found that when glucose was injected intraperitoneally into rats fasted overnight after a longer period of dietary treatment, the glucose tolerance of zinc-deficient animals was depressed compared to pair-fed controls. This finding was confirmed by Huber and Gershoff (1973) and by Hendricks and Mahoney (1972) who also showed that zinc depleted rats, which had the same initial plasma glucose concentration as the pair fed and ad libitum-fed control animals, had a significantly lower glucose tolerance when given glucose interperitoneally.

Fasel, Hadjikhani and Felber (1970) suggested that the conflicting results obtained after oral dosing of glucose as compared to intraperitoneal injection might be explained by a greater stimulation of insulin secretion by glucose given orally.

Reasons for poorer glucose tolerance of zinc-deficient animals are not clear. In other research reviewed by Kirchgessner, Roth and Weigand (1976) no difference was found in the plasma insulin levels between zinc-deficient rats and their zinc-supplemented continuously-fed or meal-fed pair mates, though the glucose tolerance in the zinc-deficient rats was significantly lower than in the pair-weight controls. Plasma insulin levels increased after glucose injection but were not different in zinc-depleted and control animals. Even though there may have been no

difference in the insulin levels, it is possible that the physiological potency of the hormone was reduced by zinc deficiency. Zinc deficiency might also have different effects on free active and bound inactive insulin in circulation. Zinc deficiency was said to have caused a "pre-diabetic" condition. Kirchgessner, Roth and Weigand (1976) also reported that Engebartk and Kief found that acute stimulation of insulin secretion in rats also reduced the zinc content in the β-cells of the pancreas. They make the assumption that since zinc participates in the synthesis and storage of insulin in the β-cells, it is plausible that the amount of insulin stored during zinc deficiency is lower.

Liaw, Hendricks and Mahoney (1976) demonstrated in an invitro system, that zinc from the islets of Langerhans isolated from pancreas of zinc supplemented rats was secreted into a media containing glucose. There was no movement into a similar media containing no glucose.

In zinc deficient animals, the islets contained less zinc before incubation and a smaller percentage of the zinc moved into the glucose media. There was, again, no secretion of zinc, when the islets were incubated in a media containing no glucose. Insulin activity as reflected by a decrease in blood glucose, was in direct proportion to the amount of zinc released into the media.

Wound healing

Wound healing is analagous to growth and is similarly affected by zinc deficiency. It is a complex, active biological process that requires an intact protein synthetic mechanism, as does growth (Wacher, 1976). Zinc's role in wound healing was first reported by Strain and his co-workers and reviewed by Pories, et al., (1976).

Sandstead et al., (1974) demonstrated delayed wound healing of incised wounds and thermal burns in zinc deficient rats. They also showed significantly reduced tensile strength of incised wounds after twelve days in zinc deficient rats. In addition, extra zinc given to rats on a diet with normal zinc levels did not increase the rate of healing or increase the tensile strength of incised wounds.

Zinc deficits develop rapidly in patients with major burns and persist until wounds are epithelialized (Larson, 1970 as discussed by Pories, et al., 1976).

Hallbook and Lanner (1972) found that with venous leg ulcers, healing was impaired in those patients with reduced serum zinc levels. Wound healing was accelerated by the addition of zinc to their diets. Added zinc had no effect on patients with normal serum zinc levels.

Rose et al. (1978) recently reported work with liver and hepatoma poly (A) polymerase which showed that the enzyme-zinc complex was labile and that a reduction in zinc content correlated with a loss of enzyme activity. Their

data indicated that (a) poly (A) polymerase is a zinc containing protein; (b) this metal plays a role in the interaction between an enzyme and its substrate.

Wounds often heal slowly and with difficulty in individuals with diabetes. The reasons are unknown (Bennion, 1979).

Perhaps the failure of some diabetics to heal ulcers on their feet and elsewhere is related to zinc deficiency. Healing of such ulcers has been reported subsequent to zinc therapy (Sandstead, et al., 1974).

Altered taste

Henkin, et al. (1971) found zinc deficiency associated with a syndrome which manifested itself in decreased taste acuity (hypogeusia); unpleasant, obnoxious and perverted appreciation of food and drink (dysgeusia), decreased olfactory acuity (hyposmia); and unpleasant, obnoxious and perverted appreciation of odors (dysosmia). In the thirty-five cases studied, hypogeusia was found in all patients while the other symptoms were not uniformly present.

Several metals had previously been described as important for the control of taste acuity. Zinc, the least toxic and best tolerated of these, was chosen as the metal for treatment. Zinc appeared to correct many of the symptoms of the disease and to improve taste thresholds.

Zinc concentration in hair from apparently normal children from an unselected population in Denver correlated positively with appetite, growth and taste acuity in these children (Hambidge, et al., 1972). After supplementing the diets of these children with small quantities of zinc, taste acuity was normalized and hair zinc concentrations increased.

Henkin (1977) studied patients with progressive systemic sclerosis who had been zinc depleted by oral administration of histidine and who exhibited anorexia as well as taste and smell dysfunction. Zinc supplementation, even with continued histidine administration, returned each sign and symptom toward normal within 8-24 hours.

Zinc deficiency in adult male human volunteers by dietary control has been accomplished and described by Prasad (1976b). These patients manifested chemical features found in field studies: i.e., weight loss, loss of libido, rough and scaly skin, lethargy, loss of appetite and low levels of zinc in plasma, red blood cells, leukocytes and urine after receiving a 1750 calorie diet for six months which contained only 1.2 mg of zinc per day.

Zinc's major carrying protein in blood is albumin. There exists in blood, an equilibrium of zinc, albumin and amino acids. Addition of amino acids, particularly cysteine

and histidine, strips the zinc from albumin and binds it to the amino acid molecules. Henkin (1977) administered L-histidine to volunteers and produced hyperzincuria and eventually low serum zinc concentrations. In 4-6 days the young men volunteers complained of anorexia and had to be encouraged to eat. The anorexia was severe enough to produce a 2-3 pound weight loss. Breakfast was the best tolerated meal; dinner, the least.

With continued and increased doses all subjects developed decreased taste acuity, then decreased smell acuity. Distortion of taste and smell perception followed. The doses of L-histidine were continued, but exogenous zinc was administered, with rapid and complete abolition of anorexia in 24 hours. Taste and smell dysfunction eventually disappeared.

Henkin's (1977) study also led to the discovery of the parotid salivary zinc protein, gustin, which is now used to estimate rapid changes in body zinc status. Zinc also has been involved at the level of the taste bud membrane.

Henkin (1977) was successful in restoring normal appetite and taste to cancer patients who exhibited anorexia and hypogeusia and had low serum zinc values by treating the patients with zinc sulfate.

Catalanotto (1978) reviewed research on decreased or altered taste acuity, zinc deficiency and therapy. Studies with zinc deficient animals showed modified taste function.

Hussey (1974) cited a study by Schechter of patients with hypogeusia in whom the syndrome began during or soon after an illness in 57 percent of the group, 33 percent of the group could cite no illness and 10 percent had recently had an illness or surgery. Examination failed to link the gypogeusia with any underlying cause, but serum zinc levels were low and urinary zinc excretion was increased. Orally administered zinc alleviated the syndrome.

In a study of aged institutionalized persons, whose diet was adequate except for zinc (Greger, 1978) showed that the taste acuity of the aged patients did not respond to zinc supplementation as significantly as younger patients studied by Henkin, et al. (1975) and Hambidge, et al. (1972).

Urine zinc

Zinc is a normal component of urine; from 0.1 to 0.7 mg of zinc per day is excreted by normal adults (Underwood, 1977). Spencer, et al. (1976) found that on a normal zinc intake of about 12.5 mg/day, the urinary zinc excretion was to be low ranging, from 0.5 to 0.8 mg/day while most of the zinc was excreted in the stool. Ellis (1978) agrees that the urinary excretion is fairly constant, at about 500 µg/24 hours, and normally does not vary much with the zinc intake.

Prasad (1976b) stated that excretion of zinc in urine decreased as deficiency of zinc progressed, based on 24-hour

urine collections. In most cases zinc deficiency in man is associated with hypozincuria but hyperzincuria has been observed in some diseases.

Pidduck, Wren and Price Evans (1970) found a highly significant difference in the urinary zinc excretion between human diabetics and control groups. The difference did not seem to be a consequence of therapy, age of onset of the disease, proteinuria, age or weight. Mild diabetics showed a less severe zincuria than a diabetic who required insulin or oral hypoglycemic agents. They found the means of the µg/day excreted as follows: No therapy or diet controlled males, 665; females, 319; all, 492. Oral hypoglycemica agent therapy males, 587, females, 717; all, 645. Insulin therapy males, 962; females 509; and all, 776.

A high excretion of zinc in urine among newly diagnosed cases of diabetics was found by Kumar and Rao (1974). The 24-hour excretion of zinc in urine was 1,080 µg/24 hours compared to 465.4 µg/24 hours in nondiabetics; a significant difference.

Serum and plasma

Davies, Mash and Dormandy (1968) determined plasma zinc values in normal men and women who had fasted overnight and then were given 50 g of glucose. Plasma zinc levels fell within 10 minutes and reached minimum levels at 1.5 hours; then rose to about the original levels after 2 hours.

Well controlled diabetics that did not require insulin had similar zinc curves. Intervenous injections of glucose had a similar but more rapid effect on plasma zinc levels. The mean values of zerum zinc in normal adults, analyzed by atomic absorption spectrophotometry, ranged from 90 µg/100 ml to 122 µg/100 ml. This range is not as great as that in any single study cited (Fuwa, et al., Parker et al., Meret and Hankin, Kurz, et al., and Pekarek, et al. as reviewed by Halstead, Smith and Irwin, 1974).

Pekarek, et al. (1972) reported that the concentration of zinc in serum from male adults is approximately 100 µg/ 100 ml. Lower values have been reported in women and in aged persons (Lindeman, et al., 1971).

Pories, et al. (1976) reported a normal value of serum zinc as 125 µg percent.

Pidduck, Wren and Price Evans (1970) found no significant differences in plasma zinc concentrations between diabetic subjects and normals. The diabetic males had a mean of 81.56 µg/100 ml, male controls had 77.88 µg/100 ml. Diabetic females had a mean of 79.35 µg/100 ml; female control had 81.89 µg/100 mls. Pidduck pointed out that serum zinc is 16 percent higher than plasma zinc.

In recently diagnosed diabetics, Kumar and Rao (1974) found that levels of zinc in plasma and blood cells were significantly low while the 24-hour zinc excretion was significantly high.

Chooi, Todd and Boyd (1976) found that plasma zinc did not differ between men and women and remained fairly constant until about 50 years of age, after which it declined. In this study diabetics, unlike normal individuals, did not show any significant alterations in plasma zinc levels with age. The high plasma zinc concentrations exhibited by diabetics over the age of 50 years, in comparison with the control group, did not appear to be caused by diet or zinc in insulin preparation since there was no difference observed between diabetics on hypoglycemic agents and those controlled by insulin. Chooi, Todd and Boyd (1976) cited work by Chlouverakis which concludes that the amount of endogenously derived insulin required to maintain normal glucose tolerance increased with age. He reasoned that the reduction of plasma zinc levels with age in older normals may, therefore, be related to changes in insulin levels. This may also explain the observation that diabetics treated with exogenous insulin did not exhibit the same decline in plasma zinc levels.

Hair

Zinc concentration in hair reflects zinc nutriture, and if hair has been growing at a reasonable rate, hair zinc is a useful clinical index of zinc status (Klevay, 1970).

Hambidge, et al. (1972) identified a number of children from Denver as zinc deficient as a result of a survey of

trace element concentration in the hair of apparently normal children. Ten of 132 children had hair zinc concentrations less than 70 ppm, or more than 3 SD below the normal adult mean. Eight of the children were found to have below normal growth. Most of the children with low zinc levels also had a history of poor appetite, and five of six tested also showed reduced taste acuity.

Klevay (1970) found no correlation between plasma zinc and hair zinc.

Deeming and Weber (1978) in attempting to determine whether there was a relationship between mineral concentrations of hair, serum and diet, found significant differences in hair concentrations of zinc between male and female human subjects. The mean concentration of hair zinc from women was 208 ppm and only 176 ppm in men. The dietary intake of zinc for males was significantly greater than for females. The authors considered differences in hair zinc to be due to sex and not reflective of dietary intake. They also showed that hair zinc levels in both sexes declined after 40 years of age even though there were no significant differences in intake with age.

Human zinc requirements

The Food and Nutrition Board of the National Research Council (1974) has determined that the average zinc content of a mixed diet consumed by American adults is between 10 and 15 mg.

Only 5-15 percent of the zinc ingested in the diet is actually absorbed by the body (Spencer, 1965 and Prasad, 1966). Zinc absorption may be further reduced by the presence of phytate or other dietary components which act to bind zinc (Rheinhold, et al., 1973).

Zinc balances for most individuals are in equilibrium on a zinc intake of 12.5 mg/day. There are individuals for which a higher intake of about 15 mg/day is needed to attain equilibrium (Spencer, et al., 1976).

Harper (1973) recommended that the dietary allowance for zinc should be 15 mg/day for adults. The Food and Nutrition Board recommends an additional 15 mg/day during pregnancy and 10 mg/day during lactation.

Sources of zinc in the diet

A severe zinc deficiency resulting from an inadequate intake of zinc is unlikely to occur with a varied diet of natural foods. Zinc is widely distributed in food, drinking water and air. Most zinc salts are absorbed and are equally well utilized; even metallic zinc can be dissolved by gastric juice and become available for absorption (Fox, 1970). There are, however, some components which have a profound effect on the availability of zinc. The most widespread offender is phytic acid which occurs in cereal grains and legumes and binds zinc particularly in the presence of excess calcium. Other binding or chelating agents are

found in clay and become a problem when geophagia is practiced (Halstead, 1968).

The zinc content of the diet greatly depends on dietary protein content. A diet containing about 1 gm protein/kg weight for a 70 kg man is expected to contain about 12.5 mg of zinc. A diet that is adequate in calories but has a low protein content will contain much less and a high protein diet may have two to three times that zinc content (Spencer, et al., 1976).

The main source of zinc in the diet is meat. There are marked differences in the zinc content in different kinds of meat. Red meat has the highest; fish also has a relatively high zinc content. Most other food items in the daily diet have a zinc content of 1 mg or less per 100 g net weight. Whole wheat and rye bread have about 1 mg/100 g and other food items have less (Osis, et al., 1972).

Mills (1973) suggested that present food trends toward the consumption of processed and refined foods may increase dietary zinc deficiency in the future in the United States. For example, whole wheat bread has 1.04 g zinc/100 g of bread, and white bread has 0.57 g zinc/100 g.

Zinc in the environment

Zinc is widely distributed in food, drinking water and the air. A table prepared by Woolrich (1973) indicating the percent of total human intake of metals from air utilizing

the highest reported atmospheric concentration showed the maximum concentration reported for zinc as 1.69 $\mu g/m^3$; the daily intake from food and water was 14,500 µg and the daily intake from air was 33.8 µg. Carbon disulfide exposures have been shown to decrease the zinc content in tissues in both humans and animal subjects. Zinc excretion is increased following increased carbon disulfide exposure. Through chelating action, the ionic form of zinc is decreased to a metabolically ineffective concentration. Carbon disulfide exposure inhibits growth during the nontoxic phase and causes weight loss during the toxic stage (Woolrich, 1973).

Zinc is found in most water supplies. Hansen (1971) reported from 10 to 50 ppb in a number of wells in the Upper Fremont River Basin. The conduit system for the water can also change the level of zinc found in the water. Zinc levels reported in tap water in Wales were 0.203 ± 2.2229 ppb in the morning and 0.086 ±0.0110 ppb in the evening Elwood, Abernathy, and Morton, 1974).

METHODS AND PROCEDURES

Characteristics of Areas Studied

1. Loa-Bicknell area, Wayne County
   a. rural area
   b. assumed low level atmospheric chromium and zinc contamination
   c. high incidence diabetes mellitus
2. Payson area, Utah County
   a. rural area
   b. suspected higher level atmospheric chromium and/or zinc contamination (Geneva Steel Plant)
   c. low incidence of diabetes mellitus
3. Hyrum area, Cache County
   a. rural area
   b. assumed low level atmospheric chromium and/or zinc contamination
   c. low incidence diabetes mellitus

Sample Selection

Areas selected for study were determined from a Utah State Division of Health Diabetic Screening, the results of which were published in 1969. The state-wide program screened 15,371 individuals and diagnosed 528 previously

unknown cases of diabets mellitus, which accounted for 3.4 percent of the population screened.

Wayne County was selected as a site because the screening showed an incidence of 12.66 percent, the highest in the state.

The Payson area of Utah County was selected as site because the diabetic screening showed an incidence of 7.5 percent in Utah County, one of the lowest in the state.

The Hyrum area of Cache County was selected because the screening showed the incidence of diabetes in that county to be 3.79 percent, much lower than Wayne County.

A public health nurse working in each area assisted in identifying persons in that respective area with maturity-onset diabetes mellitus. These people were asked to participate in the study. Another person in that same area, of the same sex, who matched as nearly as possible in age, weight, and, if a woman, in parity, were identified and were invited to participate as controls.

Arrangements were made in each area to conduct glucose tolerance tests and collect other data. A registered medical technologist drew all blood samples and a public health nurse or medical doctor was always present. A medical doctor in internal medicine made the final diagnosis of diabetes in all cases.[1]

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[1]Cloyd G. Krebs, M.D., Provo, Utah.

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Seventy-six persons were invited to participate in this study, supposedly as diabetics and near matched controls. Of this number, 24 were diagnosed as diabetic and 52 were diagnosed as nondiabetic.

Sample Collection

Glucose tolerance test and blood collection

The glucose tolerance tests were conducted according to the set of conditions recommended by the American Diabetes Association's Committee 1968 report, the Standardization of the Oral Glucose Tolerance Test. Glucose dosing was carried out as recommended by the American Diabetes Association (1969). Blood samples were drawn by a registered medical technologist using disposable syringes fitted with stainless steel needles using sterile techniques.

A standard 3-hour glucose tolerance test was made on each subject. The fasted and 1 hour (after glucose dosing) blood samples were 13 ml in volume; 3 ml of which was mixed with fluoride as an enzyme inhibitor and were used for glucose analysis. The remaining 10 ml were dispensed (after removing the needle from the syringe) into acid washed, double distilled water rinsed, 12 ml polyethylene test tubes. The 2 hour and 3 hour blood samples drawn were only 3 ml in volume for the glucose analysis.

The 3 ml aliquots of blood were taken to Logan L.D.S. Hospital where the glucose levels were determined on a 12 channel Auto Analyzer.

Serum

Blood drawn from the subjects while fasted and 1 hour after glucose dosing was placed into an acid washed test tube. After the blood had coagulated, the clot was removed and the serum was spun in a centrifuge at 1500 R.P.U. for 15 minutes. The cell free serum was poured into clean, acid washed polyethylene test tubes and stored at 20° C until analysis was completed. Chromium, zinc, cholesterol and triglyceride levels were determined in these serum samples.

Taste acuity

Detection and recognition thresholds for representatives of each of four taste qualities were measured in each subject by a forced choice-three stimulus trop technique (Henkin, 1971). Random sequences of three drops of solution were placed onto the surface of the tongue; two of the drops were water, one of the drops contained a solute dissolved in water. Four different solutes were tested; for salt, sodium chloride; for sweet, sucrose; for bitter, urea; and for sour, hydrochloric acid.

The concentrations and the method of presentation in a varied order and a mixed design are found in Appendix C. Thresholds were determined for one taste quality before

proceeding to the next. The lowest concentration of solute which the subject could consistently distinguish as different from water for each taste quality was called perception threshold, the lowest concentration of solute which the subject could consistently recognize as salty, bitter, sour or sweet was called recognition threshold (Henkin, et al., 1971; Hambidge, et al., 1972).

Urine

Each subject was asked to collect a 24-hour urine sample. The samples were collected in plastic disposable specimen containers. Each sample was measured and the amount recorded. A 100 ml aliquot was taken, mixed with 1 ml HCl and placed in a clean acid washed polyethylene sample bottle. Samples were frozen at -20° C until analyzed.

Hair

Samples of hair were collected from the suboccipital area of the head with stainless steel scissors. Samples were placed in an envelope, sealed and taken to the laboratory.

Drinking water

A 100 cc sample of drinking water was obtained at the home of each participant. The water was allowed to run for 3 minutes before a clean acid wash polyethylene sample bottle was filled.

Dust

Three dust samples were obtained from within the home of each participant. An ashless filter paper was used over the nozzle of a vacuum cleaner to obtain a sample from (1) floor, (2) near the center (upholstered furniture, etc.), (3) high (top of drapery-window or doorway). Samples were placed in an envelope, sealed and labeled.

Chemical Analysis

Chromium

Chromium levels in serum were determined directly on serum and urine in a Model 63 Carbon Rod Atomizer mounted on a Varian Techtron AA120 Atomic Absorption Spectrophotometer and equipped with a rapid response recorder. Operational parameters were similar to those of Davidson and Secrest (1972). Sample aliquots (20 ul) were introduced into the furnace with Eppendorf micropipets. Since graphite tubes varied in electrical conductance, sample quantitation was always made between sets of standards at intervals of about 10 samples. All samples were analyzed in triplicate.

Hair chromium was determined on 20 mg samples of hair. Hair was weighed into glass cruciables which had been acid washed and triple rinsed in demineralized water which had a resistance > 5 mega ohms. The samples were then ashed in an activated oxygen plasma low temperature asher. Ashed samples were solubilized in 100 ul of 0.2 N HNO_3 and analyzed for chromium as described for serum. The ashing

phase of the programmer for the carbon furnace, however, was eliminated.

Water chromium was determined on 10 ml aliquots of water which were pipetted into clean, acid washed triple rinsed polyethylene test tubes and then covered with laboratory tissue paper. These samples were placed into a forced air oven at 60° C until totally dry. The residue was brought to 1 ml with 0.2 N HNO_3 and analyzed for chromium as described above.

Chromium levels in house dust were determined by wet ashing samples in concentrated HNO_3 followed by concentrated perchloric acid. These samples were then diluted with demineralized water and analyzed as previously described.

Zinc

Serum zinc levels were determined on samples of serum which were deproteinated with trichloro acetic acid (TCA). One-fourth ml of serum was mixed with three-fourths ml of a 12.5 percent TCA solution. Samples were allowed to stand for 10 minutes and then were centrifuged at 2500 RPM for 15 minutes. Serum zinc levels were determined from the supernatant on an atomic absorption spectrophotometer using an air acetylene flame.

Urine was diluted 1:1 with 0.2N HNO_3 and aspirated directly into the atomic absorption spectrophotometer for determination of the zinc concentrations.

Hair zinc concentration was determined on 20 mg hair samples which were ashed in a muffle furnace for 48 hours at 550° C. The residual ash was solubilized in 1 ml 0.2N HNO_3. These samples were used for the direct determination of zinc concentration as described for urinary zinc.

Water zinc levels were determined by direct aspiration on the atomic absorption spectrophotometer without any further sample preparation.

Creatinine

Urinary creatinine was determined using the Picrate Colormetric method (ICNND, 1963)

Cholesterol

Serum cholesterol was determined on samples of blood taken when the subjects were fasted and again 1 hour after they had ingested a glucose dose (50 g/m^2). Total serum cholesterol was assayed colorimetrically using the stable Liebermann-Burchard reagent (Kim and Goldberg, 1969).

Triglycerides

Determination of serum triglyceride levels was made on serum from fasting and 1 hour blood samples. A method utilizing isopropanol and washed Alumina followed by saponification was used (Neri and Frings, 1973).

Statistical analysis

Statistical analysis of data was carried out by Analysis of Variance utilizing the SPSS package on the Burroughs B6700 computer.

Significance between treatment means when the F values were significant was determined by Duncan's new multiple range test (LeClerg, Leonard and Clark, 1962). Data, where there was statistical significance, was plotted with a computer plotter.

In order to look at the influence of diabetes mellitus on certain parameters, measured paired *t* and nonpaired *t* tests were determined. Because a paired *t* test showed similar significant data to nonpaired *t* analysis, nonpaired *t* data is presented throughout the paper because a larger number of observations could be included.

RESULTS

Characteristics

Age

The mean age of the diabetics in this study was 63 years. The mean age of the nondiabetics was 56 years. There was a significant difference to the .01 level. The total population surveyed in Utah County was older than in Wayne and Cache Counties (Table 1).

Sex

There were 15 male diabetics, 19 male nondiabetics, and 9 female diabetics and 33 female nondiabetics in the population studied (Table 1).

Weight

The mean weight of the total diabetic population was 80.31 k; the mean weight of non-diabetics was 70.82 k. In every county the diabetics were heavier than nondiabetics. There was no statistical difference in weight between counties. The height/weight ratio was the same in Wayne County for diabetics and nondiabetics, but there was a marked difference in the height/weight ratios between diabetics and nondiabetics in Utah and Cache Counties (diabetics had a greater weight/height than normals).

Table 1. Characteristics of population studied

Character-istic	Cache		Utah		Wayne	
	D[a]	ND[b]	D	ND	D	ND
Male	10	7	1	2	4	10
Female	0	5	5	7	4	21
Age, years	60.5 ±11[c]	55.1 ±10	73.0 ±5	60.9 ±14	58.9 ±9	53.2 ±12
Weight, kg	83.08±11.35	74.91±12.26	78.09±12.26	70.82±8.63	78.54±18.61	74.46±35.87
Height, cm	168.0±10	167.5±10	160.7 ± 7	160.0±7	170.5±10	162.2 ±10
Wt/Ht kg/cm	.49	.45	.49	.44	.46	.46

[a] Diabetic
[b] Nondiabetic
[c] mean ± standard deviation of the mean.

Blood/glucose

Fasted glucose values of the diabetics were significantly higher than nondiabetics in Cache and Utah Counties. There was not a significant difference between diabetics and nondiabetics in Wayne County in the fasted glucose levels.

One, two and three hours post prandial blood glucose levels of all diabetics were significantly higher than nondiabetics. However, blood glucose levels in diabetics in Wayne County were significantly lower than in either Cache or Utah Counties (Figure 1).

Serum cholesterol

There was no statistical difference among the serum cholesterol levels of the diabetics and the nondiabetics in any of the three counties. Utah County people had the highest mean serum cholesterol (229±4 mg/100 ml) at the fasting state. This volume was significantly higher than fasted serum cholesterol levels (192±51 mg/100 ml) of people in Cache County.

There was a tendency for diabetics to show higher serum cholesterol values in this study; however, statistical significance was not achieved (Table 2).

Serum triglycerides

The triglyceride levels in serum in diabetics tended to be higher than in nondiabetics 1 hour after a glucose dose. This was particularly true in Cache and Wayne Counties.

*Mean significance range as determined by Duncans new multiple range test. A mean value is significantly different from another mean if the top of the bar does not bisect the lined area ($p < .05$). This is a rank test thus the last ranked value has no significance range.

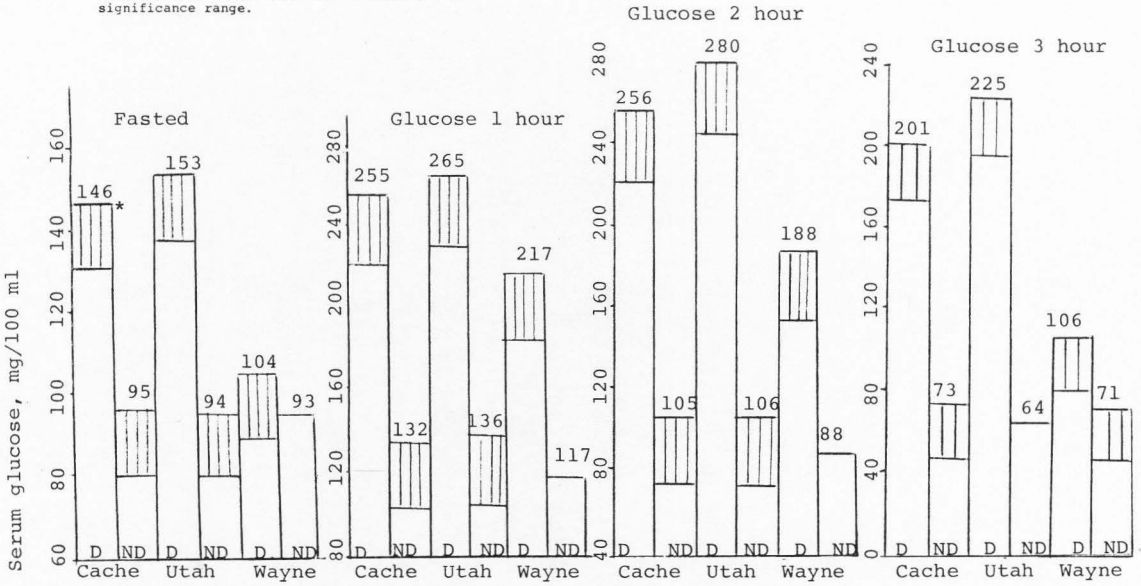

Figure 1. Serum glucose, mg/100 ml, by county and by diabetic (D) or nondiabetic (ND).

Table 2. Serum cholesterol values in diabetic and non-diabetic subjects by county

County	Cholesterol mg/100 ml Diabetics	Nondiabetics	t[a]
Cache			
fasted	210 ± 51[b]	176 ± 48	1.6
1 hour[c]	208 ± 29	179 ± 47	1.7
Utah			
fasted	216 ± 34	239 ± 44	1.1
1 hour	204 ± 53	224 ± 46	0.8
Wayne			
fasted	231 ± 42	211 ± 50	1.0
1 hour	230 ± 39	227 ± 103	0.1

[a] t value as determined by a non-paried t test

[b] Mean ± standard deviation about the mean

[c] 1 hour after glucose dosing

When combining all diabetics and all nondiabetics in the three counties, diabetics had a significantly higher circulating triglyceride level than did nondiabetics. This was true in the fasted state as well as 1 hour after glucose dosing (Figure 2).

Tissue chromium

Serum chromium levels tended to be higher in all subjects in Utah County than in Wayne County. Urine chromium per unit of creatinine tended to be higher in Utah County subjects than in Wayne County subjects (Appendix D). Chromium levels were similar in diabetics and nondiabetics (Table 3).

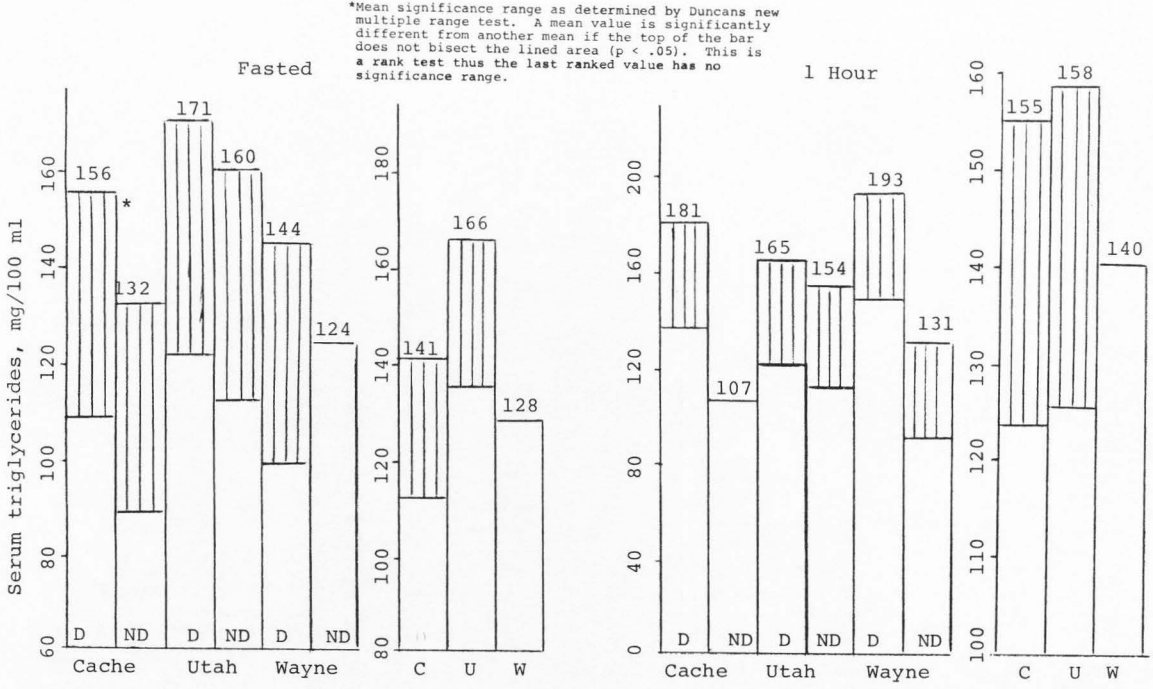

Figure 2. Serum triglycerides, mg/100 ml, by county and by diabetic (D) or nondiabetic (ND).

Table 3. Tissue levels of chromium in diabetic and non-diabetic subjects

Tissue	Diabetics	Nondiabetics	t[a]
Serum chromium µg/liter			
fasted	9.1 ± 4.9[b]	8.1 ± 3.5	0.98
1 hour[c]	10.0 ± 6.9	8.0 ± 4.7	1.39
Uring chromium			
µg/liter	6.7 ± 7.4	7.3 ± 4.1	0.39
µg/24 hrs	7.7 ± 10.1	8.3 ± 6.7	0.29
µg/mg creatinine	1.4 ± 1.6	1.3 ± 1.1	0.22
Hair chromium mg/g	490 ± 264	461 ± 256	0.45

[a] t value as determined by non-paired t test

[b] Mean ± standard deviation about the means

[c] Sample taken 1 hour after glucose dosing

Variability about the mean was very high. As a consequence, small differences were difficult to detect (Table 3).

Tissue Zinc

Serum

There was no difference in the serum zinc levels between fasted or 1 hour post prandial in diabetics. The same was true for the nondiabetics. Serum zinc levels were significantly higher in diabetics than nondiabetics (Table 4).

Serum zinc levels were higher in Utah County than in the other two counties.

Table 3. Tissue levels of chromium in diabetic and non-diabetic subjects

Tissue	Diabetics	Nondiabetics	t[a]
Serum chromium µg/liter			
fasted	9.1 ± 4.9[b]	8.1 ± 3.5	0.98
1 hour[c]	10.0 ± 6.9	8.0 ± 4.7	1.39
Uring chromium			
µg/liter	6.7 ± 7.4	7.3 ± 4.1	0.39
µg/24 hrs	7.7 ± 10.1	8.3 ± 6.7	0.29
µg/mg creatinine	1.4 ± 1.6	1.3 ± 1.1	0.22
Hair chromium mg/g	490 ± 264	461 ± 256	0.45

[a] t value as determined by non-paired t test

[b] Mean ± standard deviation about the means

[c] Sample taken 1 hour after glucose dosing

Variability about the mean was very high. As a consequence, small differences were difficult to detect (Table 3).

Tissue Zinc

Serum

There was no difference in the serum zinc levels between fasted or 1 hour post prandial in diabetics. The same was true for the nondiabetics. Serum zinc levels were significantly higher in diabetics than nondiabetics (Table 4).

Serum zinc levels were higher in Utah County than in the other two counties.

Table 4. Tissue levels of zinc in diabetic and nondiabetic subjects

Tissue	Diabetics	Nondiabetics	t[a]
Serum zinc µg/100 ml			
fasted	130 ± 39[b]	112 ± 31	2.09*
1 hour[c]	128 ± 35	109 ± 23	2.78**
Urine zinc			
µg/liter	669 ± 404	342 ± 253	4.68**
µg/24 hr	834 ± 487	377 ± 230	5.59**
Hair zinc			
µg/g	134 ± 33	140 ± 43	0.57

[a] t value as determined by non-paired t test

[b] Mean standard deviation about the mean

[c] Sample taken 1 hour after glucose dosing

*Significant at $P < .05$

** Significant at $P < .01$

Urine

The urinary zinc, whether expressed as concentration, 24 hour excretion, or zinc per unit of creatinine was significantly higher in the diabetic than in the nondiabetic.

Hair

There was no difference between diabetics and nondiabetics in tissue stores of zinc as reflected by hair zinc analyses (Table 4). Hair zinc levels tended to be lower in Cache County than in either of the other counties (118, 147, and 147 ppm).

Taste acuity and recognition

Recognition and perception of a bitter taste was significantly reduced in diabetics as evidenced by recognition and perception of the bitter taste at a higher molar concentration of urea (514 versus 342 mM for diabetics and nondiabetics respectively). Diabetics also had a significantly reduced ability to recognize salt taste.

There was no statistical difference in the perception or recognition of sweet, sour, or in the perception of salt taste between diabetics and nondiabetics. There were no consistant differences in the taste acuity between counties (Table 5).

Table 5. Taste perception and recognition thresholds of diabetics and nondiabetics

	Diabetics	Nondiabetics	t[a]
Taste perception			
Sweet, mM sucrose	72 ± 49[b]	61 ± 69	0.67
Sour, mM HCl	12 ± 14	11 ± 13	0.32
Salt, mM NaCl	72 ± 42	63 ± 32	0.98
Bitter, mM Urea	514 ± 348	342 ± 219	2.55**
Taste Recognition			
Sweet, mM sucrose	88 ± 54	70 ± 71	1.06
Sour, mM HCl	16 ± 14	14 ± 15	0.48
Salt, mM NaCl	112 ± 93	77 ± 50	2.00*
Bitter, mM Urea	583 ± 351	382 ± 252	2.69**

[a] t value as determined by non-paired t test

[b] Mean standard deviation about the mean

*Significant at $P < .05$

**Significant at $P < .01$

Water

The chromium level of drinking water was significantly lower in Wayne County than in Utah County ($P < .01$)

There was not a significant difference in the chromium level of drinking water between diabetic and nondiabetic households within each county (Table 3).

There was no differences in the zinc level found in the drinking water between diabetic and nondiabetic households or among counties (Figure 8, Appendix A).

Dust

Analytical difficulties made it impossible to obtain satisfactory information on the levels of chromium or zinc in household dust samples.

DISCUSSION

Diabetes

The diagnosis of diabetes is made by comparing the results of blood glucose levels at fasting and, how rapidly the glucose is cleared from the blood after a glucose load. The diagnosis of onset maturity diabetes becomes an arbitrary decision at the "prediabetic" and "diabetic" level. The difficulty of diagnosis became apparent in selecting subjects for this study.

A person was originally invited to participate if he or she had previously been diagnosed onset diabetic (not insulin controlled) by his or her own doctor or in a State Department of Health screening clinic. A near matched control was then sought for that subject.

In Cache County, ten previously diagnosed diabetics were invited to participate. Eight of these persons were also diagnosed diabetic by the criteria used in this study. Two of the subjects, who came in as diabetics and who were also using prescribed hypoglycemic agents (not taken for 72 hours perior to the glucose tolerance test), were found to be nondiabetic. Two of the control subjects were found to be diabetic.

Similar results were found in Utah County. Two previously diagnosed diabetics were found to be nondiabetic, one of whom had been taking a hypoglycemic agent. Two controls were found to be diabetic.

A much different pattern emerged in Wayne County where the problem for the study had originated. Many of the subjects invited to participate had been diagnosed diabetic at the screening clinics conducted by the Health Department. Sixteen subjects who had previously been diagnosed diabetic were diagnosed nondiabetic by the criteria used in this study. Four of the sixteen subjects were taking prescribed hypoglycemic agents at the time of the test (not taken for 72 hours before test), and five subjects had taken hypoglycemic agents at some previous time. Three of the persons who had been asked to participate as controls were diagnosed diabetic in this study. Only eight of thirty-nine subjects tested in that county were diagnosed diabetic.

Nineteen people who originally agreed to participate in this study as diabetic were diagnosed nondiabetic. Twelve of these people were presently taking or had, in recent years, taken hypoglycemic agents.

Because of the nature of the approach of obtaining subjects for this study, population characteristics were not random nor uniform.

From county to county there was considerable variation in age. There were more older people represented in the

diabetic population. Utah county diabetics were much older than Wayne County diabetics (Table 1). Wayne County diabetics and nondiabetics had the same height/weight ratio. This was not true in the other counties. The weight/height ratio was higher in the diabetic than in the nondiabetics in both Cache and Utah Counties. Age, however, was a characteristic of the disease and any diabetic who was under 35 years of age was eliminated from all statistical analysis and was not included in this report.

Wayne County diabetics also showed a different pattern in blood glucose levels than did diabetics from Cache or Utah Counties. There was not a significant difference between diabetics and nondiabetics in Wayne County at the fasting level. This could help explain why so many of the Wayne County people had previously been diagnosed diabetic and were found to be nondiabetic in this study. Wayne County blood glucose levels were much lower at the fasting level and at every interval after glucose dosing than either Utah or Cache. The nondiabetics were similar to each other in blood glucose levels.

The diabetics tended to be younger in Wayne than in the other areas, which could be attributed to the lower levels of chromium found in the tissue of Wayne subjects than in others (Table 3). Chromium is considered essential for normal glucose levels in man and experimental chromium deficiency results in elevated blood glucose levels

(Mertz, et al., 1974). The effects of lower stores of chromium in Wayne County subjects could manifest itself as glucose intolerance at a younger age.

There is a discrepancy, however, in this theory in that chromium deficiencies also are manifested in elevated serum cholesterol levels which accompany the glucose intolerance (Mertz, et al., 1974). Wayne County diabetics tend to have higher serum cholesterol levels than Utah County diabetics, but this was not true of the nondiabetics; those from Wayne County tended to be lower (Table 2).

The level of physical activity between the two populations was unknown, but because the Wayne subjects were younger and the area is one in which many people participate or make their livelihood by outside activity, it is suspected that the difference in exercise could be responsible for some of the differences found.

Another parameter that might be considered is altitude. The west end of Wayne County is all above 7,000 feet in altitude. Seven of the eight diabetics for Wayne County were long time residents of that area. The altitude of both the Hyrum area and the Payson area are near 4,500 feet in altitude. Published data relating diabetic severity to altitude were not found.

Body Tissues and Chromium

Hambidge (1971) found 7 ppb chromium to be the most frequent level in serum in normal adults. This is in

agreement with the levels of serum chromium found in this study (8.1 ± 3.5 and 8.0 ± 4.7 µg/liter) (Table 3).

Hambidge (1971) showed, as did this study, that 1 hour after glucose dosing, there was no change in serum chromium levels in normal subjects (Table 3).

Pekarek et al. (1975) showed, however, that serum chromium concentrations in normal subjects fell precipitiously after glucose loading. In this study, the serum chromium concentrations for both diabetics and nondiabetics were very similar in the fasted and 1 hour post prandial states (Table 3).

Hambidge (1971) found that the 24 hour urinary chromium excretion in normal adults was 8.4 µg with individual results ranging from 1.6 to 21 µg/24 hours. Mitman et al. (1975) found 24 hour excretion from nondiabetic adult women to be 7.2 ± 0.4 µg/24 hours. In this study the mean of all diabetics 24 hour urine excretion was 7.7 ± 10.1 µg and the mean of all normals was 8.3 ± 6.7 µg which agrees with Mitman and Hambidge (Table 3).

Doisy et al. (1971) found that normal adults and maturity onset diabetics excreted similar amounts of chromium in the urine, but the adults with chemical diabetes excreted significantly greater amounts.

Gurson and Saner (1978) found very little difference in the 24 hour excretion of chromium between diabetics and nondiabetics. This study showed similar results. They also

found an increased urinary chromium/creatinine ratio in diabetics which this study did not find.

Chromium hair values in this study for all diabetics had a mean of 490 ± 264 ng/g and 461 ± 256 ng/g in nondiabetics. Benjanuvatra and Bennion (1975) found the mean hair chromium level of adult nondiabetics to be 241 ppb with the range of 78-473. The mean value of maturity onset diabetics was 94 ppb with a range of 35-298 ppb, a considerable difference.

Gurson et al. (1975) reported a mean value of 240 ± 130 µg/g in older hospitalized adults. These values are lower than the ones found in this study.

Analysis of chromium biological tissues is difficult. This is true of hair. Human hair can provide an index of chromium nutrition but interpretation of the results can be difficult because, unlike other body tissues, it has been exposed to an external environment. Hambidge et al. (1972) tested eleven hair shampoos and found that none of them either added or depleted chromium from the hair tested. There was no change beyond the removal of adsorbed chromium. They found also that atmospheric chromium did not contribute chromium to the hair. The chromium sources that were found to contribute tightly bound chromium to the hair were from hair bleaches and hair dyes. Each participant in this study was asked about any preparation that had been used on his or her hair. Fifteen Wayne County subjects reported having

used a hair rinse, dye or bleach within sixty days. The Wayne County mean value for all subjects for hair chromium was 421 ppb as compared to that of Utah County subjects, which was 496 ppb, and the overall mean of Cache County subjects was 550 ppb. Only two other subjects, both from Cache County, reported having used hair dye. Perhaps, had subjects been available for the study from Wayne County who had not used these hair preparations, an even greater difference would have been found in the mean level of hair chromium concentration.

Body Tissues and Zinc

Fisher, Hendricks and Mahoney (1978) found mean serum zinc values for older men to be 118 ± 43 µg/100 ml and for older women to be 197 ± 26 µg/100 ml. Henkin et al. (1975) reported a mean value of 86 ± 21 µg/100 ml in an adult population. Halstead, Smith and Irwin (1974) reported values of different normal adult populations in which means ranged from 90 µg/100 ml to 122 µg/100 ml. Serum mean values in diabetics and nondiabetics in Wayne and Cache Counties were similar (Table 4). Serum zinc values in both diabetics and nondiabetics in Utah County tended to be higher (Appendix D).

Diabetics in this study excreted significantly greater amounts of zinc in the urine than did nondiabetics. Pidduck Wren and Price Evans (1970b) had found this to be true between diabetics and control groups. They found that mild

diabetics showed a less severe zincuria than diabetics who required insulin or hypoglycemic agents.

In this study, overall mean values for serum zinc are higher in diabetics than in nondiabetics. Urine zinc excretion is higher in diabetics. Deep body stores of zinc as reflected by hair zinc levels tend to be lower in diabetics (Appendix D).

Henkin (1977) dosed patients with histidine and cystein to chelate zinc to make patients zinc deficient and alter and/or lower their taste acuity. It is known that diabetics do not metabolize protein normally. This could be related to the fact that diabetics often have altered taste acuity. In this study the diabetics had altered taste acuity in perceiving and recognizing bitter taste (Table 5) and in recognizing salt taste (Table 5). It is not known if diabetics had a higher salt intake and thus increased difficulty in recognizing salt taste at lower concentrations.

Klevay (1970) found that there was no correlation between hair zinc values and serum zinc values in this study.

Hair zinc values have been found to decline with age even when zinc intake has not declined (Deeming and Weber, 1978). They found the mean concentration of older men to be 208 ppm and 176 ppm for older women. This study did not take the sex of the subjects into account, but the overall mean was 136 ppm, a lower value than that of Deeming and Weber (1978). The mean for Cache County Subjects was

114 ppm, the mean hair zinc value in Wayne County was 147 ppm and also 147 ppm in Utah County.

Even though no statistical correlation was found between hair zinc and serum zinc, Utah County serum mean values and hair zinc mean values were higher than the zinc tissue mean values of Wayne and Cache Counties.

Cholesterol and Triglycerides

Mildly impaired glucose tolerance, hypertriglyceridemia, insulin resistance and mild obesity are often associated. Total cholesterol and triglycerides tends to increase with age up to 60 years (Sharkey, 1971); the incidence of maturity onset diabetes also increases with age.

West and Kalbfleish (1971) found cholesterol levels substantially greater in subjects with impaired glucose tolerance. Males had higher serum cholesterol levels at all levels of glucose intolerance. The females in their study had no significant change in cholesterol levels until their 2 hour post prandial glucose values reached 200 mg/100 ml.

The diabetics in Cache and Wayne Counties tended to have higher serum cholesterol levels than did nondiabetics. In all cases, the fasted serum cholesterol level was greater than the 1 hour post prandial level. In Utah County, however, the serum cholesterol level was higher in nondiabetics than in diabetics (Table 2).

In this study it was found that serum triglycerides were significantly higher in diabetics than in nondiabetics (Figure 2).

The data from this study relating cholesterol values to chromium body stores and water chromium supplies was not clear. It has been shown (Schroeder and Nason, 1969) that chromium supplementation of a previously low chromium diet decreased serum cholesterol levels. In rats, this occurred only if the previous diet had been chromium deficient. In humans, it occurred in some cases, but not in all. Perhaps those in which the cholesterol level did not drop with chromium supplementation were not chromium deficient.

It appears that even though there are differences, perhaps diabetics in this study were not chromium deficient to an extent that different levels of environmental supplies of chromium had a measureable effect on cholesterol levels.

A paired t test analysis of all data, utilizing diabetics and near matched control subjects, revealed that serum glucose levels were indeed higher in diabetics as was their urinary zinc excretion. Diabetics had reduced taste acuity and recognition ability (Appendix D). Thus, age and weight differences observed when utilizing all diabetic and nondiabetic subjects did not bias the statistical analysis of data by ANOV and Duncan's New Multiple Range Test.

SUMMARY AND CONCLUSIONS

This study was an attempt to determine if there is a relationship between human tissue and environmental levels of chromium and/or zinc and maturity onset diabetes.

Diabetics were studied in three populations. A Utah State Department of Health (1969) screening showed Wayne County to have a high incidence of diabetes. It was assumed that there were low levels of environmental zinc and chromium. Utah County had been shown to have low incidence of diabetes and was assumed to have a higher environmental level of zinc and chromium. Cache County had a low incidence of diabetes and assumed low levels of environmental zinc and chromium.

Glucose Tolerance tests were conducted and diabetic subjects were diagnosed. Nondiabetics served as controls. Body tissues (serum, urine, and hair) from all populations were analyzed for zinc and chromium levels. Serum cholesterol and serum triglyceride levels, weight/height, which have all been associated with diabetes were determined.

Altered taste acuity, which has been related to the diabetic condition and zinc deficiency was also determined.

Environmental levels of zinc and chromium were determined from household drinking water.

Comparisons were made between near matched controls within each county, diabetics and nondiabetics within each county and all diabetics and all nondiabetics in the populations from all three counties.

There were characteristics that were found in the total diabetic population as compared to the total nondiabetic population. The diabetics were heavier for their height. They had significantly higher tryglyceride levels at both the fasted state and 1 hour post prandial. Diabetics also tended to have higher serum cholesterol levels.

Tissue levels of chromium in diabetics and nondiabetics were similar. There was not a difference in chromium levels of the drinking water from the households of diabetics and nondiabetic.

Diabetics had higher serum zinc values than did nondiabetics. Neither group showed any difference in serum zinc values between the fasted state and 1 hour post prandial.

Diabetics had a significantly higher urinary zinc excretion and showed a significantly decreased ability to recognize a bitter taste. Hair zinc values did not differ between diabetics and nondiabetics.

There were some definite county differences. The Wayne County diabetic population was younger than either of the other counties. The weight/height ratio for Wayne County diabetics and nondiabetics was the same. In the other

counties, diabetics were heavier for their height than were nondiabetics.

There was not a significant difference in fasted glucose levels and 1 hour post prandial levels between diabetics and nondiabetics in Wayne County. These differences were significant in Utah and Cache Counties. The blood glucose levels in diabetics from Wayne County were much lower than in the other two counties. The total Wayne County population studied had lower serum cholesterol levels than was found in Utah County.

Tissue levels of chromium were lowest in Wayne County and were the highest in Utah County. This was also true of levels of chromium found in household drinking water.

Utah County subjects showed the highest levels of chromium and zinc in body tissues and the highest chromium/creatinine ratio in urine samples.

Cache County levels fell between Wayne and Utah Counties in many parameters; Cache subjects did show the lowest serum cholesterols at the fasting state and the lowest levels of hair zinc.

A different diabetic pattern emerges in Wayne County. Whether or not this is related to environmental and thus body stores of chromium is difficult to assess. Environmental chromium would only make a difference if there was a true body chromium deficiency.

Differences found between the populations of Wayne County could be due to exercise, different eating patterns and a total life style. The great differences in altitude is another parameter which could be explored.

LITERATURE CITED

American Diabetes Association. 1969. Standardization of the oral glucose tolerance test. Report of the Committee on Statistics. Diabetes 18:299-310.

Andrus, R. 1971. Aging and diabetes. In P. Felig and P. K. Bondy (Eds.). The Medical Clinics of North America Symposium of Diabetes Mellitus. Vol. 55. Saunders, Philadelphia.

Baird, J. D. 1973. Diabetes mellitus and obesity. Proc. Nutr. Soc. 32:199-204.

Baladimos, M. C., and A. Marble. 1971. Tolazamide in the treatment of diabetic mellitus, clinic experience and review of literature. Curr. Therap. Res. 13:6-12.

Baumslag, N., and H. G. Petering. 1976. Trace metal studies in Bushman hair. Arch. Environ. Health, Sept.:254-257.

Beisel, W. R., R. S. Pekarek, and J. Wannenacher. 1976. Homestatic mechanisms affecting plasma zinc levels in acute stress. In A. S. Prasad and D. Oberleas (Eds.). Trace Elements in Human Health and Disease. Vol. 1. Academic Press, New York.

Benjanuvatra, N. K., and M. Bennion. 1975. Hair chromium concentrations of Thai subjects with and without diabetes mellitus. Nutr. Reports Inter. 12:326-330.

Bennion, M. 1979. Diabetes mellitus--treatment and complications. In Clinical Nutrition. Harper and Row, New York.

Briggs, M. H., M. Briggs, and A. W. Lusaka. 1972. Trace elements in human hair. Separatum. Exper. 28:404-412.

Boyle, E., B. Mondschein, and H. H. Dash. 1977. Chromium depletion in the pathogenesis of diabetes and atherosclerosis. South. Med. J. 70:1449-1453.

Burt, R. L. 1960. Carbohydrate metabolism in pregnancy. Clin. Obstet. Gyn. 3:310-316.

Burt, R. L., and I. W. F. Davidson. 1973. Carbohydrate metabolism in pregnancy: a possible role of chromium. Acta. Diabet. Lat. 10:770-778.

Catalanotto, F. A. 1978. The trace metal zinc and taste. Am. J. Clin. Nutr. 31:1098-1103.

Chooi, M. K., J. K. L. Todd, and N. D. Boyd. 1976. Influence of age and sex on plasma zinc levels in normal and diabetic individuals. Nutr. Meta. 20:135-142.

Cohen, A. M., A. Teitelbaum, and R. Saliternik. 1972. Genetics and diet as factors in development of diabetes mellitus. Metab. 3:235-240.

Cohen, I. K., P. J. Schechter, and R. I. Henkin. 1973. Hypogeusia, anorexia and altered zinc metabolism following thermal burn. J. Am. Med. Assoc. 223:914-916.

Collins, R. J., P. O. Fromm, W. D. Collings. 1961. Chromium excretion in the dog. Am. J. Physiol. 201:795-799.

Davidson, I. W. F., W. L. Screst. 1972. Determination in biological materials by atomic absorption spectrometry. Anal. Chem. 44:1808-1813.

Davies, I. J. T., M. Mash, and T. L. Dormandy. 1968. Measurements of plasma zinc. J. Clin. Path. 21:359-365.

Deeming, S. B., and C. W. Weber. 1978. Hair analysis of trace minerals in human subjects as influenced by age, sex, and contraceptive drugs. Am. J. Clin. Nutr. 31:1175-1180.

Doisy, R. J. 1963. Plasma insulin assay and adipose tissue metabolism. Endocrinology 72:273-278.

Doisy, R. J., D. H. Streeten, J. M. Freiberg, and A. J. Schneider. 1976. Chromium metabolism in man and biochemical effects. In A. S. Prasad, and D. Oberlas (Eds.). Trace Elements in Human Health and Disease. Vol. 2. Academic Press, New York.

Doisy, R. J., M. L. Streeten, M. L. Souma, M. E. Kalafer, S. I. Rekant, T. C. Dalakas. 1971. Metabolism of chromium in human subjects--normal, elderly and diabetic subjects. In A. S. Prasad, and D. Oberlas (Eds.). Trace Elements in Human Health and Disease. Vol. 2. Academic Press, New York.

Ellis, L. 1978. Serum zinc levels and urinary zinc excretion in patients with renal transplants. Clinica Chemica Acta. 82:105-111.

Ellwood, P. C., M. Abernathy, and M. Morton. 1974. Mor tality in adults and trace elements in water. Lancet. Dec.:1470-1482.

Evans, G. W., E. E. Roginski, and M. Mertz. 1973. Interaction of the glucose tolerance factor (GTF) with insulin. Biochem & Biophys. Research Communication, 50:718-723.

Fasel, J., M. D. H. Hadjikhani, and J. P. Felber. 1970. The insulin secretory effect of the human duodenal mucosa. Gastroenterology 59:109-113.

Fisher, S., D. G. Hendricks, and A. W. Mahoney. 1978. Nutritional assessment of senior rural Utahns by biochemical and physical measurements. J. Clin. Nutr. 31:667-672.

Food and Nutrition Board, National Research Council. 1974. Zinc. In Recommended Dietary Allowances. National Academy of Sciences, Washington, D. C.

Fox, M. R. S. 1970. The status of zinc in human nutrition. World Rev. Nutr. & Diet. 12:208-226.

Fredrickson, D. S., R. I. Levy, and R. S. Lees. 1967. Fat transport in lipoproteins--an integrated approach to mechanisms and disorders. New Eng. J. Med. 276: 148-165.

Galloway, J. A., E. Marler, E. W. Shuey, and M. Kory. 1973. Diabetes mellitus. Ely Lilly Research Co., Indianapolis.

Glinnsman, W. H., F. J. Feldman, and W. Mertz. 1966. Plasma chromium after glucose administration. Science 152:1243-1245.

Glinnsman, W. J., and W. Mertz. 1966. Effect of trivalent chromium on glucose tolerance. Metabolism 15:510-520.

Greger, J. L., and A. H. Geissler. 1978. Effect of zinc supplementation of taste acuity on the aged. Am. J. Clin. Nutr. 31:633-637.

Grobin, W. 1970. Diabetes in the aged: underdiagnosis and overtreatment. C. M. A. Jour. 103:915-923.

Gurson, C. T., and G. Saner. 1971. Effect on glucose utilization in marasmic protein--calorie malnutrition. Am. J. Clin. Nutr. 24:1313-1319.

Gurson, C. T., and G. Saner. 1978. The effect of glucose loading on urinary excretion of chromium in normal adults, in individuals from diabetic families and in diabetics. Amer. J. Clin. Nutr. 31:1158-1161.

Gurson, C. T., G. Saner, M. Mertz, W. R. Wolf, and S. Sokucu. 1975. Nutritional significance of chromium in different chronological age groups and populations differing in nutritional backgrounds. Nutr. Reports Inter. 12: 9-16.

Hallbook, T., and E. Lanner. 1972. Serum zinc and healing of venus leg ulcers. Lancet 2:780-782.

Halstead, J. A. 1968. Geophagia in man: its native and its nutritional effects. Am. J. Clin. Nutr. 21:1384-1393.

Halstead, J. A., and J. C. Smith. 1970. Plasma zinc in health and disease. Lancet 322-324.

Halstead, J. A., J. C. Smith, and M. I. Irwin. 1974. A conspectus of research on the zinc requirements of man. J. Nutr. 104:345-378.

Hambidge, K. M. 1971. Chromium nutrition in the mother and the growing child. In W. Mertz, and W. E. Cornatizer (Eds.). Newer Trace Elements in Nutrition. Marcel Dekker, Inc., New York.

Hambidge, K. M., J. D. Baum. 1972. Hair chromium concentrations of human newborn and changes during infancy. Am. J. Clin. Nutr. 24:376-379.

Hambidge, K. M., M. L. Franklin, and M. A. Jacobs. 1972. Hair chromium concentration: effects of sample washing and external environment. Am. J. Clin. Nutr. 24:384-389.

Hambidge, K. M., C. Hambidge, M. Jacobs, and J. D. Baum. 1972. Low levels of zinc in hair, anorexia, poor growth and hypogeusia in children. Ped. Res. 6:868-874.

Hambidge, K. M., and D. O. Rodgerson. 1969. Comparison of hair chromium levels of nullparous and parous women. Am. J. Obstet. Gyn. 103:320-321.

Hambidge, K. M., D. O. Rodgerson, and D. O'brien. 1968. Concentrations of chromium in the hair of normal children and children with juvenile diabetes mellitus. Diabetes 17:517-522.

Hansen, V. E. 1971. Water supply in the upper Fremont River Basin. Mountain States Resources Corp., Utah Division Water Resources, Nielson, Maxwell, Wangsguard Consulting Engineers, Salt Lake City, Utah.

Hardy, S. L. 1978. The sensory evaluation of food products made with varying levels of sucrose and fructose and of threshold measurements of individuals with diabetes mellitus. MS thesis, Utah State University.

Harper, A. F. 1973. Recommended dietary allowances. Nutr. Rev. 31:393-396.

Hendricks, D. G., and A. W. Mahoney. 1972. Glucose tolerance in zinc-deficient rats. J. Nutr. 102:1079-1084.

Henkin, R. I. 1971. Newer aspects of copper and zinc metabolism. In W. Mertz and W. E. Cornatzer (Eds.). Newer Trace Elements in Nutrition. Marcel Dekker, Inc., New York.

Henkin, R. I. 1977. New aspects in the control of food intake and appetite. An. New York Acad. Sci. 300:321-324.

Henkin, R. I., B. M. Patten, K. R. Peter, and D. A. Bronzert. 1975. A syndrome of acute zinc loss. Arch. Neurol. 32:745-751.

Henkin, R. I., P. J. Schechter, R. Hoye, and C. F. T. Mattern. 1971. Idiopathic hypogeusia with dysgeusia, hyposmia and dysosmia, a new syndrome. J.A.M.A. 217:434-440.

Hondel, D. C., F. W. Sunderman, M. W. Neckay, and M. D. McNelly. 1973. Atomic absorption spectometry of nickel, copper, zinc and lead collected from healthy subjects during sauna bathing. Clin. Chem. 19:1288-1292.

Hopkins, I. L., K. O. Ransome, and A. S. Majaj. 1968. Improvement of impaired carbohydrate metabolism by chromium III in malnourished infants. Am. J. Clin. Nutr. 21:203-211.

Hopkins, I. L., and K. Schwarz. 1964. Chromium III binding to serum proteins, specifically siderophilin. Biochem. Biophys. Acta. 90:484-491.

Houssay, B. A., V. C. Foglia, and R. R. Rodriguez. 1954. Production or prevention of some types of experimental diabetes by extrogens or corticosteriods. Acta. Endocr. 17:146-151.

Huber, A. M., and S. M. Gershoff. 1973. Effects of zinc deficiency in rats on insulin release from the pancreas. J. Nutr. 103:1739-1744.

Hussey, H. H. 1974. Taste and smell deviations: importance of zinc. J.A.M.A. 228(13):1669-1670.

Hutcheson, D. P., D. H. Gray, B. Venogopal, and T. D. Luckey. 1975. Studies of nutritional safety of some heavy metals in mic. J. Nutr. 105:670-675.

Interdepartmental Committee on Nutrition for National Defense (ICNND). 1963. Manual for Nutrition Surveys. 2nd ed. Superintendent of Documents, U. S. Government Printing Office, Washington, D. C.

Jackson, W. P. U. 1972. Diabetes and related variable among the five main racial groups in South Africa. Postgrad. Med. J. 48:391-398.

Keen, J., and R. J. Jarrett. 1969. Modern concepts in the diagnosis of diabetics. In C. Weller (Ed.). The New Management of Stable Adult Diabetes. C. Thomas, Springfield, Illinois.

Kim, E., and M. Goldberg. 1969. Serum cholesterol assay using a stable Liebermann Burchard reagent. Clinical Chem. 15:1171-1179.

Kirchgessner, M., H. P. Roth, and E. Weigand. 1976. Biochemical changes in zinc deficiency. In A. S. Prasad, and D. Oberleas. (Eds.). Trace Elements in Human Health and Disease. Vol. 1. Academic Press, New York.

Klevay, L. M. 1970. Hair as a biopsy material in the assessment of zinc nutriture. Am. J. Clin. Nutr. 23:284-289.

Klimt, C. R., C. L. Meinert, I. P. Ho, and F. W. Briese. 1967. Study of familial patterns of reported diabetes. Diabetes. 16:40-46.

Kumar, S., and K. S. Joya Rao. 1974. Blood and urinary zinc levels in diabetes mellitus. Nutr. Metabol. 17:231-235.

Kurz, D. L., E. J. Eyring, and J. E. Roach. 1973. Serum zinc in the newborn. Biol. Neonate. 23:180-183.

LeClerg, E. L., W. H. Leonard, and A. G. Clark. 1962. Field Plot Technique. Burgess Publishing Co., Minneapolis, Minnesota.

Levine, R. A., D. H. P. Streetan, and R. J. Doisy. 1968. Effects of oral chromium supplementation on the glucose tolerance of elderly human subjects. Metabolism. 17: 114-125.

Liaw, C. C., D. G. Hendricks, and A. W. Mahoney. 1976. Factors affecting zinc movement from pancreatic islets. Fed. Proc. 35:659.

Lindeman, R. D., R. G. Bottomley, R. L. Cornelison, and L. A. Jacobs. 1972. Influence of acute tissue injury on zinc metabolism in man. J. Lab. and Clin. Med. 79:452-460.

Liu, V. J., and J. S. Morris. 1978. Relative chromium response as an indicator of chromium status. Am. J. Clin. Nutr. 31:972-976.

Macapinlac, M. P., W. M. Pearson, G. H. Barney, and W. J. Darby. 1968. Protein and nucleic acid metabolism in the testes of zinc deficient rats. J. Nutr. 95: 569-577.

Mahalko, J., and M. Bennion. 1976. The effect of parity and time between pregnancies in maternal hair chromium concentration. Am. J. Clin. Nutr. 29:1060-1072.

Masironi, R., W. Wolf, and W. Mertz. 1973. Chromium in refined and unrefined sugars, possible nutritional implications in the etiology of cardiovascular diseases. World Health Organization Bulletin 49:322-324.

Mayer, J. 1971. Clinical nutrition, chromium in medicine. Post Grad. Med. 49:235-237.

McBean, L. D., J. T. Dave, J. A. Halstead, and J. C. Smith. 1972. Zinc concentration in numan tissues. Am. J. Clin. Nutr. 25:672-676.

Mertz, W. 1961. Diet and glucose uptake by rat epididymal fat tissue. Fed. Proc. 20:364.

Mertz, W. 1969. Chromium occurrence and function in biological systems. Phys. Rev. 49:163-237.

Mertz, W. 1974. The newer essential trace elements, chromium, tin, vanadium, nickel and silicon. Proc. Nutr. Soc. 33:307-311.

Mertz, W. 1975. Effects and metabolism of glucose tolerance factor. Nutr. Rev. 33:129-135.

Mertz, W., and K. Schwarz. 1955. Impaired intravenous glucose tolerance as an early sign of dietary necrotic liver degeneration. Arch. Biochem. Biophys. 58:504.

Mertz, W., and K. Schwarz. 1959. Relation of glucose tolerance factor to impaired intervenous glucose tolerance of rats on stock diets. Am. J. Physiol. 196: 614-618.

Mertz, W., E. W. Toepfer, E. E. Roginski, and M. W. Polansky. 1974. Present knowledge in the role of chromium. Fed. Pro. 33:2275.

Mills, C. F. 1973. Nutritional deficiencies in a modern society. A. M. Howard and I. M. Baird, (Ed.). Books, Ltd., New York.

Mitman, F. W., W. R. Wolf, J. L. Kelsay, and E. S. Prather. 1975. Urinary chromium levels of nine young women eating freely chosen diets. J. of Nutr. 105:64-68.

Morgan, J. 1972. Hepatic chromium content in diabetic subjects. Metabolism. 21:313-316.

Mouratoff, G. J., N. V. Carroll, and E. M. Scott. 1969. Diabetes mellitus in Athabashar Indians in Alaska. Diabetes. 18:29-32.

Neri, B. P., and C. S. Frings. 1973. Improved methods for determination of triglycerides in serum. Clin. Chem. 19:1201-1202.

Osis, D., L, Kramer, E. Wiatrowski, and H. Spencer. 1972. Dietary zinc intake in man. Am. J. Clin. Nutr. 25: 582-588.

Pekarek, R. S., W. R. Beisel, P. J. Bartelloni, and K. A. Bostian. 1972. Determinations of serum zinc concentrations in normal adult subjects by atomic absorption spectrophotometry. Am. J. Clin. Path. 57:506-510.

Pekarek, R. S., E. C. Hauer, E. J. Rayfield, R. W. Wannemacher, and W. R. Beisel. 1959. Relationship between serum chromium concentrations and glucose utilization in normal and infected subjects. Diabetes. 24:350-357.

Pidduck, H. G., P. J. J. Wren, and D. A. PriceEvans. 1970a. Plasma zinc and copper in diabetes mellitus. Diabetes. 19:234-239.

Pidduck, H. G., P. J. J. Wren, D. A. PriceEvans. 1970b. Hyperzincuria of diabetes mellitus and possible genetical implications of this observation. Diabetes. 19:240-247.

Pories, W. J., E. G. Mansour, F. R. Plecka, A. Flynn, and W. H. Strain. 1976. Metabolic factors affecting zinc metabolism in the surgical patient. In A. S. Prasad, and D. Oberleas. (Eds.). Trace Elements in Human Health and Disease. Vol. 1. Academic Press, New York.

Prasad, A. S. 1976a. Zinc in human studies. In I. M. Hsu, and R. L. Davies (Eds.). The Biomedical Role of Trace Elements in Aging. Eckerd College Cerontology Center, St. Petersburg, Florida.

Prasad, A. S. 1976b. Deficiency of zinc in man and its toxicity. In A. S. Prasad and D. Oberleas (Eds.). Trace Elements in Human Health and Disease. Vol. 1. Academic Press, New York.

Prasad, A. S., J. A. Halstead, and M. Nadimi. 1961. Syndrome of iron deficiency anemia, hepatosplenomegoly, dwarfism, and geophagia. Am. J. Med. 31:532-546.

Prasad, A. S., A. Miale, Z. Farid, A. Schubert, and H. H. Sanstead. 1963. Zinc metabolism in patients with the syndrome of iron deficiency anemia, hypogonadism and dwarfism. J. Lab. Clin. Med. 61:537-549.

Prasad, A. S., D. Oberleas, E. R. Miller, and R. W. Luecke. 1971. Biochemical effects of zinc deficiency: change in activities of zinc dependent enzymes and ribonecleic acid and deoxyribonucleic acid content of tissues. J. Lab. Clin. Med. 77:144-152.

Prasad, A. S., A. R. Schubert, H. H. Sandstead, A. J. Miak, and Z. Farid. 1963. Zinc, iron and nitrogen content of sweat in normal and deficient subjects. J. Lab. Clin. Med. 62:85-89.

Preston, A. M., R. P. Dowdy, M. A. Preston, and J. N. Freeman. 1976. Effect of dietary chromium on glucose tolerance and serum cholesterol in guinea pigs. J. Nutr. 106:1391-1397.

Public Health Service. 1967. Characteristics of persons with diabetes. United States Public Health Service Publication No. 1000, Series 10(40).

Punsar, S., W. Wolf, W. Mertz, and M. J. Karvonen. 1977. Urinary chromium excretion and atherosclerotic manifestations in two Finnish male populations. An. Clin. Research. 9:79-83.

Quarterman, J. 1969. The effect of zinc on the uptake of glucose by adipose tissue. Biochem. Biophys. Acta. 177:644-646.

Quarterman, J., C. F. Mills, W. R. Humphries. 1966. The reduced secretion of and sensitivity to insulin in zinc-deficient rats. Biochem. Biophys. Res. Communication. 25:354-358.

Reinhold, J. G., K. Nasr, A. Lahimgarzadeh, H. Hedayat. 1973. Effects of phytate-rich bread upon metabolism of zinc, calcium phosphorus and nitrogen in man. Lancet. 1:283-291.

Riordan, J. R., and B. L. Vallee. 1976. Structure and function of zinc metalloenzymes. In A. S. Prasad and D. Oberleas (Eds.). Trace Elements in Human Health and Disease. Vol. 1. Academic Press, New York.

Ronaghy, H. A., J. G. Reinhold, M. Makloudy, R. Ghavami, M. R. S. Fox, and J. A. Halstead. 1974. Zinc supplementation of malnourished school boys in Iran: increased growth and other effects. Am. J. Clin. Nutr. 27:112-121.

Ronaghy, H., M. R. S. Fox, S. M. Garn, H. Israel, A. Harp, P. G. Moe, and J. A. Halstead. 1969. Controlled zinc supplementation for malnourished school boys: a pilot experiment. Am. J. Clin. Nutr. 22:1279-1289.

Rose, K. M., M. S. Allen, I. L. Crawford, and S. T. Jacob. 1978. Functional role of zinc in poly(a) synthesis catalyzed by nuclear poly (A) polymerase. Eur. J. Biochem. 88:29-36.

Sanstead, H. H., M. Terhune, R. N. Brady, D. Gillespie, and W. L. Halloway. 1971. Zinc deficiency: Brain DNA, protein and lipids and liver ribosomes and RNA polymerase. Clin. Res. 19:83.

Sanstead, H. R., V. C. Lanier, G. H. Shephard, and D. D. Gillispie. 1974. Zinc and wound healing. Am. J. Clin. Nutr. 23:514-519.

Saner, G., and C. T. Gurson. 1976. Hair chromium concentra tions in newborn and their mothers. Nutr. Reports Inter. 14:155-164.

Schroeder, H. A. 1969. Serum cholesterol and glucose levels in rats fed refined and less refined sugars and chrom-ium. J. Nutr. 97:237-242.

Schroeder, H. A., J. J. Balassa, and I. H. Tipton. 1962. Abnormal trace metals in man-chromium. J. Chron. Dis. 15:941-964.

Schroeder, H. A., and B. A. Nason. 1968. The role of chromium in mammalian nutrition. Am. J. Clin. Nutr. 21:230-244.

Schroeder, H. A., and B. A. Nason. 1969. Trace metals in human hair. J. Invest. Derm. 53:71-78.

Schroeder, H. A., B. A. Nason, and J. S. Tipton. 1970. Chromium deficiency as a factor in astherosclerosis. J. Chronic Dis. 23:112-141.

Schwarz, K., and W. Mertz. 1959. Chromium III and the glu-cose tolerance factor. Arch. Biochem. Biophys. 85:292.

Selby, L. A., C. J. Marienfeld, and J. O. Pierce. 1970. The effects of trace elements on human and animal health. J.A.M.A. 157:1800-1808.

Sharkey, T. P. 1971. Diabetes mellitus--prevalence in the United States. J. Amer. Diet. Assoc. 58:201-208.

Solomons, N. W., R. L. Rosenfield, R. A. Jacob, and H. H. Sandstead. 1976. Growth retardation and zinc nutri-tion. Pediat. Res. 10:923-927.

Spencer, H. 1965. Zince-65 metabolism during low and high calcium intake in man. J. Nutr. 86:169-177.

Spencer, H., D. Osis, K. Kramer, and C. Norris. 1976. Intake, excretion and retention of zinc in man. In A. S. Prasad and D. Oberleas (Eds.). Trace Elements in Human Health and Disease. Vol. 1. Academic Press, New York.

Staub, H. W., G. Reussner, and R. Thiessner. 1969. Serum cholesterol reduction by chromium in hypercholesterolemic rats. Science 166:746-747.

Strain, W. H., T. S. Luville, C. A. Lankau, W. P. Berliner, and W. J. Pories. 1966. Analysis of zinc levels in hair for the diagnosis of zinc deficiency in man. J. Lab. Clin. Med. 68:244-249.

Surender, K., and J. S. K. Rao. 1974. Blood and urinary zinc levels in diabetes mellitus. Nutr. Meta. 17: 231-235.

Toepfer, E. W., W. Mertz, E. E. Roginski and M. M. Polansky. 1973. Chromium in foods in relation to biological activity. Agri. Food Chem. 21:69-73.

Toepfer, E. W., W. Mertz, E. E. Roginski, M. M. Polansky, and W. R. Wolf. 1977. Preparation of chromium containing material of glucose tolerance factor activity from brewer's yeast extracts and by synthesis. J. Agric. Food Chem. 25:162-164.

Underwood, E. J. 1971. Zinc and chromium. In Trace Elements in Human and Animal Nutrition. Academic Press, New York.

Underwood, E. J. 1977. Zinc and chromium. In Trace Elements in Human and Animal Nutrition. Academic Press, New York.

Utah State Division of Health. 1969. Results of diabetes screening, FY 1964-FY1969.

Vallee, B. L. 1959. Biochemistry, physiology and pathology of zinc. Phys. Rev. 29:443-490.

Wacher, W. E. C. 1976. Role of zinc in wound healing: a critical review. In A. S. Prasad and D. Oberleas (Eds.). The Trace Elements in Human Health and Disease. Vol. 1. Academic Press, New York.

Wacher, W. E. C., and B. L. Vallee. 1959. Nucleic acids and metals, chromium manganese, nickel, iron, and other metals in ribonucleic acid form diverse biological sources. J. Biol. Chem. 234:3257-3262.

Weller, E. 1969. The new management of stable onset diabetes. C. Thomas, Springfield, Illinois.

West, K. M., and J. M. Kalbfleisch. 1971. Influence of nutritional factors on prevalence of diabetes. Diabetes. 29:99-108.

Westfall, D. M., and A. L. Rosenbloom. 1971. Diabetes mellitus among the Florida Seminoles. Diabetes. 85: 1037-1041.

Wintz, M., D. A. Seedman, and J. Graff. 1970. Studies in metabolic nutrition employing chemically defined diets. Am. J. Clin. Nutr. 23:525-545.

Woolrich, P. F. 1973. Occurrence of trace metals in the environment, an overview. Am. Ind. Hyg. Assoc. J. 34:217-226.

World Health Organization (WHO). 1973. WHO Tech. Rep. Serv. 532.

Yalow, R. S., and S. A. Berson. 1961. Immunoassay of plasma in man. Diabetes. 10:339-342.

APPENDIXES

Appendix A

Protocol and Instructions for Subjects

Protocol for use of human subjects is as follows:

1. Glucose tolerance test. This test will be a standard glucose tolerance test based on fasted 1, 2, and 3 hours post prandial blood samples. Subjects will be given the attached instruction sheet and will be tiven a glucose dose of 40 g per m^2 of body surface area as determined from charts based on height and weight. This test in Utah and Wayne Counties will be monitored by Dr. G. Cloyd Krebs, Provo. Samples from subjects in Cache County will be taken in the Logan L.D.S. Hospital by Marie Viebel.

   In each county a public health nurse is cooperating in identifying subjects for the study. Blood and hair samples for chromium and zinc determination will be taken at the same time as glucose tolerance tests are performed.

2. 24-hour urine samples will be collected by the individual subjects andpicked up by Carol Williams at the subjects home.

3. At the time the 24-hour urine sample is picked up, samples of culinary water will be obtained at the subject's home. Samples of atmospheric dust will be collected on pre-weighed filter paper by attaching to a vacuum and vacuuming a dusty spot such as the top of a refrigerator or a window sill.

4. Responsible personnel

Person	Function
Deloy Hendricks, Ph.D.	Coordination and supervision
G. Cloyd Krebs, M.D.	Glucose tolerance test, blood sampling and examination in Utah, Cache and Wayne counties
Carol Williams, M.S. student	Coordination and supervision

A consent form will be signed by each subject prior to their inclusion in the project.

Instructions for Subjects

Subject must be:

1. Nondiabetic (normal*) or
2. Maturity onset diabetic controlled by diet or diet plus an oral hypoglycemic agent
3. Must not be obese

Subject must be willing to:

1. Have a glucose tolerance test conducted.
2. Donate a 2 g clip of hair from the nape of the neck
3. Collect an accurate 24-hour total urine collection in containers provided.
4. Allow atmospheric dust collection to be made in his home.
5. Allow a sample of culinary water to be taken in his home.

Instructions for Glucose Tolerance Test:

Diet Instructions

1. Eat the diet as listed daily for three (3) days, plus anything else you desire.

Breakfast: Cereal (1/2 cup), cooked or dry
Bread, white (2 slices)
Skimmed milk (1 cup)
Sugar (2 tablespoonfuls) plus anything else you want

Lunch: (noon) Potato (1 medium, 2 1/2" diam.)
Vegetable (1/2 cup) cooked
Bread, white (2 slices)
Dessert, pie (one 4" sector of 9" diam.) or cake (2 sectors of 8" diam.)
Sugar (2 tablespoonfuls)
(A packed lunch may consist of two (2) meat, cheese or egg sandwiches, fruit, cake or cookies, and a candy bar.)
Plus anything else you want.

Dinner: (evening) Follow the same menu as specified for lunch, plus anything else you want.

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*Normals must be paired to diabetics by sex, age (±2 years), weight (±5 lbs), height (±2 in.) and parity (±1 child).

This diet has been specially prepared for you. It is designed to supply the proper amounts of food needed to obtain an accurate test of how well your body burns carbohydrate. It is very important that you eat at least the amounts shown on the diet. You may also add to the diet any other foods you like. For example, it is all right to add fruit, fruit juice, butter or jelly for breakfast. At lunch and dinner it is permissible to add meat, fish, cheese, butter or salad. Just be certain you eat everything listed on the diet. Snacks are permitted.

No food or drink is to taken after 10 p.m. the night before the test.

Appendix B

Diabetes Study Questionnaire and Consent

Diabetes Study Questionnaire

Name:

Present Address:

Birth Date:

Age:

How long have you lived at this address?

Weight:
What is the most you have weighed as an adult?
What is the least you have weighed as an adult?

In what community have you lived the longest?

How many miles have you travelled to participate in this test?

Height:

When was your last baby born?

No. of children?

Have you ever taken birth control pills? Yes_____ No_____
When did you last take birth control pills? _____
Do you now take birth control pills? Yes _____No_____

What medication are you taking (if any)? _____
_____

Have you ever used hair dye? Yes_____No_____
How long since you last used hair dye? _____

Have you had any illness in the last year? Yes_____No_____
What illnesses have you had? _____
_____
_____

Did you follow a high carbohydrate diet the last 3 days? Yes_____No_____
Have you been at least 12 hours and not more than 16 hours without food? Yes_____No_____
Have you had tea or coffee in the last 8 hours? Yes_____No_____
Have you had any strenuous exercise in the last 8 hours? Yes_____No_____

Is any member of your immediate family diabetic? Yes_____No_____
If yes, list the relation to you. _____

Have you had a previous Glucose Tolerance Test? Yes_____No_____
Were you diagnosed as diabetic? _____
If yes, when were you diagnosed as diabetic? _____

Are you taking hypoglycemic agents (diabetic pills)? Yes_____No_____

Have you ever taken insulin? Yes_____No_____

List the foods that would constitute a typical breakfast for you.

List the foods that would constitute a typical lunch for you.

List the foods that would constitute a typical dinner for you.

How has your food pattern changed?

What snack foods do you eat?

How many times a day do you snack?

Do you eat products made from white flour:

Several times each day	_____
Once each day	_____
Occasionally	_____
Never	_____

Do you eat products made from whole wheat flour:

Several times each day	_____
Once each day	_____
Occasionally	_____
Never	_____

Do you eat:	white sugar	Yes_____	No_____
	brown sugar	Yes_____	No_____
	raw sugar	Yes_____	No_____
	honey	Yes_____	No_____
	molasses	Yes_____	No_____

Which of the above do you use most frequently? _____
Which do you use the least? _____

What is your favorite food? _____
What is your least favorite food? _____

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ENVIRONMENT AND MAN V 58-28

I hereby give my consent to participate in the chromium project involving human subjects. I understand the procedure to be followed in the Glucose Tolerance Tests and am aware of the discomforts and risks involved by my participation. I will receive answers to any inquiries regarding the project and am free to withdraw my consent and discontinue participation in the project at any time.

_____

Signed

_____

Date

Appendix C

Taste Sensitivity Scoring Sheet

NAME _____

SOUR			SWEET		
CONCENTRATION	TIME 1 ORDER ID	TIME 2 ORDER ID	CONCENTRATION	TIME 1 ORDER ID	TIME 2 ORDER ID
3 MM HCL			15 MM SUCROSE		
6			30		
15			60		
30			150		
60			300		

SALT			BITTER		
CONCENTRATION	TIME 1 ORDER ID	TIME 2 ORDER ID	CONCENTRATION	TIME 1 ORDER ID	TIME 2 ORDER ID
30 MM NACL			120 MM UREA		
60			150		
90			300		
150			500		
300			1000		

ID CODE
M - MISSED
C - CORRECT
R - RECOGNIZED TASTE

RANDOM ORDER
1 X B B
2 B X B
3 B B X

Appendix D

Characteristics of Subjects

Table 6. Statistics nonpaired t on diabetic versus nondiabetics

Variable	Diabetic			Nondiabetic			
	$\bar{X}$	SD	N	$\bar{X}$	SD	N	t
Age, yrs	63.3	10.8	23	55.9	10.1	52	2.86
Weight, kg	79.61	13.91	24	70.25	12.42	52	2.94
Serum glucose, fasted, mg/100 ml	133	33	24	90	8	52	8.64
Serum glucose, 1 hr, mg/100 ml	244	48	24	123	29	52	13.45
Serum glucose, 2 hr, mg/100 ml	239	64	24	95	22	52	14.31
Serum glucose, 3 hr, mg/100 ml	179	65	23	70	14	52	7.32
Taste perception, sweet, mM suc.	72.4	49.3	23	61.5	69.3	51	---
Taste perception, sour, mM HCl	12.5	13.7	22	11.4	13.1	51	---
Taste perception, salt, mM NaCl	71.7	42.2	23	63.0	31.6	50	---
Taste perception, bitter, mM Urea	513.9	374.7	23	342.0	219.0	49	---
Taste recog., sweet, mM sucrose	87.0	54.4	22	69.8	71.1	49	---
Taste recog., sour, mM HCl	16.2	13.2	22	14.4	14.8	46	---
Taste recog., salt, mM NaCl	112.1	92.6	19	76.6	50.4	47	2.00
Taste recog., bitter, mM Urea	583	351	21	382	252	48	2.69
Urine vol, ml	1351	484	24	1382	589	52	---
Serum chromium, fasted, µg/l	9.10	4.94	23	8.11	3.48	49	---
Serum chromium, 1 hr, µg/l	9.98	6.92	21	8.02	4.72	51	---
Urine chrom, µg/24 hr	7.7	10.0	24	8.3	6.7	52	---
Urine chromium µg/l	6.71	7.45	22	7.25	4.10	46	---
Urine Cr/creatinine	1.4	1.6	24	1.3	1.1	52	---
Hair chromium ng/g	490	264	23	461	256	50	---
Water chromium µg/l	2.24	1.17	22	1.92	0.93	49	---
Serum zinc, fasted, µg/100 ml	130	39	24	112	31	44	2.09
Serum zinc, 1 hr, µg/100 ml	128	35	24	109	23	49	---
Urine zinc, µg/24 hr	050	491	24	394	236	52	5.59
Urine zinc, µg/ml	.680	.410	24	.330	.240	52	4.68
Urine zinc/creatinine	.14	.20	24	.07	.11	52	---
Hair zinc, µg/g	134	33	21	140	43	45	---
Water zinc, µg/100 ml	248	206	16	199	166	42	---
Cholesterol, fasted, mg/100 ml	218	43	24	205	50	50	---
Cholesterol, 1 hr, mg/100 ml	214	39	23	204	47	49	---
Triglyceride, fasted, mg/100 ml	156	51	24	131	44	50	2.12
Triglyceride, 1 hr, mg/100 ml	182	41	22	134	36	45	4.90

Table 7. Paired t test statistical analysis

		Diabetic		Nondiabetic	
	N	$\bar{X}$	t	$\bar{X}$	SD
Age, yrs	21	62.5	1.08	61.1	11.0
Weight, kg	21	78.3	.0212	78.3	31.8
Glucose 0	21	133	4.37**	98	34.7
Glucose 1	21	249	14.6**	132	45.1
Glucose 2	21	240	10.5**	103	60.7
Glucose 3	20	179	6.26**	74	65.7
Sweet p	20	75.8	1.04	57.0	51.8
Sour p	19	13.7	.099	13.3	14.5
Salt p	19	74.8	.411	71.1	44.0
Bitter p	19	521	2.72*	305	351
Sweet r	19	91.1	1.22	68.7	59.2
Sour r	17	16.8	0.475	14.1	15.0
Salty r	16	118	0.777	101	97.7
Bitter r	17	556	1.70	388	355
Urine vol.	21	1.388	0.432	1.328	505
Creat. mg/ml	21	4.7	-.961	5.22	1.98
Creat. 24 hr	21	6.0	-.253	6.21	2.29
Urine zinc µg/ml	21	0.64	2.53*	0.39	0.423
Urine zinc µg/24 hr	21	0.839	2.00	0.581	0.528
Urine zinc µg/ml creat.	21	0.13	3.17**	0.07	0.062
Hair zinc	16	140	1.36	125	323
Urine Cr. µg/l	20	27.8	-.283	28.5	9.91
Urine Cr. µg/24 hr	20	38.4	0.0495	38.1	21.2
Urine Cr. µg/g creat.	20	6.3	-.298	6.5	3.30

p = taste perception
r = taste recognition
*Significant P < .05
**Significant P < .01

*Mean significance range as determined by Duncans new multiple range test. A mean value is significantly different from another mean if the top of the bar does not bisect the lined area ($p < .05$). This is a rank test thus the last ranked value has no significance range.

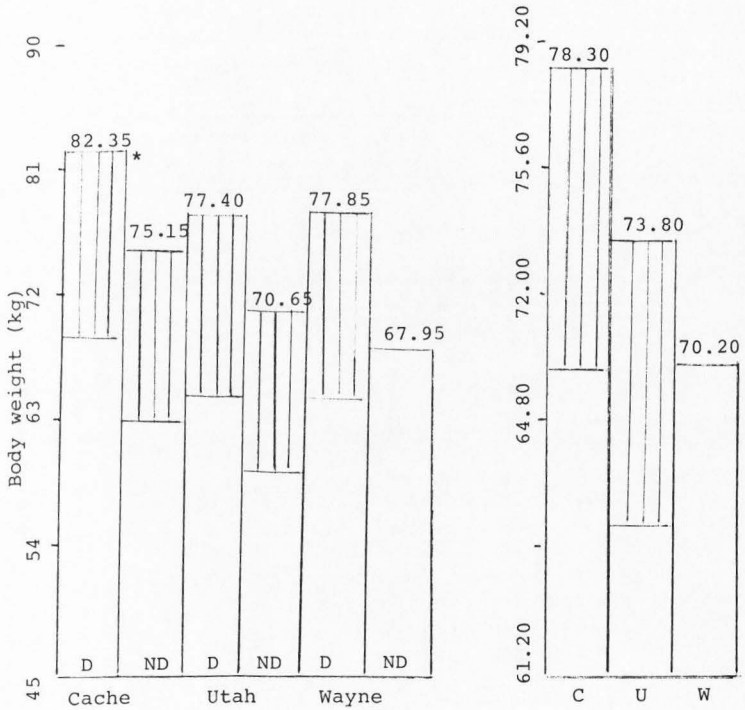

Figure 3. Body weight in kg by county and by diabetic (D) or nondiabetic (ND).

*Mean significance range as determined by Duncans new multiple range test. A mean value is significantly different from another mean if the top of the bar does not bisect the lined area ($p < .05$). This is a rank test thus the last ranked value has no significance range.

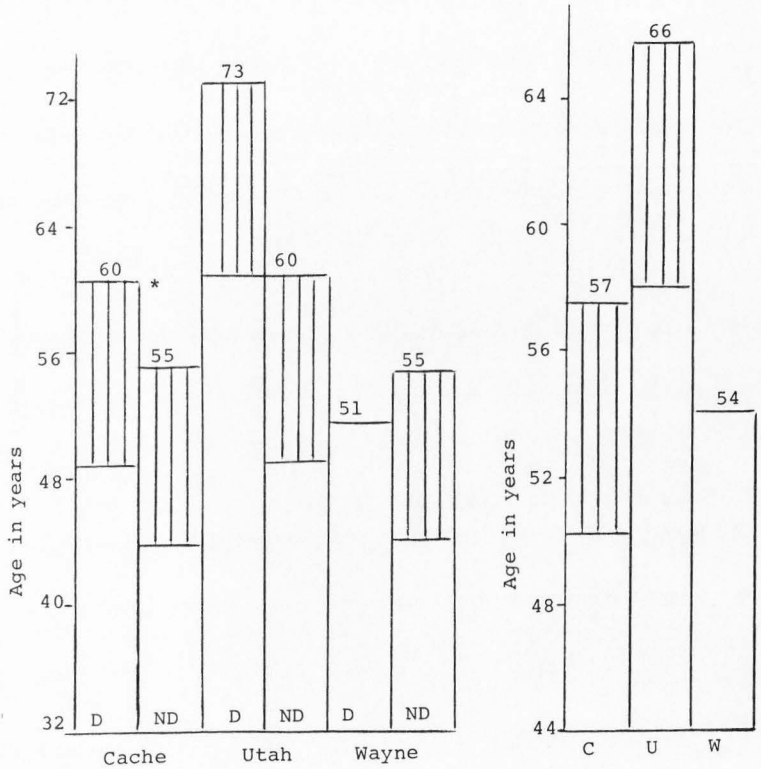

Figure 4. Age in years by county and by diabetic (D) or nondiabetic (ND).

*Mean significance range as determined by Duncans new multiple range test. A mean value is significantly different from another mean if the top of the bar does not bisect the lined area ($p < .05$). This is a rank test thus the last ranked value has no significance range.

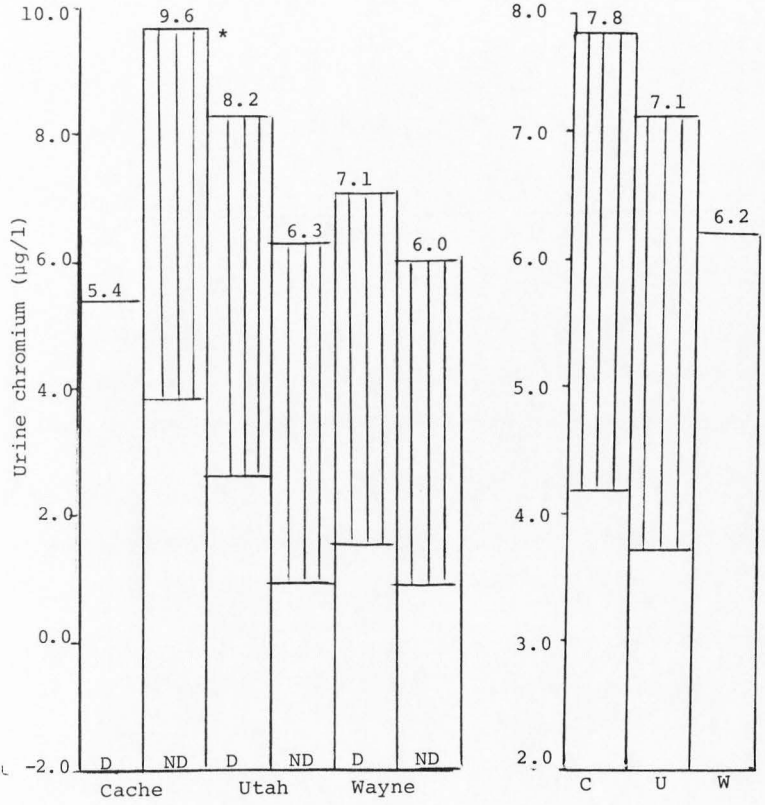

Figure 5. Urine chromium, µg/1, by county and by diabetic (D) or nondiabetic (ND).

*Mean significance range as determined by Duncans new multiple range test. A mean value is significantly different from another mean if the top of the bar does not bisect the lined area ($p < .05$). This is a rank test thus the last ranked value has no significance range.

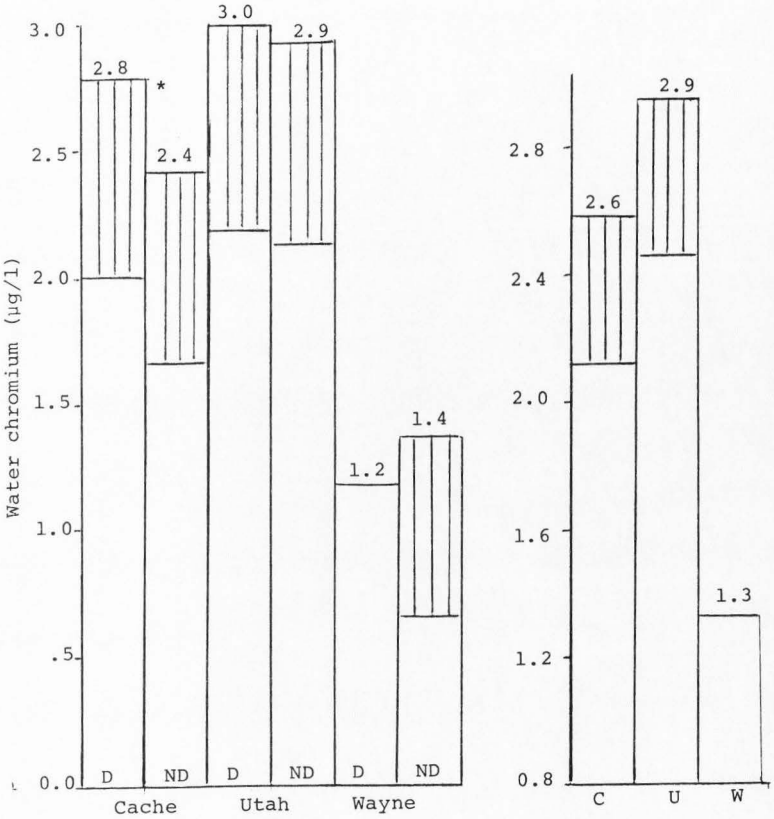

Figure 6. Water chromium, µg/1, by county and by diabetic (D) or nondiabetic (ND) household.

*Mean significance range as determined by Duncans new multiple range test. A mean value is significantly different from another mean if the top of the bar does not bisect the lined area ($p < .05$). This is a rank test thus the last ranked value has no significance range.

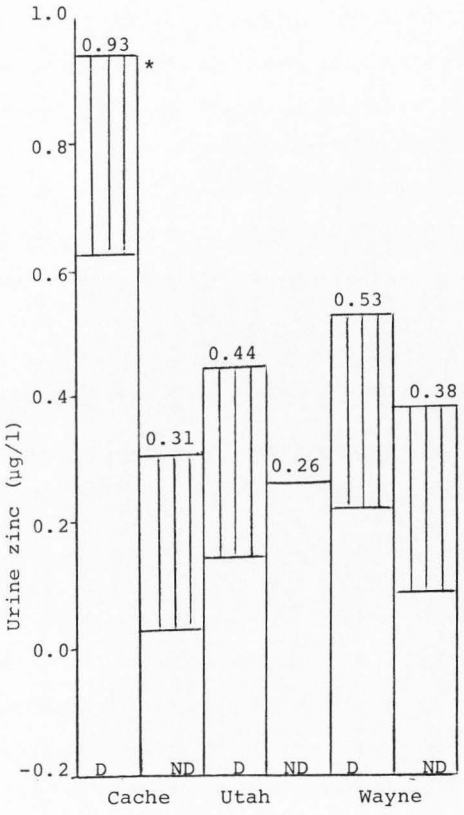

Figure 7. Urine zinc, µg/l, by county and by diabetic (D) or nondiabetic (ND).

*Mean significance range as determined by Duncans new multiple range test. A mean value is significantly different from another mean if the top of the bar does not bisect the lined area ($p < .05$). This is a rank test thus the last ranked value has no significance range.

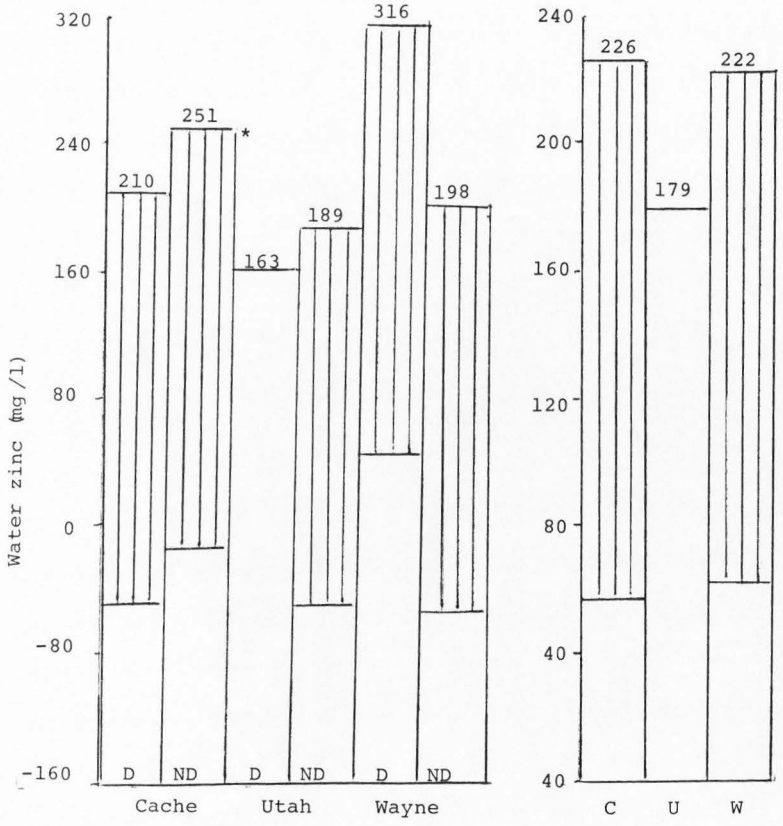

Figure 8. Water zinc, ml/l, by county and by diabetic (D) or nondiabetic (ND) household.

Table 8. Characteristics of subjects--Cache County

	County N 22		Diabetic N=10		Non-diabetic N=12		
	Mean	SD	Mean	SD	Mean	SD	t
Age, yrs	57.5	10.9	60.5	11.4	55.1	10.3	1.17
Weight, kg	78.75	12.15	82.35	11.30	75.15	12.33	1.42
Height, cm	167.75	9.93	168	11.3	167.75	9.15	0.057
Serum glucose, fasted, mg/100 ml	118	32	146	29	94	7.	5.89**
Serum glucose, 1 hr mg/100 ml	188	73	255	51	132	25.	7.29**
Serum glucose, 2 hr mg/100 ml	174	90	256	70	105	16.	7.19**
Serum glucose, 3 hr mg/100 ml	132	75	202	55	73	15	7.72**
Taste perception, sweet, mM sucrose	60.0	47.2	80.0	54.1	45.0	36.7	1.80
Taste perception, sour, mM HCl	10.3	13.0	16.3	18.4	5.75	3.25	1.96
Taste perception, salt, mM NaCl	57.1	26.7	66.7	36.1	50.0	14.8	1.47
Taste perception, bitter, mM Urea	387	286	463	331	329	247	1.09
Taste recognition, sweet, mM Suc.	83.7	68.2	101	53.0	70.9	77.4	1.04
Taste recognition, sour, mM HCl	13.7	13.4	21.3	16.9	7.36	3.88	2.78*
Taste recognition, salt, mM NaCl	118	102	176	122	85.0	75.5	2.14*
Taste recognition, bitter, mM Urea	475	328	588	348	400	306	1.35
Serum chromium, fasted, µg/l	8.64	3.33	8.69	3.92	8.59	2.94	0.068
Serum chromium, 1 hr, µg/l	8.27	2.97	8.72	3.05	7.93	2.99	0.612
Urine chromium, µg/24 hr	9.08	5.84	5.20	3.07	12.30	5.69	-3.53**
Urine chromium, µg/l	7.79	5.26	5.38	1.84	9.60	6.29	-2.04
Urine Cr/creatinine	1.39	0.867	0.879	0.641	1.82	0.814	-2.97**
Hair chromium, ng/g	550	219	569	188	534	250	0.364
Water chromium, µg/l	2.59	0.969	2.79	1.08	2.43	0.876	0.864
Serum zinc, fasted µg/100 ml	109	21.5	114	30.1	105	7.75	1.00
Serum zinc, 1 hr µg/100 ml	114	31.0	126	42.0	104	12.3	1.74
Urine zinc, µg/24	713	503	108	499	410	241	4.12**
Urine zinc, µg/ml	0.595	0.462	0.939	0.477	0.308	0.152	4.34**
Hair zinc, µg/g	114	29.6	112	27.8	116	32.1	-.309
Water zinc, µg/100 ml	226	107	210	38.8	251	202	-.630
Cholesterol, fasted, mg/100 ml	192	51.2	210	50.6	176	48.5	1.61
Cholesterol, 1 hr mg/100 ml	192	41.6	208	28.9	179	46.7	1.71
Triglyceride, fasted, mg/100 ml	141	52.2	156	59.8	127	41.3	1.34
Triglyceride, 1 hr mg/100 ml	155	47.2	181	45.0	122	25.0	3.89

**Significant at P < .01

Table 9. Characteristics of subjects--Utah County

	County mean	N=15 SD	Diabetic mean	N=6 SD	Nondiabetic mean	SD	t
Age, yrs	65.7	13.0	73.0	4.77	60.9	14.6	1.94
Weight, kg	73.8	10.26	78.08	12.16	71.73	8.62	1.20
Height, cm	160.25	7.35	160.75	7.7	159.75	7.55	0.249
Serum glucose, fasted, mg/100 ml	118	37	153	34	93	7	5.03**
Serum glucose, 1 hr mg/100 ml	187	75	26	57	136	16	6.46**
Serum glucose, 2 hr mg/100 ml	176	96	280	55	106	20	8.61**
Serum glucose, 3 hr mg/100 ml	129	85	225	41	64	10	11.3**
Taste perception, sweet, mM sucrose	44.0	18.3	50.0	15.5	40.0	19.8	1.04
Taste perception, sour, mM HCl	13.5	16.1	5.40	1.34	18.0	18.9	-1.61
Taste perception, salt, mM NaCl	84.0	44.2	80.0	55.9	86.7	38.1	-2.78
Taste perception, bitter, mM Urea	405	277	542	372	313	156	1.66
Taste recognition, sweet, mM sucrose	53.0	31.5	50.0	15.5	55.0	39.7	-.2911
Taste recognition, sour, mM HCl	16.6	16.7	5.40	1.34	23.6	18.2	-2.41*
Taste recognition, salt, mM NaCl	85.0	44.0	75.0	57.4	90.0	39.3	-.604
Taste recognition, bitter, mM Urea	405	297	590	394	290	150	2.10
Serum chromium, fasted, µg/l	9.64	6.58	11.5	8.28	8.33	5.36	.906
Serum chromium, 1 hr, µg/l	13.2	9.58	14.2	11.2	13.4	8.91	.347
Urine chromium, µg/24 hr	8.85	9.68	9.79	14.69	82.30	53.00	.296
Urine chromium, µg/l	7.14	8.31	8.28	13.2	6.29	1.22	.458
Urine Cr/creatinine	1.60	1.46	1.67	2.09	1.546	0.996	.156
Hair chromium, ng/g	496	284	573	409	437	148	.925
Water chromium, µg/l	2.95	0.782	3.00	1.00	2.93	0.735	.157
Serum zinc, fasted, µg/100 ml	136	29.0	147	39.5	126	12.1	1.52
Serum zinc, 1 hr µg/100 ml	120	22.6	133	30.4	111	10.6	2.03
Urine zinc, µg/24 hr	471	262	596	318	387	194	1.59
Urine zinc, µg/ml	0.334	0.195	0.438	0.218	0.264	.154	1.82
Hair zinc, µg/g	147	33.7	148	31.7	146	37.9	0.107
Water zinc, µg/100 ml	179	118	163	114	189	126	-.406
Cholesterol, fasted, mg/100 ml	229	40.5	216	34.1	239	44.2	-1.07
Cholesterol, 1 hr, mg/100 ml	216	48.3	204	52.7	224	46.5	.775
Triglyceride, fasted, mg/100 ml	166	39.2	173	19.7	162	48.9	.518
Triglyceride, 1 hr, mg/100 ml	159	38.1	165	22.2	155	46.5	.487

*Significant at P < .05
**Significant at P < .01

Table 10. Characteristics of subjects--Wayne County

	County mean	N=39 SD	Diabetic mean	N=8 SD	Nondiabetic mean	N=31 SD	t
Age, yrs	55.5	8.4	58.9	9.17	53.2	12.5	1.2
Weight, kg	70.69	14.76	78.54	18.80	74.46	35.91	0.309
Height, cm	164.25	0.75	170.75	.98	198.5	20.05	-.388
Serum glucose, fasted, mg/100 ml	95	11	104	14	93	9	-.223
Serum glucose, 1 hr mg/100 ml	137	51	217	27	124	58	4.37**
Serum glucose, 2 hr mg/100 ml	109	46	188	17	101	77	3.11**
Serum glucose, 3 hr mg/100 ml	77	21	107	23	70.3	14	5.69**
Taste perception, sweet, mM sucrose	75.8	79.6	80.6	59.4	75.0	86.4	0.172
Taste perception, sour, mM HCl	11.8	12.4	12.8	11.2	11.9	12.9	0.180
Taste perception, salt, mM NaCl	63.2	33.8	71.3	42.2	62.1	31.5	0.687
Taste perception, bitter, mM Urea	400	279	550	388	364	231	1.75
Taste recognition, sweet, mM sucrose	80.3	75.0	103	64.9	74.5	78.8	0.941
Taste recognition, sour, mM HCl	15.2	14.5	17.3	11.2	15.0	15.6	0.390
Taste recognition, salt, mM NaCl	70.3	38.5	75.0	39.3	70.4	38.8	0.298
Taste recognition, bitter, mM Urea	439	287	575	376	410	252	1.49
Serum chromium, fasted, g/l	7.92	3.28	8.11	3.53	7.81	3.31	0.226
Serum chromium, 1 hr, µg/l	7.05	3.25	7.67	4.59	6.70	2.77	0.766
Urine chromium, µg/24	7.30	8.26	9.36	12.60	6.82	6.87	0.775
Urine chromium, µg/l	6.59	3.77	7.07	6.22	6.47	2.97	0.3977
Urine Cr/creatinine	1.28	1.45	1.76	2.11	1.20	1.22	0.987
Hair chromium, ng/g	421	260	338	140	602	919	-.802
Water chromium, µg/l	1.33	0.509	1.19	0.368	1.37	0.551	-.871
Serum zinc, fasted, µg/100 ml	118	41.0	138	45.1	112	39.3	1.62
Serum zinc, 1 hr µg/100 ml	115	30.2	127	33.3	110	29.4	1.42
Urine zinc, µg/24 hr	470	354	784	518	363	248	3.35**
Urine zinc, µg/ml	0.398	1.98	0.528	0.237	0.358	-.283	1.56
Hair zinc, µg/g	147	43.1	143	31.7	149	46.4	-.343
Water zinc, µg/100 ml	223	202	316	269	202	181	1.43
Cholesterol, fasted, mg/100 ml	211	47.4	231	41.9	211	50.1	1.04
Cholesterol, 1 hr mg/100 ml	213	44.2	230	38.8	227	103	0.080
Triglyceride, fasted, mg/100 ml	128	46.1	145	58.3	140	98.1	0.137
Triglyceride, 1 hr mg/100 ml	144	44.9	193	46.2	146	94.3	1.36

**Significant at P < .01

VITA

Carol H. Williams

Candidate for the Degree of

Master of Science

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