

INTERVIEW

Diet, the Glycemic Index and Type 2 diabetes: the past and the future



Dr David J Jenkins* speaks to Sarah Jones, Commissioning Editor: Educated at Oxford University (Oxford, UK), Dr Jenkins is currently a professor in both the Departments of Nutritional Sciences and Medicine, Faculty of Medicine, University of Toronto (ON, Canada), a staff physician in the Division of Endocrinology and Metabolism, the Director of the Clinical Nutrition and Risk Factor Modification Center, and a Scientist in the Li Ka Shing Knowledge Institute of St. Michael's Hospital (ON, Canada). He has served on committees in Canada and the

USA that have formulated nutritional guidelines for the treatment of diabetes and recommendations for fiber and macronutrient intake for the general population under the joint USA–Canada DRI system (RDAs) of the National Academy of Sciences (DC, USA). His team was the first to define and explore the concept of the glycemic index of foods and demonstrate the breadth of metabolic effects of viscous soluble fiber, including blood glucose and cholesterol lowering. His studies on combining cholesterol-lowering food components (dietary portfolio) have been recognized as creating an effective dietary alternative to drug therapy (statins) for many people and was the only dietary approach referenced in 2004 Guidelines update of the US National Cholesterol Education Program (ATP III) and the Canadian Cardiovascular Society (CCS) guidelines for 2012. He has received many National and International awards in recognition of his contribution to nutrition research. He believes in the value of plant-based diets but that a major effort is required to mount large studies to determine their health benefits. He believes that overall diets have to be environmentally sustainable.

Q Could you summarize your scientific career so far & explain what led you to the field of diabetes?

For my research career I owe a great debt of gratitude to Dr Dennis Shirley Parsons, my tutor and mentor (Merton College Oxford, Oxford, UK). After an early interview with him, where I said that research was my goal, he ensured that I obtained College entrance and satisfied university requirements for medicine, a major achievement considering that I had (have) no mathematical ability and had a habit of failing physics exams. He on the other hand was a physician, biologist and mathematician and said that he would regard my education as a significant challenge to teach me concepts rather than mathematical formulae. The environment was rich, Hans Krebs taught us biochemistry and Eric Newsholme had just arrived from Phillip Randle's group in Cambridge bringing with him the very fresh concepts of the glucose fatty acid cycle with implications for diabetes etiology and treatment. In that environment it is not surprising that many of us developed an interest in diabetes research. As an undergraduate Dennis Parsons encouraged me to construct my own research projects and Dan Cunningham in human physiology allowed me to use the University physiology laboratory facilities. I was

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further encouraged by Dennis to publish our results in the *Lancet* showing that nicotinic acid suppressed free fatty acids release and acutely improved glucose tolerance. Dan Cunningham then said that I should break my medical studies to undertake a PhD (D. Phil). I agreed, under some duress since I wanted first to finish my clinical training. During my research I had the good fortune to be advised by an informal group including Dennis, Eric and Dan (there were no formal advisory committees, in fact very little red tape in general). My thesis was on FFA metabolism, diabetes and CHD risk with a dietary component influenced by Bob Goode a fellow PhD student who had previously been looking at vegetarian diets and CHD risk for his MSc in Toronto (ON, Canada). This dietary interest continued through my clinical years during which I was immensely impressed by Francis Avery Jones, perhaps the father of British Gastroenterology, who also acted as a mentor and after I had qualified in medicine offered me a fellowship in his MRC clinical gastroenterology unit and later as a clinical scientist; as such I was funded to assess the effects of dietary fiber. The diabetes, gastrointestinal absorption and dietary fiber interests therefore come together with those of additional mentors, including Denis Burkitt, Hugh Trowell and later Richard Doll (of smoking and lung cancer fame) who together had convinced the British MRC to invest in dietary fiber research. It was there that I became aware of the effects of viscous fibers in reducing serum cholesterol and also in reducing the postprandial glucose response. From the realization that the nature of the food and even unabsorbed components could alter the postprandial glycemic and endocrine response, it was not long before we all realized that not all carbohydrate foods were the same and so had to be tested individually to determine their glycemic responses. We could no longer rely on chemical analyses to predict their glycemic effects, potentially very important if one wished to construct diets for diabetics. For that reason we started to systematically test carbohydrate foods and index them to a standard, first as glucose and later to bread (50 g available carbohydrate). This work started in Oxford and continued after the move to Toronto. At the same time we were involved with early studies on acarbose, the α -glucosidase inhibitor that demonstrated the possible value of slowing carbohydrate absorption by drugs.

We felt that the same should apply to slowing carbohydrate absorption by dietary means. However, to compare foods in order to construct a lower glycemic response diet we needed to index foods. Hence, the glycemic index was created and has remained a topic of research for many of us since that time. Our colleague, Walter Willett at the Harvard School of Public Health created the concept of the glycemic load (the glycemic index X the dietary carbohydrate) and demonstrated the benefits of low glycemic load diets in reducing the risk of diabetes and coronary heart disease [1,2]. Jennie Brand Miller of the University of Sydney greatly extended the number of foods assessed and has made available invaluable tables of glycemic index, updated at regular intervals together with demonstrating the therapeutic benefits of low glycemic index diets [3,4].

Q What research are you currently involved in?

We're looking at ways that we can enhance the glycemic index (GI) and glycemic load to make them more effective as a clinical tools. Our group is also concerned with cardiovascular risk, which is the major cause of mortality in diabetes. We are looking at a joint treatment that would both reduce cardiovascular risk in diabetes and facilitate blood glucose control.

To this end we combine the GI with other components of the diet to reduce CHD risk; we have found that vegetable proteins may be useful in terms of reducing blood pressure and preserving renal function. For example, legumes may reduce blood pressure as they are high in vegetable protein. We have also found that nuts with vegetable oils have a positive impact on reducing the blood glucose response and also lower serum cholesterol, similarly to legumes.

We are currently looking at food types that we can put into a dietary portfolio that will both reduce glycemia, cholesterol and cardiovascular risk. If we can put these together as total diets we may be able to encourage the food industry to produce the appropriate foods that will make high impact diets feasible. Widely available 'functional foods' could then mean that this approach would not be restricted simply to treatment strategies but could also benefit the general public as a preventive strategy. Food has to be enjoyable to be eaten so producing food that is desirable for the whole population would be a major benefit for those at higher risk.

Q You are credited with creating the glycemic index; how do you think this has shaped diet-based medicine & diabetes management since then?

I think these are still early days. It has been helpful mainly in Australia due to Jennie Brand Miller's perseverance in interacting with her regulatory environment. The diabetes associations in many jurisdictions actually suggest selecting lower GI foods, which I think is reasonable. The therapeutic goals of a low glycemic index diet are analogous to those of the drug acarbose that converts the entire diet very effectively to low GI. This drug has proved very useful especially with the high carbohydrate diets consumed in the Orient. What we are doing with a low GI diet is a mild form of what is achieved with acarbose. If they are analogous there will not just be benefits in terms of glycaemia, but if we lower GI in the right way I think we can also help cardiovascular disease.

Ironically since we have launched this concept the population has become obese, and there are more people with diabetes so we cannot claim to have had a significant beneficial impact on diabetes prevention and management at this point. However, I hope we are heading in the right direction, but again we need to see some indication of major success. One of the things we are trying to do now is launch a major international study to look at what the long-term effects of these dietary strategies are under clinical trial conditions. Hopefully there will be a large number of international, including European, centers involved in this activity. It is worth mentioning that these studies may cost several hundred million dollars in order to run, so there is a lot of hard work to be done before such studies can actually be undertaken.

Q What type of diet would you currently recommend for diabetics & do you think this research is taking us in the right direction in terms of diabetes management?

Dietary restraint and exercise have, in the past, been associated with low diabetes rates. If we are saying that diabetes has doubled over the last 20 years and it will double again over the next then I think we have to retrace our steps to plant-based diets with more traditional starchy foods, a more active lifestyle and pay more attention to total calorie intake. The answer to the diabetes epidemic remains increased exercise and calorie restraint, which are very difficult

to reintroduce into the western lifestyle. The Look AHEAD study was a valiant attempt to increase exercise and reduce bodyweight. To an extent the study was quite successful [5]. The test participants needed fewer medications than control participants but the controls ended up with similar CVD event rates to the test and both had very low cardiovascular event rates. I believe that dietary restraint and exercise should work in diabetes. We just haven't been able to show it clearly in a therapeutic trial although there has been success in using this strategy for prevention of high-risk individuals developing diabetes.

However, there is some encouragement that we are now going in the right direction from research results of studies such as the PREDIMED study, which came out recently and contained a large proportion of diabetes sufferers. It included a few of the components that we would have put into our recommended dietary portfolio, for example nuts or olive oil, in the context of a Mediterranean diet, and they managed to show a 30% reduction in cardiovascular event rates in their population [6]. These findings and the results of Neal Barnard's studies of vegan diets in diabetes give confidence that advice to eat more plant foods and their components may have use in the treatment of diabetes [7,8].

Q What do you think has been the biggest achievement of your career so far?

I suppose, up to now, keeping the research running. It is becoming increasingly difficult to keep dietary trials funded on a continuous basis to enable one to follow a line of research and assess its clinical implications.

My greatest blessing has been to have had the mentors I have had and the friends with whom I have collaborated and exchanged ideas over the years. The generosity of colleagues in the food industry (Loblaw, Unilever, Kellogg among others) has made it possible to conduct many of the studies we have undertaken and have allowed the integrity of the team to be maintained.

Q What do you think is the most exciting development & what work holds the most promise for the future of the diabetes field?

There are many lines of really exciting research. I think that possibly islet cell culture and transplantation are going to be very exciting fields as they evolve. However, they do carry with them

the same problems as insulin, which was a great innovation from Toronto in its time, and that is that we still have insulin resistance, which ends up being so much of the problem with Type 2 diabetes.

A big innovation is going to be a strategy for successful healthy weight maintenance, including healthier diets and exercise, which will be key to reducing insulin resistance. It will not only be the reduction in bodyweight and especially intra-abdominal fat mass that will be exciting but the effects of exercise and diet in combination in achieving these objectives alongside reducing insulin resistance.

Q In your opinion, how close do you think we are to developing a cure for diabetes, whether this is in diet-based medicine or otherwise?

I think we are fairly close in theory for Type 2 diabetes, operationalizing it will then really be the big issue as we continue to treat individuals in an obesogenic/diabetogenic environment. People are calling ‘diabesity’, the issue of our time. These things go hand in hand with inactivity; we are constantly encouraged to do less physical activity and we have more readily available food. I believe that diabetes is an indicator of the stresses imposed by contemporary life. We will need to find strategies to deal with the availability of food and the lack of activity, but perhaps a far greater societal problem is dealing with the reason for people’s ‘frustrational’ eating.

Disclaimer

The opinions expressed in this interview are those of the interviewee and do not necessarily reflect the views of Future Medicine Ltd.

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DJ Jenkins has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. DJ Jenkins reported serving on the Scientific Advisory Board of Unilever, Sanitarium Company, California Strawberry Commission, Loblaw Supermarket, Herbal Life International, Nutritional Fundamental for Health, Pacific Health Laboratories, Metagenics, Bayer Consumer Care, Orafiti, Dean Foods, Kellogg’s, Quaker Oats, Procter & Gamble, Coca-Cola, NuVal Griffin Hospital, Abbott, Pulse Canada, Saskatchewan Pulse Growers, and Canola Council of Canada; receiving honoraria for scientific advice from the Almond Board of California, International Tree Nut Council Nutrition Research and Education Foundation, Barilla, Unilever Canada, Solae, Oldways, Kellogg’s, Quaker Oats, Procter & Gamble, Coca-Cola, NuVal Griffin Hospital, Abbott, Canola Council of Canada, Dean Foods, California Strawberry Commission, Haine Celestial, and Alpro Foundation; being on the speakers panel for the Almond Board of California; receiving research grants from Loblaw Brands Ltd, Unilever, Barilla, Almond Board of California, Solae, Haine Celestial, Sanitarium Company, Orafiti, International Tree Nut Council, and Peanut Institute; and receiving travel support to meetings from the Almond Board of California, Unilever, Alpro Foundation, and International Tree Nut Council, Canadian Institutes for Health Research, Canada Foundation for Innovation, Ontario Research Fund. DJ Jenkins receives salary support as a Canada Research Chair from the federal government of Canada. Dr Jenkins’ wife is a director of Glycemic Index Laboratories, Toronto, Ontario, Canada. The author has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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