**SESSION III: THE CHALLENGE OF OVER-NUTRITION AND OBESITY**
October 14, 2005 - 9:00 a.m. to Noon
The Challenge of Over-Nutrition and Obesity

**DR. DAVID LUDWIG**
Director, Obesity Program
Children's Hospital Boston
Associate Professor, Harvard Medical School

Thank you, Dr. Woteki and Dr. Quinn. Again, it's a great honor to be here today. Perhaps one of the most controversial and provocative notions in popular nutrition today is depicted by this cover story in *Time* magazine recently, which asked the question – Should we be eating low-fat, high-carbohydrate diets or high-fat, low-carbohydrate diets?

Billion-dollar food industries have come, and in some cases gone, based on these diet fads. Well, Dr. Willett had summarized the data relating to dietary fat and body weight, so I'd like to begin with a historical overview of dietary carbohydrate.

For most of the last century, carbohydrates have been characterized according to saccharide chain length into the categories simple sugars, single units or short chains and complex carbohydrate, or starch, which is simply a polymer glucose. In fact, this is one of the two main design principles in addition to the overall preference for carbohydrate over fat that went into the first iteration of the Food Guide Pyramid. Among carbohydrates, sugars were said to be inherently unhealthful and should be consumed sparingly. Whereas starchy foods were said to be really the base of our nutrition and should be consumed in abundance. So up to earlier this year, this teaching tool recommended up to 11 servings of starchy food per day for Americans.

This notion has been questioned for more than a quarter century. Back in 1978, Walquist, an Australian, reported that consumption of glucose or starch produced identical changes in blood glucose and insulin levels – similar findings in the *New England Journal of Medicine* a decade level. Paradoxical. It's saying that you could eat a bowl of Wheaties with no added sugar or a bowl of sugar, while they may taste different, they're biologically going to do the same thing to our blood sugar or insulin and our metabolism. How do we explain this paradoxical finding.

Let's have a look at what happens after consumption of an unprocessed grain product. The digestive enzymes beginning in the mouth, but more powerfully from the pancreatic enzymes in the small intestines, have to work their way through the intact grain structure and then through the fiber before getting to this starchy endosperm. Of course, most grain products consumed in the United States are not unprocessed; they're highly processed, in which the grain kernel has been milled into a fine, particulate flour and the fiber stripped away, leaving this denatured starch molecule. Now digestive enzymes have rapid access to these highly susceptible bonds, rapidly digesting them into a concentrated solution of glucose in the digestive tract. Thus, for this reason the distinction between simple sugar and complex carbohydrate has little if any biological significance.

If that's the case, are all carbohydrates alike? Or might there be a better system for classifying them? In 1981, David Jenkins as the University of Toronto and colleagues proposed the glycemic index for this purpose, which is an empirical system for classifying carbohydrate quality not based on a theoretical physiochemical notion like chain length, but something that's actually measured. It's defined a the area under the glucose curve after eating a controlled amount of a test food, divided by the area under the curve after eating a controlled amount of a controlled food.

So for reasons just discussed, the refined starchy foods – white bread, prepared breakfast cereals, potato products and most rice preparations – have glycemic indices equal or higher to that of table sugar. Whereas, fruits, vegetables, unprocessed grain products, legumes have a much lower glycemic index, carbohydrate calorie for carbohydrate calorie.

A related term proposed by Dr. Willett's group in the 1990s, glycemic load, takes into account the fact that we all don't eat 50-gram identical portions of carbohydrates. So it's in effect the average glycemic index multiplied by the amount of carbohydrate consumed.

And this slide shows some representative values for glycemic index and glycemic load from the refined starchy foods at the top to the less-refined grain products down through fruits and then nonstarchy vegetables at the bottom, which are in fact too low to even be measured. Note that there's a very wide range, a log order or more in the case of glycemic load, through which these foods can be distributed. So if these principles do have relevance to biology, to body weight regulation, there's a really large window through which these dietary factors could operate.

Does glycemic index or glycemic load effect appetite in the short term? To begin to look at this issue, we studied three meals with identical calories, differing in glycemic index or load. The high glycemic index meal was instant oatmeal with a little milk and sugar, 64% carbohydrate, 20% fat – perfectly consistent with previous recommendations to eat a high complex carbohydrate, low-fat meal.

The medium glycemic meal had virtually identical foods, same macronutrients, same energy density, but the oats were less processed. They are steel-cut, sometimes marketed as McCann's Oatmeal. This was the kind of oatmeal that grandmother ate and unfortunately very few people have the time anymore to cook oatmeal for 30 minutes. But because it takes longer to cook, it also takes longer to digest and thus has this slower impact on blood sugar.

And a third meal that we included for comparative purposes was a vegetable omelet with fruit that had less carbohydrate and more fat.

This slide shows that, as expected, blood glucose was highest after the instant oatmeal, in yellow, compared to the steel-cut oats, magenta, or the vegetable omelet, in green. But note that, while initially being higher, blood sugar fell rapidly and then into a relatively low range after the instant oatmeal, the high glycemic meal. The difference in conventional terms was 10 milligrams per deciliter, which could be clinically significant. It was also statistically significant.

And notice that what happened as blood sugar dropped. The stress hormone, epinephrine, or adrenalin, which responds it to stress but importantly low blood sugar, surged to very high levels, only after the instant oatmeal, the high glycemic meal – suggesting that that drop-off in blood

sugar was a true metabolic stress. And how does an individual with blood sugar dropping fast enough to cause stress hormones to be secreted feel? Probably if you're a ten-year-old child, you might not be – after that bagel with fat-free cream cheese for breakfast – you might not be sitting quietly and concentrating in the classroom. But for many of us, low blood sugar is a potent stimulus for hunger. When we gave subjects free access to food in the second meal, they consumed six or seven hundred calories more after the high glycemic meal than after the medium or low.

Now, admittedly, this is just a one-day study. But if only a fraction of this difference were maintained meal after meal, day after day, it might explain some of the increased weight gain as observed, as you heard from previous speakers, as the carbohydrate intake of our diet has increased. But more importantly, the processing of that carbohydrate is increased, so the glycemic impact has really gone up, has really skyrocketed.

Our findings are consistent with most of the other studies published in the literature in which macronutrient controlled low and high glycemic index meals have been compared. Seven of twelve found statistically significant, greater food intake after the high than after the low glycemic meal. Two showed a trend in the same direction, two showed no difference, one showed a nonsignificant trend in the other direction.

What about the other end of the energy balance equation? We talked about how food intake, appetite might be affected. But could diet affect energy expenditure? One obvious way might be if we're feeling better and more likely to get off of the couch and exercise, we could. What we are looking at in this study relates to resting energy expenditure and metabolic rate. The background for this is as follows.

The poor, long-term outcome of conventional diets has given rise to a notion of a body weight set point or more recently termed "settling point" or "settling range." According to this notion, changes in body weight elicit physiological adaptations that antagonize further weight change. This is a scientific way of putting a very commonly observed notion that as we lose weight, it's harder and harder to keep it off. And it's reflected in most of the long-term data that anybody can lose weight for a few months, but almost nobody can keep that weight off on conventional diets for the long term.

Rudy Leibel and colleagues took weight-stable individuals who were overweight or normal weight and brought their weight down by 10%. And they found that their resting energy expenditure, metabolic rate, decreased by more than would be expected by the weight loss. So that our motor is functioning more efficiently, we're holding onto those calories more. And that's going to fight weight loss.

Genetic factors are thought to specified the so-called body weight setpoint, but that's a pretty dispiriting notion, isn't it, that if you have genes that are set somewhere in the obese range, everything that you can do to lose weight is going to ultimately bump up against this ironclad weight, and sooner or later metabolism is going to win out over our mind. Of course, it can't be that simple, otherwise how do we explain the rising body mass index among genetically stable populations.

So to look at this question with regard to glycemic index, we conducted a study modeled after that of Dr. Leibel in which we looked at young adults who had been weight stable and brought their weight down by 10%, by feeding them everything that they ate for about 10 weeks, on one of two diets – either a low glycemic load higher-fat diet, or a conventional, low-fat, higher glycemic load diet. And then we measured their resting energy expenditure, and we measured the body composition. I'll point out that their body composition didn't change between groups. Everybody lost the same amount of weight, and they lost the same amount of lean tissue and fat tissue.

So this slide shows what happened to metabolic rate with weight loss. Those in the low-fat, high-glycemic group showed a decrease in their metabolic rate of 175 calories approximately per day, consistent with other findings in the literature. At the same degree of weight loss, those in the low glycemic group showed a lesser decline in their metabolic rate. In other words, their metabolism was operating at about 80 calories per day faster.

Now, that's not a big enough change to explain some of the claims by popular diets, popular low-carb diets – that you can keep eating the same amount of food and through a magical metabolic switch, the fat will melt off. Eighty calories per day is really less than one pound per month. Over a year or many years, it could add up if these changes were persistent.

But perhaps more importantly, it suggests that the body is under less metabolic stress during weight loss on a diet that doesn't raise blood sugar and insulin levels as much. We have better access to our stored fuel. The brain doesn't perceive the same deprivation. Metabolic rate doesn't fall as much. You may be feeling less cold, tired and hungry. And the bottom line is, you may be less likely to fall off the diet.

I'll just point out that we looked at a range of cardiovascular disease risk factors on this low glycemic load diet that was not only higher in fat but also higher in saturated fat and higher in salt and higher in cholesterol. And in most cases, the low glycemic load diet showed greater improvements in heart disease risk factors, including blood pressure than the conventionally recommended low-fat diet.

How about over the long term? Unfortunately, there are yet no large-scale, well-controlled multicenter studies addressing this point. But thee are some short-term or observational studies, or some pilot studies.

Earlier this year, my colleagues looked at the diets of 500 adults in Massachusetts and found that BMI was directly associated with glycemic index in both cross-sectional and longitudinal analysis. An increase of .75 BMI units with every 5% increase in glycemic index. And diets can range by much more than 5%. So this is potentially a very large effect. By comparison, BMI was not associated with the macronutrients – didn't matter how much carbohydrate you were eating; the quality of the carbohydrate mattered in this study.

Slabber did a three-month parallel, cross-over design study with 15 obese females, basically telling subjects to exchange low and high glycemic index foods on an out-patient basis. So it's a real-life setting. And the bottom line here is that body weight increased significantly more during the low glycemic than the high glycemic treatment.

We conducted a 12-month pilot study with arguably the most difficult group of subjects ever to study in the history of clinical research – obese adolescents. I can assure you that they don't want to be listening to doctors in white coats telling them what to eat. This was designed to be, again, a real-life study, not a feeding study. We randomly assigned them to either low fat or low glycemic diets and instructed them and their parents in how to put this into effect in their own life. And we tried to be fair in that we controlled treatment intensity, behavioral approaches and physical activity prescriptions between groups. And we measured diet changes, using food records. We had one dropout per group.

Can obese adolescents make these changes in a real-life changes in a real-life setting? Our process measures suggest yes. Those in the low glycemic load group showed a significant decrease in glycemic load. Those in the reduced fat group showed a significant decrease in dietary fat.

And how did this translate into a hard endpoint, well, at least in terms of BMI? This slide shows the change in BMI over the 12 months of the study. By way of theoretical comparison, an adolescent who is overweight would show a one to two BMI unit increase over a year without intervention. So the low-fat group arguably did better than that, stabilizing their body composition. Whereas the low glycemic group did even better than that at two BMI unit improvement with no evidence of weight regain from six to twelve months, as is characteristic of long-term studies. Though I do want to emphasize this is of course a small pilot study.

There's one negative study, a ten-week study by a Danish group. Comparing low and high glycemic index diets on an out-patient basis, they report no difference in body weight; however, body weight appears to be decreasing at a faster rate in the low glycemic index group. So with the study not to be ten weeks but conducted over a year or more, perhaps this negative study would actually have shown a significant difference.

Now, can these effects be attributed specifically to glycemic index or load? Clearly not. Anytime one dietary factor is changed on an out-patient basis, other factors will change that can be measured, or factors that we don't even know how to measure well, such as palatability. From a public health standpoint, it arguably doesn't matter. Because for example, if you told somebody to eat whatever they wanted as long as they were wearing an orange shirt, and people were able to do that and lose weight and be happy about it and reduce their long-term risk factors, we'd have a public health intervention to apply. But from a scientific perspective, it remains unresolved.

So we went back to the basic laboratory to a species whose diets we can control meticulously, and that was in this case mice and rats. I'm showing you data from the rats. We gave them identical diets, differing only in glycemic index, and we further controlled… We did a controlled feeding, in which we kept their weights identical through 18 weeks. So even if one group wanted to eat more, it wouldn't have been able to.

At the end of 18 weeks, the two groups weighed virtually the same, one gram difference. The high glycemic group, however, had 70% more body fat, but since they were the same weight, they had a commensurate reduction in lean tissue. And the results were quite visually dramatic. I'll just show one graphic slide. These are two weight-matched animals. The low glycemic

animal had very little visceral fat. The high glycemic index animal at the same weight, it's visceral really could not be visualized because of the massive amount of visceral anapestic.

How about diabetes? If blood sugar rises higher – it might, three or four times a day with each meal or snack – it would put more stress on beta cells. And if those beta cells in the pancreas have been compromised by obesity, a sedentary lifestyle or genetic factors, it could conceivably push the individual over the precipice into diabetes.

And I'll just summarize one of several studies, the Nurses' Health Study that provides support for this notion. After controlling for body mass index, those in the highest quintile of glycemic index had a 37% greater risk for developing type 2 diabetes than those in the lowest category. And in terms of heart disease from the study, those in the highest quintile of glycemic load had a twofold greater relative risk of having heart attack. Put the other way, those in the lowest quintile, 20%, had a 50% reduction in heard disease risk.

Now if we had a drug that could reduce heart attack risk by 50%, it would be a blockbuster. You'd see it on the front page of *Time* magazine, the stock would be worth many billions of dollars. Perhaps three or five years later it would be taken off the market because of life-threatening complications. But what if we had a dietary factor that can do this in a tasty way?

Just a brief report on cancer – there are many studies now, over a dozen, that link glycemic index or load to increased risk for breast cancer, prostate cancer, colorectal cancer, pancreatic cancer, and gastric cancer. This is just one of several studies showing an 87% increased risk of breast cancer in the highest versus lowest category took place in the index. And this may relate to the increased amounts of insulin that are produced, insulin which can stimulate cell growth and proliferation, maybe a causal link there.

Now, the notion of glycemic index is arguably taken to an extreme in a very common dietary pattern today that might be called "fast food and soda, American style." These foods are commonly believed to be high in fat, and in a gram amount they are. But they're actually much higher in refined carbohydrate than fat. Of course, the soda here is a hundred percent high glycemic carbohydrate. The potatoes, the cookies, the bun. The main ingredients in the catsup is probably sugar. And if that weren't enough, it's got the worst of almost every imaginable dietary factor – massive sizes, a sort of a primordial palatability appealing to our infantile preferences for sugar, salt and fat, high energy density, transfats, low fiber, low micronutrients. The list goes on and on.

We looked at 3,000 young adults over a 15-year period and found that individuals in the highest third of fast food intake gained an extra ten pounds compared to those in the lowest third, and that insulin resistance increased twice as fast in that category, the highest category, after controlling for confounding factors.

And with regard to soft drinks, we looked at 500 middle school children in Cambridge, Massachusetts. For every additional serving of soft drink consumed a day, the risk of becoming obese increased by 60%, even after controlling for other factors that might affect body weight such as the dietary factors, exercise and socioeconomic factors.

So what is the optimal diet for the prevention and treatment of obesity and related diseases? Clearly, much more research is needed in this area. And there may be no single optimal dietary prescription for everybody, as recent research has suggested. Interesting genotype nutrient, genotype interactions, which deserve much more attention.

But the original Food Guide Pyramid with its emphasis on reducing fat and increasing carbohydrate, without regard to carbohydrate quality, is potentially high glycemic index. And a current pyramid, My Pyramid, might arguably be an improvement. Some of the low-fat message still carries over. And many of these foods are potentially very high in glycemic index.

And another concern that I have is that we've lost a public health focus on what we should be eating less of. So if there's ambiguity here, the results, when translated by certain aspects of the industry, can wind up being a hormonal nightmare.

The low-fat Twinkie has been marketed as a health food. It's in reality no different than an oral glucose tolerance test. An alternative low glycemic pyramid would look something like this: Abundant quantities of fruits, vegetables, nuts and legumes, adequate amounts of protein, which could certainly be vegetarian protein. There probably aren't enough animals in the world to feed six billion of us. I think oils can be used liberally. At least there doesn't need to be a focus on reducing oils more than any other contributor to calories. As long as they're healthful oils, they can actually increase the palatability of the vegetables, which we are clearly not eating enough of. Grains, in their least processed state possible. Fine to have the occasional white rice or bagel or breakfast cereal, but let's try to do that as part of an otherwise well-balanced meal.

And these recommendations, I would argue, are compatible with – we could call this a low-energy density diet. We could call it a high fiber diet.

Finally, low-fat diets, as practiced in the United States have not been very effective, and they have adverse effects on serum lipids, oftentimes. Low-carb diets, at least according to the recent studies, do cause more weight loss at six months, but by twelve months so much weight regain has occurred that they're no longer significantly different. How long can you go on eating a bacon double cheeseburger and "hold the bun, thank you." Their long-term risks, especially with children, are unknown. Thus, a low glycemic diet might be a perfect compromise. It allows quite a lot of flexibility in macronutrients. You can eat low fat if you prefer. If you do, it would be especially important to lower the glycemic index of all that extra carbohydrate to avoid the increase in hunger and the adverse effects on triglycerides.

I'd say that it probably operations by the same principles as a low carbohydrate diet, but it can do so in a more sophisticated way, without eliminating carbohydrate entirely. In fact, we can eat from the abundance of nature, as long as adequate attention is paid to the quality of those carbohydrates.

And if I have two minutes left, I'd like to come back to a political issue that's been raised in various ways through this conference. And that is that the best diet, as many speakers have said, will have little practical impact unless measures have been taken to address what Kelly Burnell has termed "the toxic environment" that places private profit across a range of societal interests over public health.

For example, each year $12 billion is spent to influence the eating habits of children overwhelming for high-calorie, low-quality products. Marketing campaigns specifically target children, linking brand names with toys, games, movies, etc., etc. The food industry has extensive political influence, close relationships with scientists, ties to professional associations. And might this produce a coercive effect on nutritional policy?

Fast foods and soft drinks pervade all aspects of society, and I have to say children's hospitals are no exception. There are fast food outlets in the lobbies of top children's hospitals in the country.

So I'd offer a common-sense approach. This will clearly be controversial, and we would each perhaps come up with our own list. I would begin in the home. Set aside time for family meals. There is a growing body of research suggesting the beneficial effects of this. It may be just one meal where the parents could control the nutritional quality for their children. And limit TV viewing. This, limiting TV viewing may not act through altering physical activity levels. It's a sad comment, but American children are so inactive that watching television doesn't really make them a whole lot less active.

The main effect – and there are research studies that are in press or published already that make this point – that the main effect may be that television viewing is acting through the food commercials by altering food habits in children, decreasing the quality of food choices, not just at that point in time but establishing these food habits that then last a lifetime. There are very interesting data published in The Lancet a couple years ago from New Zealand that make this point.

In terms of media, I would argue for a ban on food advertisements to children, as consistent with the American Academy of Pediatrics recommendations and American Psychological Association recommendations.

Tax fast food and sugar-sweetened soft drinks, subsidize fruits and vegetables. This is a very controversial notion, but we're in fact doing the opposite right now. We are subsidizing junk foods. The farm subsidies bills, which give over a hundred billion dollars a year per decade overwhelmingly for commodities with relatively low nutrient quality –corn for high fructose corn syrup, wheat, predominantly for these highly processed snack foods. And so it makes these already cheap foods that are inherently of low quality even cheaper and making the fruits and vegetables relatively more expensive. If anything, let's level the playing field. If we are to give an advantage to one food product, let's choose that from a public health perspective.

Schools, these points have been made by others. And lastly, improve reimbursement for obesity prevention treatment.