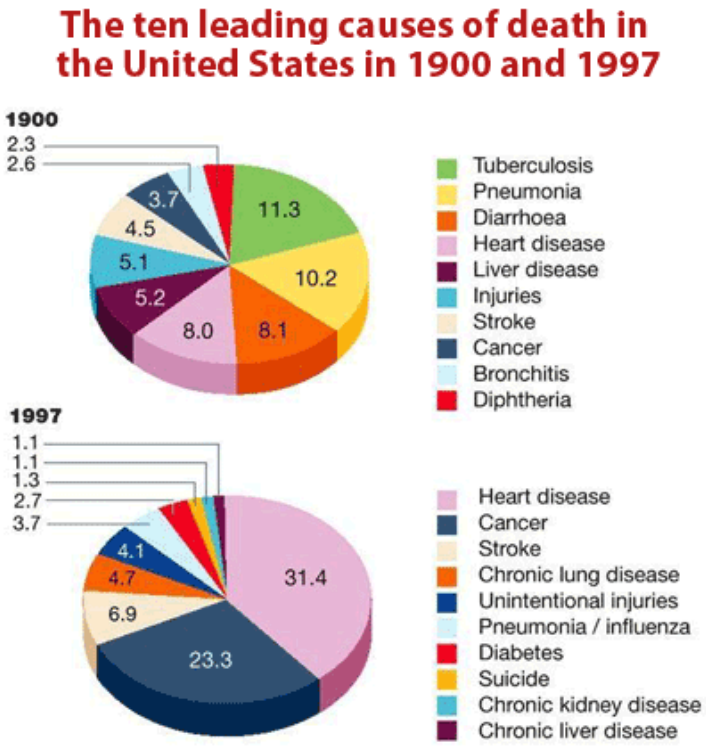
**Eating, Endocrinology, and Correcting Type II Diabetes**

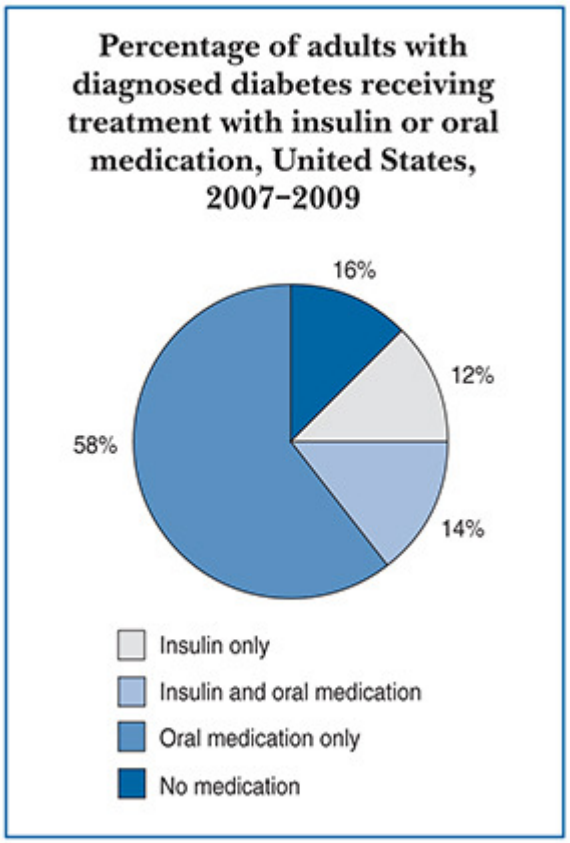
*Dr. Richard Sauerheber B.A. Biology*
*Ph.D. Chemistry, UCSD, former NIH diabetes principal investigator,*
*and supervisor, Rees Stealy Clinic Research Laboratory,*
*currently educator at Palomar College STAR center*




**Number of deaths for leading causes of death 2009:**

- Heart disease: 599,413
- Cancer: 567,628
- Chronic lower respiratory diseases: 137,353
- Stroke (cerebrovascular diseases): 128,842
- Accidents (unintentional injuries): 118,021
- Alzheimer's disease: 79,003
- Diabetes: 68,705
- Influenza and Pneumonia: 53,692
- Nephritis, nephrotic syndrome, and nephrosis: 48,935
- Intentional self-harm (suicide): 36,909  Infant mortality 29,000 34$^{th}$ in world list.

Source: U.S. CDC 2009 report. Diabetes is ranked as the 5$^{th}$ to 7$^{th}$ leading cause of death, since the exact extent that diabetes is known to contribute to other lethal diseases is not easily quantified. Diabetes and Alzheimer's were not listed as significant in 1900, diabetes entering the top 10 in 1939 and Alzheimer's in 1994 (not shown in graph), both increasing in prevalence ever since. Knew Randle, Walaas, Lazarow, Taylor, Wick, Olefsky, Levine.




**Definition.** Diabetes (siphon) mellitus (sweet) insipidus (tasteless). Known since B.C. Egypt, Type I is due to deficiency of insulin and is a true disease and has no actual cure but is remedied with exogenous insulin injection. Type II is a condition that can be corrected through isocaloric eating.

**Incidence.** 25.5 million diabetics in U.S., 24 million type II (8% incidence in 315 million population), 1.5 million type I (0.3%) (overestimated by improper definition of diabetes with blood glucose from 110-130, but underestimated since many type II cases remain undiagnosed). The incidence was lower in 1991, with 10 million Type II of 250 million population (4.0%) and 1.5 million Type I (0.5%). Type I has increased only from 0.019% to 0.020% from 2001-2009 in children. 'Type III' is misnomer, merely Type II condition during pregnancy.

**Causes.** Type I caused by inherited pancreatic islet deficiency, certain viral infections, iron hemochromatosis, car accidents. 'Type III' caused by high caloric intake during pregnancy. Type II caused by longterm higher than required caloric intake after eventual filling of fat cells. Insulin resistance does not explain the condition and it is not a disease. The condition can be corrected through isocaloric eating. Does not require a cure because is not a disease. What is inherited is healthy islets able to efficiently store ingested foodstuffs so that diabetic condition appears after fat and muscle cells are full of glycogen and triglyceride.
Classic case occurs after many decades of eating somewhat more calories daily than necessary with weight gain until eventually the fat cells one is born with become filled. Continuing to eat in the usual way causes blood sugar to increase since it cannot be stored well and spills into urine. NO new cases of Type II were ever recorded during WWI or WWII during food rationing. Increased incidence from 4 to 8% likely due to advertising and prevalence of high calorie foods containing high fat and carbohydrate. Metabolic changes with aging also can be involved.

**Insulin.** Insulin (island) 51 amino acids, molecular weight 5,808. Only hormone that functions to lower glucose, store lipid and increase protein synthesis and to block lipid and protein and glycogn breakdown. 14 other hormones oppose insulin to elevate blood glucose. Banting, McLeod Nobel Prize shared with Best and Collip (Toronto, 1923) for clean purification and use in children's death ward. Normal blood range 0 – 2 ng/ml (0 – 60 uIU/ml, 0 – 344 pM). Langerhans 1882 Germany discovered islets and role in digestion, Minkowski discovered removal in depancreatectomized dogs led to flies swarming over urine (Germany 1886); Banting/Best purified and used

(1921); Sanger sequenced (1958) Nobel Prize; Dorothy Hodgkin crystallography Nobel 3-D shape (1963); Roselyn Yalow Nobel (1977) for RIA assay.

**Glucose.** Glucose normal range 90-130 mg% (ADA). Renal threshold varies from 170-200 mg% with exceptions that are normal. Insulin dose response curve 0 – 2 ng/ml, obese diabetic curve also has full stimulation, an insignificant shift in Kd due to size of cell. Insulin binds to receptors on muscle, fat and liver (at high levels from portal vein) and decreases protein kinase and cAMP, blocks lipolysis, glygogenolysis and proteolysis, increases syntheis of protein, fat and glycogen, increases glucose transport activity two fold through an allosteric effect on transporter conformation (rather than recruitment of extra transporters or an increase more than 2 fold) in 1 minute. This discovery caused an NIH official to not renew my research grant. Glucose > 170-200 mg% spills into urine = diabetes. Long term 10-15 years causes microangiopathy.

**Diabetes Treatment and Lethality**. Insulin treatment of type I without eating = immediate hypoglycemic shock (< 50mg%) (dizziness, sweating, headache, increased heart rate due to epinephrine counteraction, paleness, weakness, vomiting, coma, death if untreated; treat with orange or fruit juice or soda or candy unless unconscious, then inject glucagon if prescribed or call 911) (cause of death in Type I children using insulin pumps). Oppositely, uncontrolled type I, hyperglycemia in three days causes hyperglycemic coma (400-1000 mg%) (rapid heart rate, shallow rapid breathing, pallor, shock, exhaustion, ketotic acidosis, coma if untreated; treat with insulin). Poor control of type I during growth years causes stunted growth. Poor control for 10 years (type I or type II) causes retinopathy, neuropathy, capillary thickening. Type II nonketotic coma from diabetic drugs plus forgetting to eat.

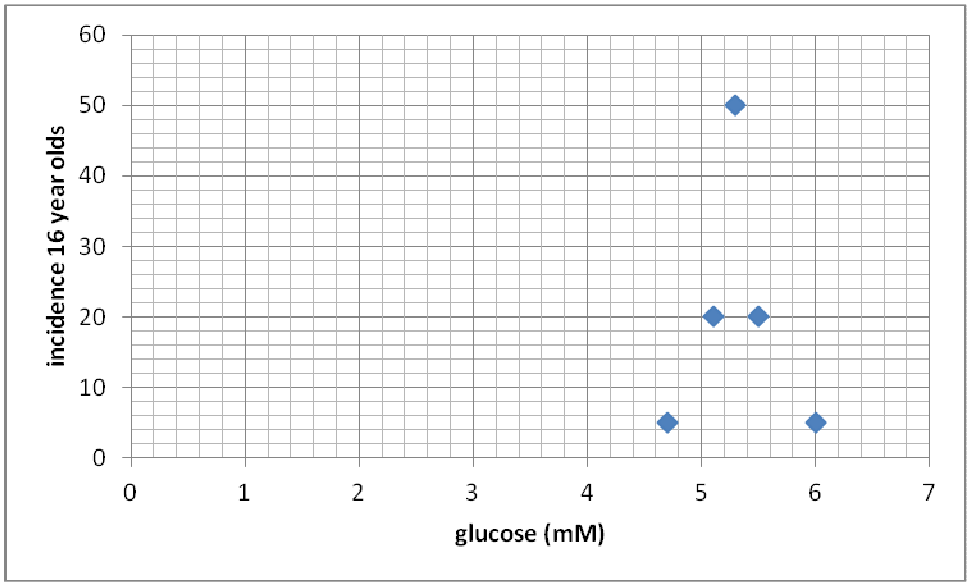
Eastern U.S.: MASS General Hospital and Joslin Diabetes Center (Harvard, Boston), Mayo Clinic Diet (Rochester, MINN), see Current Therapeutic Research, 1988; metabolic ward with cafeteria square meals only. Weight loss unnecessary, use no diabetic drugs, then eat to almost full for isocaloric eating after stopping eating to normalize glucose.

Gestational diabetes some refer to as Type III is type II during pregnancy is a temporary condition that occurs in 10% of pregnancies and is best corrected with daily exercise and caloric restriction until blood sugar is normal, but if this is not possible then insulin injections can be used, rather than synthetic unnatural drugs. Normal glucose level maintenance is important since hyperglycemia during pregnancy causes 3 times the incidence of birth defects in the newborn to occur, usually heart deformities (sugar above 140 mg% in third trimester at the time of eating).

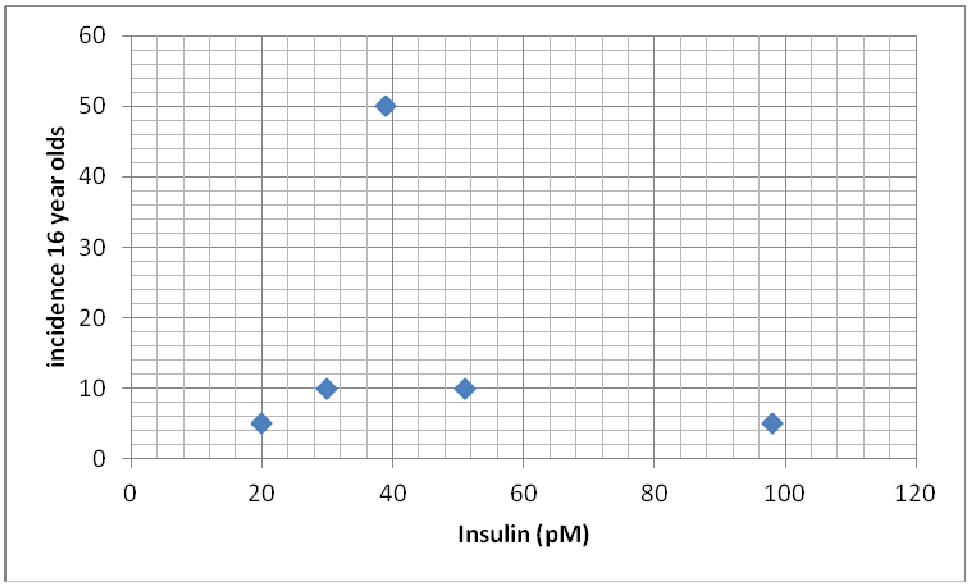
Western U.S.: outpatient oral 'antidiabetic drugs'. Sulfonylureas first generation banned by FDA 1965 for increased heart attack incidence; second generation long term failure and islet degeneration, lower rate of heart disease incidence increase, not yet banned. Lost my grandfather to heart attack on diabetic drugs just before they were banned. Drug first purpose was to induce Type I diabetes in research animals, diabetic dog 1 = DBI.

Coronary heart disease CHD is the leading lethal disease in the U.S. Diabetes contributes to this significantly from oral medications that increase heart attack incidence by converting heart tissue from fatty acid to glucose consuming tissue and by blood vessel thickening in heart vessels exacerbating atherosclerosis when condition is not controlled well (elevated fasting insulin levels due to overeating correlate with increased CHD incidence where insulin blocks lipolysis and lowers the level of preferred fatty acid fuel for the heart).

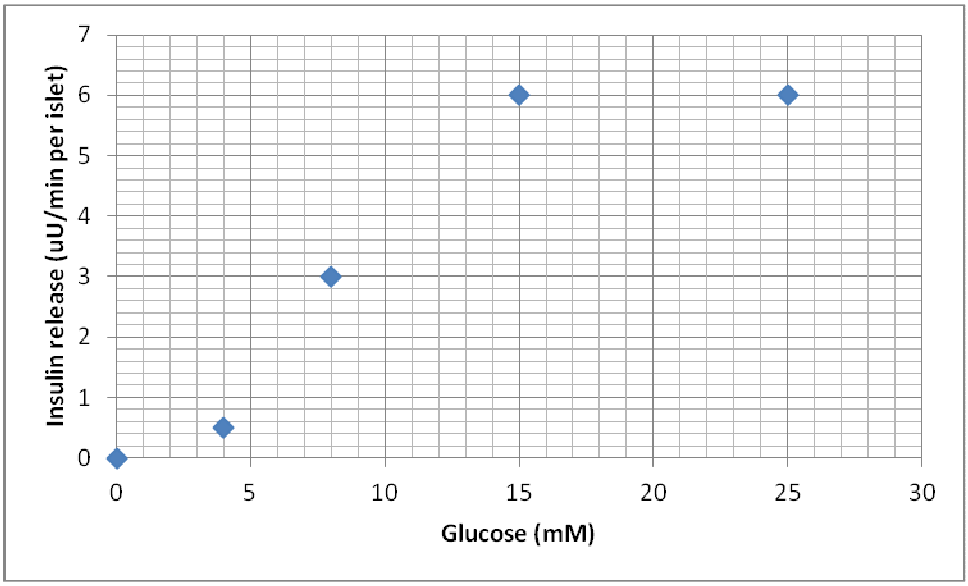
**Insulin Regulation of Foodstuffs.** The pancreas is an endocrine and exocrine organ behind the stomach and peritoneal cavity in the fold of the duodenum. Exocrine secretes bicarbonate and digestive enzymes into small intestine. Endocrine islets have alpha A (glucagon), beta B (insulin), gamma C (pancreatic polypeptide) and delta D (somatostatin) cells that control handling of assimilated foodstuffs, chiefly by insulin secretion during eating that quickly tapers off between meals. After eating, glucose goes up, causing insulin to go up, causing glucose to go down, causing insulin to go down, allowing glucagon to go up if glucose < 70 mg%, preventing hypoglycemia and increasing fatty acids. Insulin increases glucose uptake and blocks lipolysis, thereby lowering glucose and fatty acids and promoting glycogen and triglyceride energy storage.



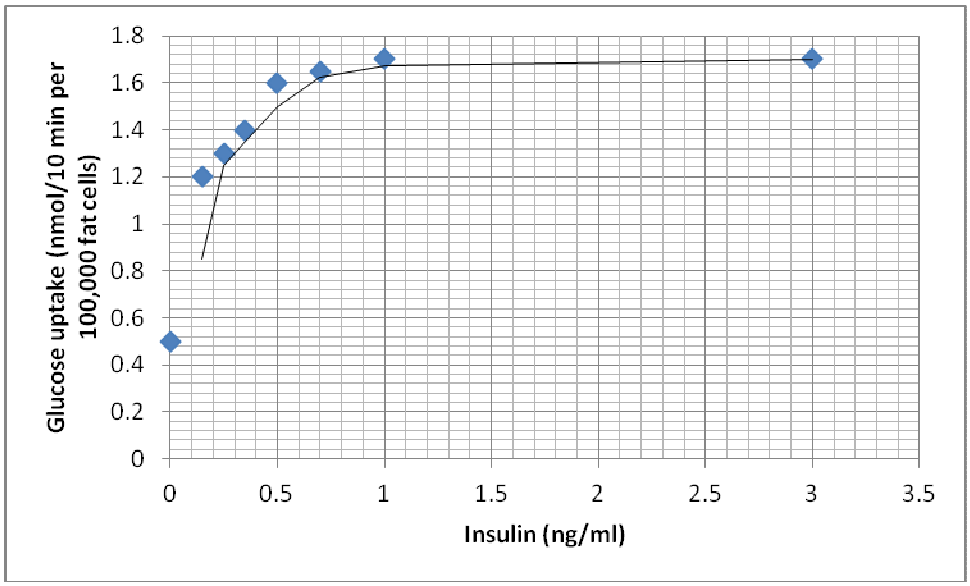

Normal fasting glucose range in human blood. 4.5 mM = 81 mg%, 5.3 mM = 95 mg%, 6 mM = 108 mg% (Allard, Pierre, 2003, **Clinical Chemistry**, vol 49, 644 Canadian teens). After eating in the fed state glucose levels rise normally to near the renal threshold (170-200 mg% = 10 mM). Normal glucose is 80-150 in elderly and in pregnancy. (Glucagon release is inhibited by 2-7 mM glucose).



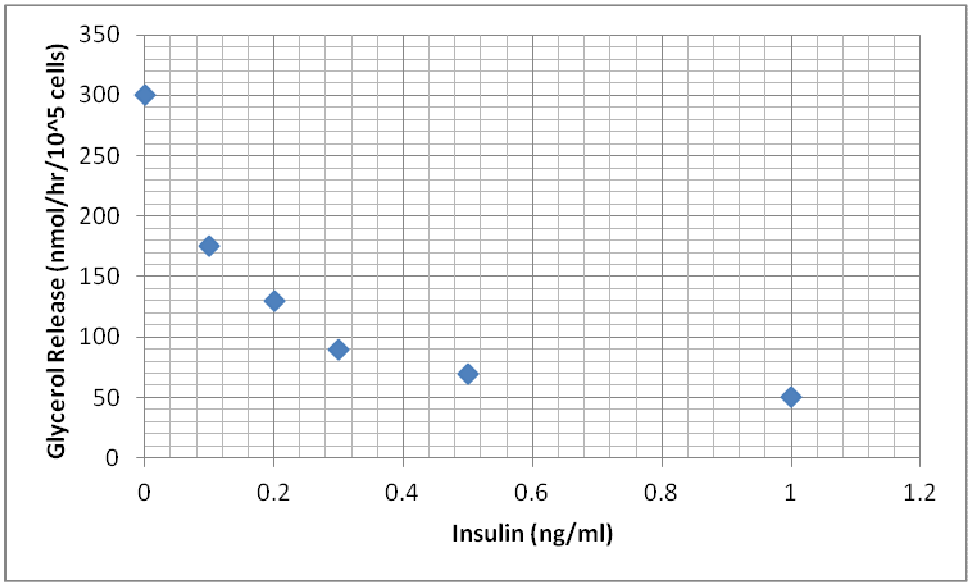

Normal fasting insulin levels in human blood. 39 pM = 0.2 ng/ml = 6 *u*IU/ml; 98 pM = 0.5 ng/ml = 15 *u*IU/ml (Allard). Normal range (Merck Manual) 6 – 26 *u*IU/ml (0.2 – 0.9 ng/ml, or 39 – 170 pM), Teitz, Clinical Chemistry 0 – 60 *u*IU/ml (0-1 ng/ml), or Merck 0– 200 pM). After eating, in the fed state insulin rises to approximately 5 ng/ml (Merck) (150 *u*IU/ml, 980 pM).




Insulin release from pancreatic islets as a function of glucose concentration (Cooperstein and Watkins, **The Islets of Langerhans**, 1981). Note maximal insulin release at 200mg%, the renal threshold for glucose.

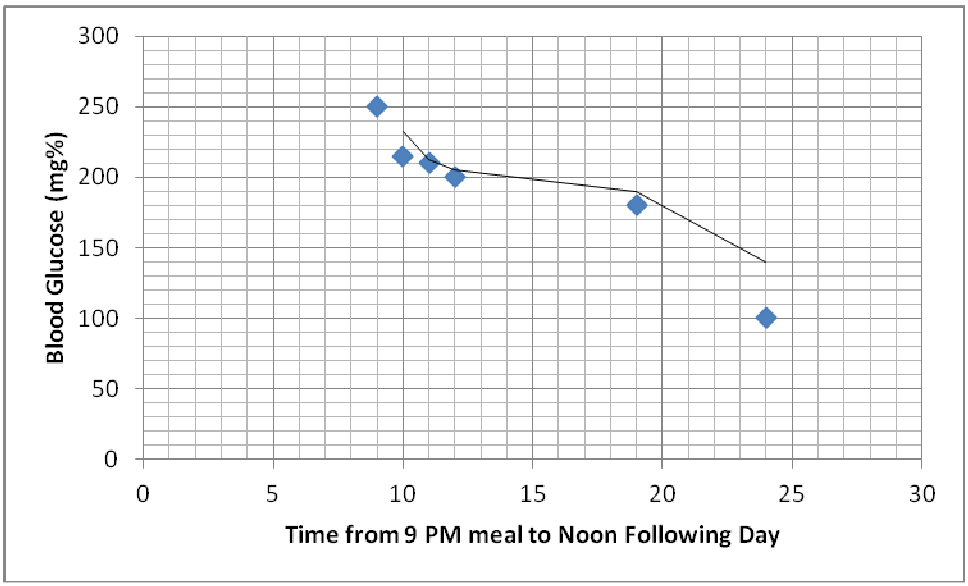



Glucose uptake as a function of insulin concentration. (Sauerheber, et.al. (1987) **Biochemical Pharmacology** 36, p. 2305, *Insulin Stimulation of Adipocyte Membrane Glucose Transport*). 200 pM = 1 ng/ml = 30 IU/ml. Similar curve in skeletal and heart muscle. Insulin does not stimulate tranport in liver which has freely permeable transporters to glucose. The appearance of this curve compares with the time dependent increases in insulin level over a 9 month period of normal pregnancy. In gestational diabetes it is imortant to adjust to this situation and not eat until blood sugar is normal (< 140-150 mg%) first due to the higher frequency of congenital heart defects caued by the prolonged hyperlgycmeia during pregnancy. Simply wait until sugar levels drop before eating the next meal.

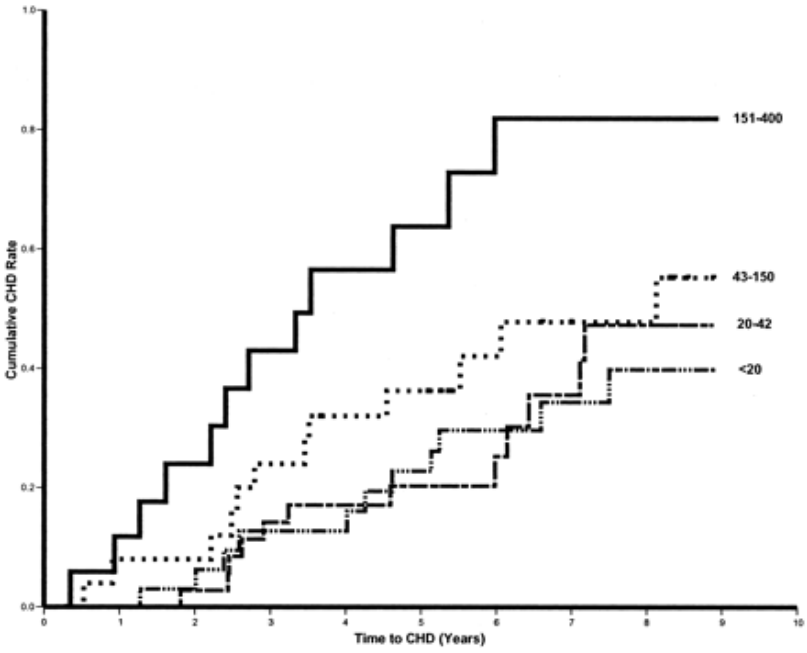



Insulin blocks lipolysis in fat cells (and in liver) over a range similar to that which increases glucose transport. Fatty acid levels in blood are decreased by insulin after meals and increase again between meals. Fatty acids potentiate insulin release only when glucose is present. (from Olefsky, J., **Journal of Lipid Research** 18:459,1977). Free fatty acids rise during fasting to 7 *u*M from 3-4 *u*M in the fed state. Insulin lowers heart-preferred fatty acid fuel. Normally heart alternates between fatty acids and glucose as fed and fasting states alternate. Long term elevated insulin between meals (due to overeating, oral diabetic drugs or insulin) forces long term reliance on glucose rather than the preferred fuel fatty acids, changing composition of heart muscle.

**Control of Type II Diabetes to Curb Heart Disease (fatty acid under-use, collagen storage) and Microangiopathy (atherosclerosis of cardiac arteries and glucose reaction with vessel surfaces).**
Low calorie diets are necessary to control type II hyperglycemia. First it is necessary to eliminate diabetic drugs, then stop eating until hyperglyceia normalizes, then resume isocaloric eating that maintains body weight rather than weight gain. Hyperglycemia always normalizes by stopping eating after an evening meal and skipping breakfast the next morning, as seen in the graph for human Type II diabetics (taken from Sauerheber, et al. (1988) *Noninsulin Dependent Diabetes Mellitus in Obese Hyperglycemic Mice in Relation to Feeding: Comparison with the Human Obese Diabetic Condition* **Current Therapeutic Research** 44(4) pp. 612-618).



At MASS General and the Joslin Diabetes Center at Harvard University, diabetics are always admitted into the hospital, placed in a metabolic ward and fed 3 square cafeteria meals daily. No diabetic drugs are or have ever been used. In each case the diabetic hyperglycemia disappears and the patient learns how to prevent it. Allen diet first used fasting on 4 bran muffins plus fluids, then gradual feeding of low to higher caloric intake. Krall, 1540 calories daily in diabetic pilots allowed them to maintain normal weight without gaining more weight, kept flying licenses.



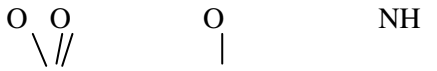
Cumulative incidence of CHD categorized by baseline intervals of fasting radioimmune insulin levels (intervals in microunits per milliliter shown to the *right* of each *curve*). Kronmal, R., et.al., (2004) **Journal of Clinical Endocrinology and Medicine.**
Heart muscle relies on fatty acids mostly, glucose is not the preferred fuel. So hyperglycemia and high insulin cause heart to use glucose for fuel, blocking normal utilization of fatty acids.

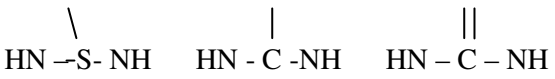
**Complications.** Diabetes lethality can be divided into three types, acute, semi-acute and chronic:

| | Type I | Type II |
|---|---|---|
| Low blood glucose, coma, death minutes. | Insulin without eating | Drugs without eating |
| High blood glucose, coma death 3 days. | Insulin lack | 600 mg%, no water intake |
| Microangiopathy, heart disease, 10 years. | Poor glucose control | Poor glucose control |

**Improper Overcorrection with Drugs**. Diabetes misdiagnosis is a prime example where diabetic drugs are given that are causing harm and given to people who do not actually have diabetes. Diabetes incidence is overestimated due to false diagnosis. Recent trends spurned by drug companies is to chemicalize a person who has fasting glucose of 101 mg% or higher, even though the ADA recognizes that normal glucose ranges from 90-130 mg% and that glucose does not spill into urine and thus cause a diabetic condition until the 170-200 mg% renal thereshold is exceded. The exuberance is fostered by the UDPG studies showing that good control of blood sugar prevents microangiopathy longterm, but sadly the treatment can be worse than the condition in the case when drugs are used, rather than isocaloric eating to maintain fasting glucose below 130 mg%.

**Oral Diabetic Drugs.** Sadly, chemicals synthesized to alter the beta cell membrane, originally designed to inflict a diabetic state in research animals, are now used in low doses as though they are legitimate to treat type II diabetes as 'oral diabetic' agents. Most of these are sulfonylurea or alloxan derivatives with chemical groups that intreact with glucose transporters in the beta cell membrane to react with disulfides in the protein abnormally causing insulin secretion. These agents in many people eventually stop having hypoglycemic effect and instead may be involved in converting type II diabetics into an insulin-requiring condition resembling Type I. The chemical group responsible contains an electron rich polar moiety surrounded by two amine groups.





The first, *sulfonylurea*s, are in tolazamide (= tolinsase), tolbutamide (= orinase), diabenes (= chlropropamide), sulfonamide, diabeta (= micronase = glyburide), and the second in the protein-conformation-altering natural metabolic poisonous waste product *urea* in in alloxan and streptozotocin used to destroy beta cells in research animals for type I diabetes research and in glucotrol and glynase and the third *metformin*, phenformin and dibiguanides (DBI) the original research drugs designed to induce permanent type I diabetes in animals. The first two groups cause insulin, already at fed state levels in Type II, to be higher, causing low fatty acid levels, blocked proteolysis reliance on glucose as only fuel, microangiopathy and cardiomyopathy longterm and often eventually requiring insulin injections. The third group causes accelerated glucose metaolism with lactic acid buildup. Drugs should never be used in Type II diabetes. Sulfonylureas and phenformin were banned by the FDA in the 1960's due to twice the heart mortality. There are great drugs such as aspirin and nitroglycerin for angina victims and platelet aggregation inhibitors for stents and those with cardiovacular disease, and statins but only being safe in those who actually need the normalization they achieve. The problem with drugs is that the person is converted from inappropriate hyperlgycemia (with normal or elevated insulin from overeating) to a condition of inappropriate hyperinsulinemia (with normalized glucose levels caused by insulin abnormal insulin secretion by the drug), where heart tissue then relies exclusively on glucose for fuel, since it is insulin, not glucose, that determines the rate of glucose entry into cells-- in fact type I diabetes is known as the disease of 'starving in the midst of plenty' because glucose at extremely high levels still does not prevent lipolysis, fatty acid breakdown and ketosis—only insulin exhibits that function.

**Specific dietary recommendations** are available in the Mayo Clinic Diet Manual and the American Diabetes Association for diabetic diets.

Note that typical foods eaten per person per week during the food rationing of World War II:

1 egg per WEEK
4 ounces of margarine
4 ounces of bacon
2 ounces cheese
1/8 lb jam = 2 ounces
3 ounces of sweets
one quart of milk

Home gardens grew in popularity. Canned and frozen fruits and vegetables, meats, butter and cheese were rationed in the U.S. from 1941-1946 to conserve food for soldiers overseas. Two boxes of macaroni and cheese could be substituted for an amount of meat that was smaller for one coupon, so its production skyrocketed. Today's idea of carbohydrate restriction in the paleo diet works because too much carbohydrate in total is consumed, not because no one should eat any carbohydrate. No new diabetes cases occurred during food rationing of WWII even though starch (as well as meat the paleo diet recommends) was still a foodstuff. Yes we are designed to eat meat, with pancreatic lipases and proteases to digest meat, and the Bible even says not to listen to those saying we're not supposed to eat any meat.

**Health for all:** It is time to return to being an organic Nation and to recognize that industrialization has its place but must be kept in its proper place, and that does not include the chemicalization of the human blood supply through water and air contamination, or the use of useless harmful drugs such as industrial fluoride taken internally and diabetic drugs, or the use of useful drugs in those who do not need them, such as statins necessary for health in victims born with hypercholesterolemia, but which in those with only slight cholesterol elevation that brain cholesterol can become depleted with drug use.

**Industrial Fluoride Toxicity.** Diabetics drink more water than normal so clean pristine fresh drinkng water without drugs should be used by diabetics. Water treated with industrial fluorosilicic acid for its fluoride causes 0.21 ppm of the ion in the blood (50% from the added drug and 35% from toothpaste, the rest from foods) but in diabetics consuming twice as much water average 0.42 ppm fluoride in the blood and accumulate fluoride to 4,000 mg/kg in bone permanently over the same years others accumulate fluoride to 2,000 mg/kg. Once bone levels exceed 3,000 mg/kg bone is weakend and more subject to fracture. The U.S. now has an endemic of hip fractures in

U.S. elderly with 1/3 million cases yearly, many perishing while wating for bone to heal that will never heal in the aged, being fluoridated. This is a National problem that contributes to bone weakening and other adverse pathology all from adding fluorosilicic acid into 70% of U.S. public water supplies.

Greater L.A. area began infusing industrial fluorides into all water suplies in 2007 which includes most of North County other than Poway and old Oceanside and Camp Pendleton, Escondido began in 2005, San Diego city began in 2011 at the time HHS suggested only the lowest range suggested by CDC dental officials be used at 0.7 ppm. This also adds 2-3 ppm sodium ion and 0.6 ppm silicic acid into water, and all three do not belong in normal pristine fresh drinking water. Teitz, Merck, Lohan, etc. list all normal constituents in the human bloodstream and of course do not have a listing for either fluoride or silicic acid because these are contaminants of the blood. Fluoride in fact is a listed toxic calcium chelator that binds calcium in all calcium-rich regions of the body and interferes with calcium homeostasis. Long-term consumption even in non-diabetics can lower thyroid function, produce slight iron deficiency anemia and lower IQ and degenerates intracellular organelles in brain cells after crossing the blood brain barrier and incorporates into atherosclerotic plaque in coronary arteries of cardiovascular disease patients (NRC, 2006, Yuxin, **Nuclear Med. Comm**, 2012).

Zero fluoride water is available from Glacier or Aquafill water RO machines outside grocery stores, or one can purchase distilled water or your own distiller and fortify it with minerals or a bone char filter or a home undersink RO of the modern type that has a pore size smaller than the diameter of the fluoride ionic sphere, or can haul water from Palomar Mountain Spring water or from Carlsbad alkaline water which both test zero fluoride.

Arsenic levels are increasing in National water supplies and soils due largely to the former use of arsenic insecticides sprayed on farmlands. Arsenic is a type class IA certain human carcinogen that accumulates under skin and causes lung and skin and other cancers. Schools built on such land have huge increases in cancer incidence in children and is a National problem (CDC, 2005). Lead is elevated by use of fluorosilicic acid infusions in public water and acts synergistically with arsenic as carcinogens. Aluminum is used in water supplies to remove dirt particles cheaply and is eliminated after ingestion except in water supplies that are fluoridated where the complexes are assimilated and incorporate into brain and bind the abnormal proteins present in Alzheimer's disease and may worsen this condition.

**Pollution.** As far as cancer is concerned, it is not only our water supplies that are being onslaughted but our air. Filthy nuclear fission reactors such as at San Onofre and around the country spew massive amounts of radionuclides into the air from vents that are simply too low in density as gaseous particles to be trapped with pollution scrubbers. The NRC and owners of these of course argue it is incidental and compares the exposure to that of a few chest X rays regularly, but there is no such comparison when particles are inhaled and can become long-term irradiating sources inside a person.