Smart Life Forum

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NEXT MEETING: Thursday, October 21, 2010, at 7pm

Robert H. Lustig, MD

on

The Fructose Epidemic

SHORT PRESENTATION before Dr. Lustig's talk:

Understanding the importance of basal metabolic rate.
by Steve Fowkes

Basal metabolic rate is the level of metabolism that is inherent in your cells. Low metabolic rate is associated with much pathology, and is widespread in our population. Low metabolism is commonly experienced as hypothyroid symptoms (cold hands and feet, a tendency towards constipation, sleeping problems, cognitive impairments, poor healing, low energy, lack of stamina, and below-normal body temperature. The early morning body temperature (taken immediately after waking, before any physical activity) is the best indication of low basal metabolism, next to whole body calorimetry. Whole body calorimeters are rare, difficult to calibrate, and psychologically challenging (they are coffin-sized to minimize air volume), but fortunately thermometers are readily available and support a self-care model. Early AM body temperature within 1 degree F of 98.6 is fine, but 1-2 degrees low is problematic, 2-3 degrees low can be serious, and 3-4 degrees low is usually deeply debilitating. Causes can be hormonal (lack of progesterone, testosterone, T3, T4, and cortisol, or too much estradiol and/or estrone), toxicity (pesticides and heavy metals), inflammatory (chronic infection, allergy, or delayed hypersensitivity), neuroendocrine (circadian phase maladaption, jet lag, unhappiness, chronic stress, spiritual disconnection, or light deficiency), or nutritional. Bring your questions.

FMBR (Foundation for Mind Being Research) next meeting:
Near Death Experiences, with a panel of three experienced experts:
Nadia McCaffrey, Yolaine Stout, and Ellie Schamber, Ph.D.
Friday, October 22, 7:30 pm, at Unity Palo Alto, 3391 Middlefield Rd.
See FMBR.org for more details.

Presentation Location:

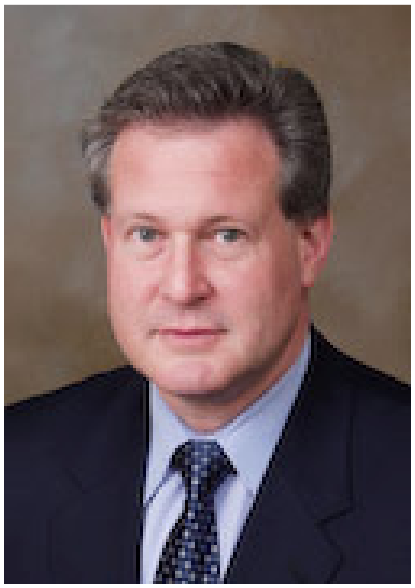
Cubberley Community Ctr.
Room H1

4000 Middlefield Rd.

Palo Alto, CA

In This Issue

Meet Robert H. Lustig, MD



Robert H. Lustig, M.D. is Professor of Pediatrics in the Division of Endocrinology at University of California, San Francisco, and Director of the Weight Assessment for Teen and Child Health (WATCH) Program at UCSF.

Dr. Lustig is a neuroendocrinologist, with basic and clinical training relative to hypothalamic development, anatomy, and function. Prior to coming to San Francisco in 2001, he worked at St. Jude Children's Research Hospital in Memphis, TN. There, he was charged with the endocrine care of many children whose hypothalami had been damaged by brain tumors, or subsequent surgery, radiation, or chemotherapy. Many patients who survived became massively obese. Dr. Lustig theorized that hypothalamic damage led to the inability to sense the hormone leptin, which in turn led to the starvation response. Since repairing the hypothalamus was not an option, he looked downstream, and noted that these patients had increased activity of the vagus nerve (a manifestation of starvation) which increased insulin secretion. By administering the insulin suppressive agent octreotide, he was able to get them to lose weight; but more remarkably, they started to exercise spontaneously. He then demonstrated the same phenomenon in obese adults without CNS lesions. The universality of these findings has enabled Dr. Lustig to weave these threads together into a novel unifying hypothesis regarding the etiology, prevention, and treatment of the current obesity epidemic. This has led him to explore the specific role of fructose (half of sucrose and high-fructose corn syrup) as a specific mediator of both chronic disease, and continued caloric consumption. His now notorious YouTube video, "Sugar – the bitter truth" continues its popularity with the lay public.

A native of Brooklyn, NY, Dr. Lustig went to Stuyvesant H.S. in Manhattan, graduated from MIT in 1976, and received his M.D. from Cornell University Medical College in 1980. He completed his pediatric residency at St. Louis Children's Hospital in 1983 and his clinical fellowship at UCSF in 1984. From there, he spent six years as a post-doctoral fellow and research associate in neuroendocrinology at The

Future Speakers:

November 18,
Michael Mayer, PhD, on Body Mind Healing

December 16, TBA

About Smart Life Forum

Smart Life Forum, Inc. is a 501(c)(3) California nonprofit corporation whose primary mission is to provide credible health education to the public with an emphasis on optimal wellness, anti-aging medicine, and longevity.

Annual memberships in Smart Life Forum, Inc. and charitable donations are tax deductible to the extent allowed by law. For information on how to join or make a donation, please visit our website: www.smartlifeforum.org.

For questions, please contact Mike Korek at (650) 941-3058.

Rockefeller University. He has been a faculty member at the University of Wisconsin-Madison, and the University of Tennessee, Memphis. Dr. Lustig has authored 85 peer-reviewed articles and 30 reviews. He has mentored 20 pediatric endocrine fellows, and trained numerous other allied health professionals. He provides endocrinologic support to several protocols of the Children's Oncology Group. He is the former Chairman of the *Ad hoc* Obesity Task Force of the Lawson Wilkins Pediatric Endocrine Society, a member of the Pediatric Obesity Practice Guidelines Subcommittee of The Endocrine Society, a member of the Obesity Task Force of the Endocrine Society, a member of the Pediatric Obesity Devices Committee of the U.S. Food and Drug Administration, and a member of the Steering Committee of the International Endocrine Alliance to Combat Obesity. He also consults for several childhood obesity advocacy groups.

Dr. Lustig lives in San Francisco with his wife and two daughters (ages 10 and 4). Spare time (what little there is) is spent cooking, theater-going, and traveling.

MAIN PRESENTATION

The Fructose Epidemic

By Robert H. Lustig, MD

The obesity epidemic shows no signs of relenting. There is now more obesity globally than there is malnutrition. Not only has the frequency increased, but the severity of obesity in terms of BMI distribution, the prevalence of co-morbidities, and the increases in frequency of bariatric surgery document that obesity is more severe as well. The incidence of obesity-related insulin resistance, and its spinoffs — metabolic syndrome, non-alcoholic fatty liver disease, and polycystic ovarian syndrome — continue to escalate. Worse yet, the greatest increase in prevalence is in the youngest members of society. The 2-5 year old demographic is experiencing the most rapid rise in obesity, and metabolic syndrome is even more frequent among obese children than it is for obese adults. We even have an epidemic of obese 6-month olds. Obesity is said to be an interaction between genetics and environment. Our genes haven't changed in 30 years, but our environment sure has. The obese 6-month old is the "exception that proves the rule". While it is easy to ascribe blame to our current

dietary and exercise practices, how does this explain the obese 6-month old? What follows is a brief discussion of the actual biochemical alterations that promote obesity, and a suggestion of the changes in the food environment we can make to halt this childhood obesity epidemic.

Insulin and obesity

Insulin is the energy storage hormone. What you don't burn, you store in fat tissue, under the influence of insulin. This is obvious to every physician who treats diabetic patients, as their weights increase with insulin. Things that make insulin go up cause energy storage, and things that make insulin go down promote energy burning. Insulin does three things which put it front and center in obesity physiology. 1) Insulin drives energy into fat for storage. 2) Insulin interferes with leptin signaling at the hypothalamus (the energy control center of the brain). This results in leptin resistance; which results in decreased sympathetic tone, reducing energy expenditure and physical activity; and increased vagal activity, which promotes further insulin secretion, appetite, and energy storage. 3) Insulin interferes with the clearance of dopamine in the nucleus accumbens (the reward center of the brain), thus increasing the reward of food. Thus, hyperinsulinemia turns the negative feedback system of energy balance into a positive feedback or "vicious cycle", promoting obesity. Externally, this appears as "gluttony and sloth", but it is biochemically driven.

How does this work? A thin, insulin sensitive, 13 year old might consume a daily allotment of 2000 kcal, and burn 2000 kcal daily in order to remain weight-stable, with a stable leptin level. However, if that same 13 year old became hyperinsulinemic and/or insulin resistant, perhaps as many as 250 kcal of his daily allotment would be shunted to storage in adipose tissue, promoting a persistent obligate weight gain. Due to the obligate energy storage, the child now only has 1750 kcal per day to burn. The hyperinsulinemia also results in a lower level of hypothalamic leptin signaling, conveying a central signal of energy insufficiency. The remaining calories available are lower than his energy expenditure; the hypothalamus would sense starvation. Through decreased sympathetic tone, he would reduce his physical activity; and through increased vagal tone, he would increase caloric intake and insulin secretion, but now at a much higher level. Furthermore, the insulin prevents the extinguishing of the reward pathway, promoting increased intake as well.

Where did the hyperinsulinemia come from?

At least 3 separate reasons for hyperinsulinemia in children can be discerned. 1) *Genetics:* children from certain racial and ethnic groups have increased insulin dynamics even prior to the development of obesity, which may predispose them to increased weight gain. 2) *Epigenetics:* the "fetal origins of adult disease" hypothesis states that those born small- and large-for-gestational age at birth are prone to developing obesity; both birth weight extremes are states of hyperinsulinemia and insulin resistance, which may worsen beyond the neonatal period. 3) *Our food environment:* our current Western food environment is highly insulinogenic, as demonstrated by its increased energy density, high fat content, high glycemic index, decreased fiber, and decreased dairy content. But in particular, the monosaccharide fructose appears to be a cornerstone of the obesity epidemic, through its effects on insulin.

Fructose and insulin

The primary stimulus to insulin release at the pancreas is glucose; found in all forms of carbohydrate (refined starch, legumes). Carbohydrate intake increases insulin release and increases weight gain. However, the other insulin-promoting nutrient is fructose, found in sugar. Fructose does not stimulate insulin directly, but rather promotes insulin resistance.

The most commonly used sweetener in the U.S. diet is the disaccharide sucrose (e.g. table sugar), which contains 50% fructose and 50% glucose. However, in North America and other countries, non-diet soft drinks are sweetened with high-fructose corn syrup (HFCS), which contains up to 55% of the monosaccharide fructose. Thanks to its abundance, sweetness, and low price, HFCS has become the most common sweetener used in processed foods. HFCS is found in processed foods ranging from soft drinks and candy bars to crackers to hot dog buns to ketchup. It's not that HFCS is biologically more ominous than sucrose; it's that its low cost has made it available to everyone, especially low socioeconomic groups. Fructose is fructose, whatever its source. Average daily fructose consumption has doubled over the past 30 years, and increased 6-fold in the past century. The growing dependence on fructose in the Western diet may be fueling the obesity and T2DM (Type 2 Diabetes Mellitus) epidemics.

Both animal and human studies demonstrate that high-fructose diets lead to increased energy intake, decreased resting energy expenditure, excess fat deposition, and insulin resistance. **The hepatic metabolism of fructose differs significantly from glucose, clearly illustrating the point that all calories are not the same.**

The Biochemistry of Fructose Metabolism

Fructose is absorbed in the intestine and enters the liver without insulin regulation. There, fructose is converted to fructose-1-phosphate (F1P), consuming ATP (adenosine tri-phosphate, "molecular unit of currency" of intracellular energy transfer) and increasing the formation of uric acid, which suppresses the action of nitric oxide on vascular smooth muscle and promotes hypertension.

F1P enters the glycolytic pathway without regulation. This leads to an accumulation of xylulose-5-phosphate, which stimulates the process of de novo (new) lipogenesis, increasing VLDL production, which promotes atherogenesis. The glycolysis of fructose ultimately leads to an over-accumulation of acetyl-CoA in the hepatocyte, some of which cannot be metabolized through the Krebs cycle; therefore it is then reassembled into free fatty acids (which promote pancreatic insulin hypersecretion) and triglycerides (some of which precipitate in the liver and cause hepatic insulin resistance and non-alcoholic steatohepatitis).

The Krebs cycle takes place in the mitochondria and is part of a metabolic pathway involved in the chemical conversion of carbohydrates, fats and proteins into carbon dioxide and water to generate a form of usable energy

Fructose also does not suppress secretion of the so-called "hunger hormone" ghrelin, levels of which correlate with perceived hunger. Finally, fructose has both direct and indirect effects (through insulin), which activate the reward pathway to foment increased consumption, similar to the process of addiction.

In sum, fructose consumption has metabolic and hormonal consequences different from glucose that facilitates development of obesity and the complications of the Metabolic Syndrome. The highest fructose

loads are soda (1.7 gm/oz) and juice (1.8 gm/oz).

What can be done?

As you can see, if our food supply has been adulterated, obesity becomes a public health issue, not a personal responsibility issue. This is going to take an exceptional policy effort addressing the food environment, and will take parent, school, community leader, physician, food industry, and politician education and action. But in the meantime, here are some suggestions.

1) Remove ALL sugar sweetened beverages from schools and school lunches. Juice, sports drinks, and even chocolate milk are as dangerous as soda.
2) Restrict marketing of ANY AND ALL fructose-containing foods to children.
3) Provide parent education at various medical interaction points; e.g. prenatally, at birth, and at doctor office visits.
4) Consider legislation that subsidizes fresh fruit and vegetable (endogenous fructose) consumption; while taxing the consumption of fructose-added foods.
5) Change WIC (Women, Infants Children welfare program) rules so that fresh fruits are covered and juices are not.
6) The Food and Drug Administration has given fructose GRAS (generally regarded as safe) status, allowing the food industry to add as much as they want to our food. This designation must be repealed.
7) Most importantly, repeal the corn subsidy. This will prevent price distortion, and increase the price of sugar, which will naturally reduce both addition to foods, and its consumption.

There are many other ways to impact the childhood obesity epidemic, working on the energy expenditure side of the argument. But until our food supply is de-fructosified, don't expect the obesity epidemic to go away.