Islet turnover persists in long-standing type 1 diabetes

The results of a study provide some of the first evidence in humans that the pancreas continues to form beta cells even in the setting of long-standing type 1 diabetes, suggesting a possible new treatment strategy.

This finding goes against the long-held belief that T1DM leads to a complete loss of insulin-secreting beta cells and that reversal of the disease requires replacement of beta cells by islet or pancreas transplantation.

“The implication is that T1DM could be cured if we could stop the new insulin-secreting cells being destroyed,” stated Butler at the American Diabetes Association’s 65th Annual Scientific Sessions in San Diego.

In studies performed on pancreatic sections from 42 individuals who had T1DM for decades - in some cases up to 60 years - Butler found that the majority (88%) still had detectable insulin-producing beta cells in their pancreas. The number of beta cells was unrelated to the duration of diabetes and age at death but was significantly higher in individuals with lower blood glucose levels.

These cells have a high death rate by autoimmune destruction implying that there must be ongoing new insulin-producing cells being formed. Therefore, T1DM may be reversible by targeted inhibition of beta cell destruction.

“What we do not know yet, however, is what rate these cells are being produced or how they are being produced,” Butler said, adding that “these questions are currently being actively addressed in studies by our group funded by the Juvenile Diabetes Research Foundation.”

Low-Carbohydrate Diet Helps in Weight Loss

Obese women, who follow low-carbohydrate diets, may lose more weight in a four-month period than those who go on low-fat diets.

In a previous study, researchers from the University of Cincinnati, Ohio compared the effects of a low-carbohydrate diet versus a low-fat diet among obese women. They found that the women on the low-carbohydrate diet lost more than twice as much weight as compared to those on low-fat diet during a six-month period.

To investigate, researchers randomly assigned 50 moderately obese women to a low-carbohydrate diet group or a low-fat diet group. Only the low-fat group was told to restrict their caloric intake. Forty women completed the study.

By the end of the four-month study, women in both groups had lost weight and body fat. However, the low-carbohydrate group lost more than 10 per cent of their body weight, while the low-fat group lost about 7 per cent. Specifically, the low-carbohydrate group lost 9.8 kilograms of weight and 6.2 kilograms of body fat, while the low-fat group lost about 6.1 kilograms of weight and 3.2 kilograms of body fat.

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To estimate their level of physical activity, women in both groups were fitted with pedometers, which recorded the number of steps they took daily.

At the start of the study, both groups of women had similar pedometer readings, and by the end of the study, there were no significant changes. Resting energy expenditure was also similar between the two groups at the start of the study and remained comparable four months later. The thermal effect of food (TEF), which comprises up to 10 per cent of the amount of energy consumed daily, includes the energy expended during digestion. When the investigators obtained TEF measurements after the women ate breakfasts containing a similar number of calories, they found that those on the low-fat diet expended more energy in a five-hour period.

This suggests that the low-fat meal was absorbed more quickly than the low-carbohydrate meal.

These results confirm that short-term weight loss is greater in obese women on a low-carbohydrate diet than in those on a low-fat diet even when reported food intake is similar.

Journal of Clinical Endocrinology and Metabolism, March 2005

**Light drinking has immediate effects on diabetes, cardiovascular risk**

Consumption of small amounts of alcohol improves several measures of diabetes and cardiovascular risk factors in the few hours after eating a meal, according to a report in the February 2005 issue of The Journal of Clinical Endocrinology and Metabolism.

“Our current study extends the findings of our previous work, which demonstrates that people who drink small amounts of alcohol on a regular basis have better blood fat levels, better insulin sensitivity and lower amounts of abdominal or central fat than people who don’t drink at all or those who drink heavily,” Dr. Lesley V. Campbell from Garvan Institute of Medical Research, Sydney, Australia reports.

Campbell and colleagues examined the effect of 15 grams of alcohol - the amount in 1 to 1 1/2 drinks - on postprandial metabolic factors in 20 postmenopausal women during the 6 hours after eating.

Alcohol consumption was associated with lower glucose and insulin levels after a low-carbohydrate meal, but only in insulin-sensitive subjects, the authors report, whereas alcohol consumption did not affect these variables after a high-carbohydrate meal or in insulin-resistant subjects.

Alcohol consumption did not influence the postprandial levels of total or HDL cholesterol after either type of meal, the report indicates, though alcohol augmented the postprandial increment in triglyceride levels after both meals.

Alcohol enhanced the reduction in arterial stiffness after the low-carbohydrate meal and increased the postprandial increment in energy expenditure 30 to 60 minutes after both the low- and high-carbohydrate meals, the researchers note.

“The beneficial effects of adding a small amount of alcohol to a meal that we demonstrated add weight to, and indeed may explain the observation, that moderate alcohol consumers have lower risks of heart disease and diabetes,” Campbell said. “Our findings could possibly be used to convince heavy alcohol consumers to reduce their intake to a level associated with documented beneficial effects.”

The use of alcohol per se in this study, rather than a particular type of alcoholic drink, means that we may confidently attribute the benefits that were demonstrated to alcohol itself, rather than to a specific component of a particular alcoholic drink.

As only postmenopausal women were studied in this trial, future studies will need to examine similar research questions in men. (Any volunteers?)

Source: J Clin Endocrinol Metab 2005;90:661-672
Glucooses levels just above 11 mmol/L are associated with increased rates of death and in-hospital complications in patients with community-acquired pneumonia, according to a report from Canada. Glucose levels above 14 mmol/L have previously been associated with poor outcomes, but the effect of lower levels of hyperglycaemia has been unclear.

Finlay A. McAlister and colleagues from University of Alberta Hospital, Edmonton, studied the relationship between hyperglycaemia and short-term outcomes in 2471 patients with community-acquired pneumonia (CAP). Patients with an admission glucose above 11 mmol/L had a significantly increased risk of death (13%) and in-hospital complications (29%) compared with patients having an admission glucose of 11 mmol/L or below (9% and 22%, respectively), the investigators report in the April issue of Diabetes Care.

These differences were more marked among those without a prior history of diabetes, the results indicate. Similarly, the risk of stroke did not change for the pharmaceutical care subjects but increased for the usual-care subjects.

These data and those of others argue that the pharmacist can be a beneficial addition to integrated care for patients with type 2 diabetes.

Source: Diabetes Care 2005;28:771-776

Pharmaceutical care reduces risk factors in type 2 diabetes

A 12-month pharmaceutical care program can reduce vascular risk factors in patients with type 2 diabetes, according to a report in the April issue of Diabetes Care. Pharmaceutical care involves the detection, prevention, and resolution of drug-related problems, the authors explain, and has proved beneficial in other chronic diseases, including asthma and cancer.

Dr. Timothy M. E. Davis from Fremantle Hospital in Western Australia and colleagues investigated the impact of a pharmaceutical care program in a community-based sample of 180 patients with type 2 diabetes who participated in the program or received usual care.

Reductions in BMI, blood pressure, fasting plasma glucose, and glycosylated haemoglobin were greater in patients participating in pharmaceutical care than in the usual-care patients, the authors report. The pharmaceutical care group also experienced non-significant improvements in serum lipid parameters and urine albumin/creatinine ratios.

After controlling for greater use of ACE inhibitor/angiotensin 2 receptor blocker therapy, antihypertensive drug use, and anti-platelet drug therapy in the pharmaceutical care group, the researchers note, allocation to pharmaceutical care remained an independent predictor of improvements in plasma glucose and glycosylated haemoglobin.

The median 10-year risk of coronary heart disease decreased in the pharmaceutical care group but did not change significantly in the usual-care group, the results indicate. Similarly, the risk of stroke did not change for the pharmaceutical care subjects but increased for the usual-care subjects.

These data and those of others argue that the pharmacist can be a beneficial addition to integrated care for patients with type 2 diabetes.

Source: Diabetes Care 2005;28:771-776

Mild hyperglycaemia worsens outcomes in community-acquired pneumonia

Glucose levels just above 11 mmol/L are associated with increased rates of death and in-hospital complications in patients with community-acquired pneumonia, according to a report from Canada. Glucose levels above 14 mmol/L have previously been associated with poor outcomes, but the effect of lower levels of hyperglycaemia has been unclear.

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These differences were more marked among those without a prior history of diabetes, the results indicate. A history of diabetes per se was not associated with increased risk of mortality or in-hospital complications.

Patients with admission glucose levels above 11 mmol/L were also less likely than others to meet the study definition of pneumonia recovery by day 5 of hospital admission, the researchers note.

Even after adjustment for other risk factors in the Pneumonia Severity Index, the investigators report, hyperglycaemia on admission remained significantly associated with adverse outcomes. A substantial proportion of hospitalised patients with pneumonia had hyperglycaemia and this was associated with poor outcomes, even after adjusting for known prognostic factors in CAP.

While observational studies in non-intensive care unit settings echo the randomised trial evidence from critical care units suggesting that stringent glucose control benefits ill patients, a large randomised trial is required to compare stringent glycaemic control on regular inpatient wards with usual care in patients with CAP.

Weight loss reduces CRP in patients with IGT

Lifestyle changes including weight loss and increased exercise prompt a significant drop in sub-clinical inflammation as determined by levels of C reactive protein (CRP) in subjects with impaired glucose tolerance (IGT), researchers in the Diabetes Prevention Program Research Group report.

Steven Haffner and colleagues conducted a placebo-controlled study of the effects of an intensive lifestyle intervention or metformin on the progression to diabetes in 3234 adults with impaired glucose tolerance. The average BMI was 34.0 and 68% were female. The primary results, released in 2002, showed that the intensive lifestyle modification reduced the incidence of type 2 diabetes by 58% and that metformin treatment prompted a 31% reduction. In the current analysis, the researchers looked at the effect on CRP and fibrinogen levels.

At 1 year, in men, there was a median reduction of CRP by 33% in the lifestyle group and by 7% in the metformin group. There was a 5% increase in the placebo group, according to the report in the May issue of Diabetes. In women, there was a CRP reduction of 29% in the lifestyle group and of 14% in the metformin group. There was no change in the placebo group.

Most of the improvements in the lifestyle group appeared to be due to weight loss rather than to increased physical activity, say the investigators.

Compared with the metformin and placebo groups, "only modest reductions" were seen in fibrinogen levels in the lifestyle group. Nevertheless, these reached significance.

Weight loss in the lifestyle group was only about 6-7% at the end of the year, and at that point most were still obese.

However, the investigators conclude that not only does lifestyle intervention "reduce the risk of developing type 2 diabetes but also has effects on risk markers that may eventually reduce the risk of cardiovascular disease."

Source: Diabetes 2005;54:1566-1572

Metformin levels in breast milk clinically insignificant

Metformin is excreted into breast milk, but the levels are insufficient to adversely affect blood glucose levels of nursing infants, according to the findings of a small study reported in the June issue of Obstetrics & Gynaecology.

While metformin is occasionally used as monotherapy for controlling type 2 diabetes in nursing mothers, the effect of metformin on the nursing infant is unclear.

To investigate, Gerald G. Briggs from Miller Children's Hospital, Long Beach, California and colleagues measured the levels of metformin in the serum and breast milk of five women and measured the blood glucose levels in three of their infants.

Milk metformin concentrations averaged 63% of serum metformin concentrations, the authors report, resulting in average daily doses to the infants ranging from less than 0.014 to 0.070 mg/kg/day.

These doses represented, on average, 0.65% of the mother's daily dose, the report indicates.

All three infants tested had blood glucose concentrations within normal limits (higher than 40 mg/dL), the researchers note, and none of the nursing infants experienced adverse effects.

"The estimated daily doses ingested by the infants seem to be clinically insignificant," the authors conclude. "Although additional data are required, we conclude that metformin is compatible with breastfeeding."