

THE NO CANDY MAN

US endocrinologist Robert Lustig is on a crusade against sugar. He talks to **Balaji Ravichandran** about why he believes we are getting fatter and how he hopes to start tackling the sugar industry



A man who declares that sugar is a toxin in the same league as cocaine and alcohol, and one that must be regulated in the same manner as tobacco, is apt to draw public attention. But Robert Lustig, professor of clinical paediatrics at the University of California, San Francisco, is not camera shy. Indeed, he revels in the attention, even when it is not always flattering. Where other academics might feel uncomfortable, he exploits his fame to full effect. For example, at a recent symposium in London he argued that sugar was an addictive and dangerous substance, singularly responsible for the soaring rates of obesity and diabetes around the world. He began his speech with a quotation from Gandhi and concluded by declaring a war against the sugar industry. The audience responded with rapture and enthusiasm.

Lustig, a paediatric endocrinologist specialising in neuroendocrinology, owes his fame predominantly to a lecture, posted on YouTube, entitled “Sugar: The Bitter Truth” (www.youtube.com/watch?v=dBnniua6-oM). At the time of writing, it had had more than 3.3 million views. Not bad for a 90 minute lecture, the bulk of which is devoted to complex biochemical reactions that happen in the liver. But Lustig is an engaging and passionate speaker, prone to rhetorical flourishes and dramatic pronouncements, which keeps his audience, virtual and real, interested.

Lustig believes that the advice we have received from doctors and nutritionists over the past 40 years—that, in order to lose weight and keep obesity and diabetes at bay, you must eat less and exercise more—is wrong. Although he says that the first law of thermodynamics—that energy can neither be created nor be destroyed—is indeed sacrosanct, what matters is how we interpret the law. The standard interpretation is that “a calorie is a calorie,” and so, if we eat more calories than we expend, that excess will be stored as fat. But, there is another way to view it, Lustig argues. Things that make your energy expenditure go up, such as exercise and caffeine, make for higher quality of life, whereas those that lower energy expenditure, such as hypothyroidism and starvation, make us feel lousy. So, he says, we could say that our body interprets energy storage in terms of how much it expects to burn in the future.

However, he believes that both storage and expenditure are outside our control and are instead subject to regulation by biochemical processes. In other words, our interpretation of thermodynamics has reversed the cause and effect. Our behaviour has no say in the biological mechanisms that lead to obesity and metabolic syndrome. Rather, our behaviour is determined and regulated by biochemistry. Sloth and gluttony, he says, are merely symptoms of a deeper disorder, not the cause.

Importance of insulin

So why do we get fat? Lustig’s answer, described in some detail in his book *Fat Chance*, effectively comes down to two words: insulin and sugar. Insulin is the primary regulator of energy storage in the body, and it is the only hormone in the body that directs liver cells to synthesise fat from glucose and to store it in various repositories around the body, especially as visceral fat. Indeed, Lustig has argued that researchers and the media are somewhat distracted by the question of obesity, when in fact they should be paying attention to metabolic syndrome.

People of normal weight with symptoms of the metabolic syndrome far outnumber those who are overweight or obese but are metabolically healthy, he says. And the best way to define metabolic syndrome is not symptomatically, as it varies from person to person, but mechanistically. The various manifestations of metabolic syndrome all have one thing in common, he says: insulin resistance. Add leptin resistance to the recipe, and we have obesity, he argues. Leptin, a hormone synthesised by fat cells, signals satiety, and acts on the hypothalamus to control appetite and feeding behaviour. The brain interprets low levels of leptin as starvation and promotes feeding behaviour. In obese people, although the serum leptin levels are high, Lustig says, the brain is unable to recognise them and so it promotes further eating, as if it were starving.



PAUL CHINNISAN FRANCISCO CHRONICLE/POLARIS/REXUS

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So, anything that drives high levels of insulin secretion would direct the regulatory systems of the body, especially the liver, to promote synthesis and accumulation of fat, rather than shunt the available calories towards other activities of the body. But, he says, insulin also blocks the action of leptin in the hypothalamus, which in turn means that the brain continues to perceive the body as starving, inducing overeating. These, therefore, are the biochemical determinants of sloth and gluttony. While the body can cope with this for a while, the regulatory mechanisms soon break, and the feedback loop becomes a vicious cycle.

Dangers of fructose

This is where sugar and refined or processed carbohydrates enter the picture, says Lustig. Being devoid of fibre (and other nutrients), they are absorbed rapidly in the gut, and elicit large insulin spikes from the pancreas, setting in motion an obesogenic cascade. However, Lustig believes

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sugar is uniquely toxic, and much more dangerous than the refined starch found in white rice or bread. Sugar is usually consumed in the form of sucrose, composed of a molecule of glucose and fructose, or, especially in the United States, high fructose corn syrup, which usually contains about 55% fructose and 42% glucose. In addition to the insulin spikes, fructose, he says, is metabolised differently from glucose and is converted into fats that end up creating lipid droplets in the liver, which either create fatty liver or are shunted to visceral fat.

In his address to a London symposium organised by the charity Food and Behaviour Research last month, Lustig gave more detail on why he thinks fructose is so toxic.¹ He refuted the idea that it was metabolised in the same way as glucose, claiming that the five member furan ring of fructose is inherently unstable and binds to proteins more readily than glucose does. This, he said, tags proteins for self destruction, which clears insulin receptors in the liver, inducing insulin resistance. The destruction of proteins in turn releases reactive oxygen species implicated in cellular ageing and metabolic syndrome. Furthermore, he argued, fructose is what makes sugar and fruits sweet, and so it is also the molecule implicated in our addiction to sweet foods. Sugar, he said, is weakly addictive, like alcohol, and shares the same reward pathways in the brain as nicotine and cocaine.

Opposition

Lustig is a compelling proponent of his arguments, but how do academic researchers receive his ideas? Although there was some disagreement at the London symposium, Lustig says that scientists worldwide have been extremely supportive. Those who haven't received his ideas well are standard nutritionists and those who believe that all calories are equal. "I think it depends on how you were raised, how you were trained," he says. He claims to have once believed the same, but his research among children, especially into hypothalamic obesity, has convinced him otherwise. After all, he asks, how can you attribute sloth and gluttony to an obese six month old?

Lustig says that the main opposition to his arguments comes from the sugar and food industries. The bulk of his Wikipedia entry is devoted to what are described as controversies over his views on sugar and fructose. However, nearly two thirds of the studies cited there to repudiate

Lustig's views were funded by Coca Cola, and the remainder were supported by other organisations with close ties to the food industry. Was he surprised? "It doesn't shock me," he says.

In fact, Lustig believes that most of the opposition to his work comes from the sugar industry, and he says that the techniques it uses are remarkably similar to those used by the tobacco industry 50 years ago. Of these, the most insidious, he said, was to cast doubt on the strength of the evidence already accrued. The sugar industry is quick to dismiss anti-sugar findings because of lack of robustness, but ethical, financial, and temporal constraints mean that the gold standard of research—meta-analyses and randomised controlled trials—is not always possible, he says.

So, would he like to see sugar banned? "No. Absolutely not. [Instead,] make it a little harder to get," he said, as with alcohol or tobacco. He also wants the added sugars found in 80% of the American food supply to be removed. Should the sale of sugar be restricted to those over a certain age, just as with alcohol and tobacco. "Yes, absolutely. Why not?" he responded, enthusiastically.

Lustig has recently taken a sabbatical from his clinical work and enrolled as a graduate student in a law school for a year. Given the close ties between the US government and the food industry, he does not hold out much hope for political intervention, nor for regulation of the food industry. The best way forward, he says, is through the courts. Here, he returns to the analogy between sugar and tobacco and wonders whether we could do for metabolic syndrome what we did for lung cancer. "I am not going to sue," he insists. "I am just going to help the lawyers." What legal measures did he envisage as necessary to take on the food industry and reduce our addiction to sugar? "Well, let's put it this way," he says with a knowing smile. "I don't want to tell them what we're planning... Let's just say it's coming."

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Listen to the podcast of the interview at www.bmj.com/podcast/2013/03/15/are-all-calories-equal

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¹ Ravichandran B. Sugar is the new tobacco. 13 March, 2013. <http://blogs.bmj.com/bmj/2013/03/15/balaji-ravichandran-sugar-is-the-new-tobacco/>.

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