

# DIABETES IN CONTROL.com Newsletter

The Newsletter for Professionals in Diabetes Care

July 25, 2007 - Issue #374

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## Top Diabetes Stories:

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Higher Cancer Prevalence Seen Among Diabetics Taking Thiazolidinediones\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4989>

Most Internists Are Switching Patients Off Avandia\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4988>

Type 2's Improve Cardiovascular Risk After Switching From Insulin to Pioglitazone/Glimepiride\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4987>

New Study Slams Safety of Avandia for Diabetes\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4986>

Interval Training Workouts Burn More Fat Than Continuous Workouts\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4984>

Half of Diabetic Patients Not Reaching HbA1c Target\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4982>

Next DPP-4 Inhibitor Galvus Delayed Until 2010\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4979>

Food Cravings For Calories Not Carbs, Says Obesity-Related Study\*

<http://www.diabetesincontrol.com/results.php?storyarticle=4978>

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## From the editor's desk

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**Dr. James R. Bailes'** new book No More Fat Kids, A Pediatrician's Guide for Safe and Effective Weight Loss, has raised some controversy in the medical community, but I had it reviewed by one of my interns who has a 6 year old child, and to her it made a lot of sense. [Click here](#) to learn more.

<http://www.diabetesincontrol.com/results.php?storyarticle=4990>

ONE WEEK to the AADE conference in St. Louis stop by our booth #707 and say hello. You can pick up some samples and enter to win an iPod. Present Diabetes will be with us to introduce you to our Online Community for Diabetes Professionals to Learn, Share and Collaborate with colleagues around the world.

**FREE LIVE WEBCAST:** August 8, we will be having another live webcast and teleconference call with Dr. Richard K. Bernstein, who will answer questions from medical professionals and patients and it is free. Just go to <http://www.diabetes911.net/askdrb/index.php> and register.

**Lisa Long, PharmD. Candidate 2008, University of Florida** just finished her endo rotation with me and offers her personal opinion of her favourite insulin pump.

<http://www.diabetesincontrol.com/results.php?storyarticle=4991>

**Theresa L. Garnero, ARNP, CDE**, returns with a new cartoon. Check it out by [clicking here](#).

<http://www.diabetesincontrol.com/results.php?storyarticle=4992>

## July 29, 7PM ET on CNBC

dLife explores care giving - the challenges, and the rewards. Plus, Nicole Johnson pays a visit to the research labs of the NIDDK to see the search for a cure in progress. And, a college basketball coach who didn't let a severe diabetes complication, keep him from a championship season. Catch this all-new episode of dLifeTV on:

Sundays on CNBC at 7 PM ET, 6 PM CT, and 4 PM PT Check your local listings for details.

If over the past week you requested more information about Atkins, the Prodigy Voice Monitoring System, or the Diabetes Action Network, (NFB) we may not have received your information due to unforeseen database issues. If you would like to make sure you receive more information, please tell us using these links.

Prodigy Voice Monitoring System

<http://www.diabetesincontrol.com/aserver/adclick.php?n=aa2c37b8>

Atkins

<http://www.diabetesincontrol.com/aserver/adclick.php?n=a929c42d>

Diabetes Action Network

<http://www.diabetesincontrol.com/aserver/adclick.php?n=a989bec4>

**We can make a difference!**

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**This week's overview:**

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- Item #5: Flavonoids in Orange Juice Make It a Healthy Drink for Diabetics
- Item #7: Pumpkin Extract Can Improve Blood Glucose Levels for Diabetics
- Item #9: Superiority Not Proven for Rapid-Acting Insulin Analogues
- Item #10: New Diet Pill Expands 1,000 Times in Your Stomach
- Item #13: New Diet Pill Expands 1,000 Times in Your Stomach
- Item #14: Low Glycemic Index Diets Better for Weight Loss
- Item #15: Less Insulin In the Brain Key to a Long Life

Check out this weeks **"Test Your Knowledge"** question. This week's question deals with CGMS. <http://www.diabetesincontrol.com/results.php?storyarticle=4993>

Dave Joffe, *Editor-in-Chief*

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**CE CREDITS**

ARE NOW AVAILABLE FOR DM EDUCATE? , COMPREHENSIVE ONLINE DIABETES MANAGEMENT COURSE - DM Educate was created by the University of Pittsburgh, in partnership with Novo Nordisk to provide pharmacy students with the tools to meet the needs of patients with diabetes. Currently 75 colleges and universities throughout the world are registered and using the course. [Learn more here](#)

<http://www.diabetesincontrol.com/results.php?storyarticle=4904>

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**NEWS FLASH:**

**Galvus, the Next DPP-4 Inhibitor Delayed Until 2010. FDA wants more safety studies.**

**Novo Nordisk Sues Sanofi-Aventis Claiming Insulin Pen Patent Infringement:** They filed a complaint claiming Sanofi-Aventis infringed on its NovoPen 4 system.

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**Tools for your Practice:**

**The Secrets of Alternate Site Testing**

If we could get our patients to test more often we would get better results. But finger sticks hurt so why don't our patients use alternate site testing. This one page handout helps your patients understand how to get rid of the

pain.

<http://www.diabetesincontrol.com/results.php?storyarticle=4994>

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15. Less Insulin In the Brain Key to a Long Life  
<http://www.diabetesincontrol.com/results.php?storyarticle=4975>

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**ITEMS For The Week:**

Item 1

**Higher Cancer Prevalence Seen Among Diabetics Taking Thiazolidinediones**  
*Patients with diabetes, especially women, who take thiazolidinediones (TZDs) may have a 59% increased risk of developing cancer, according to a new report.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4989>

"There is more to these drugs than first meets the eye," Dr. Maria E. Ramos-Nino from the University of Vermont, Burlington, stated.. "The long -term consequences and benefits are not understood."

Dr. Ramos-Nino and colleagues investigated the association of TZDs and cancer prevalence among nearly 9000 diabetic patients participating in the Vermont Diabetes Information System. A randomly selected sample of 1003 of these participants were interviewed about personal and clinical parameters, including any history of malignancy.

The investigators found that the use of any TZD was associated with a 59% increased risk of cancer in a logistic regression model corrected for use of sulfonylureas and biguanides, age, HbA1c, BMI, smoking, comorbidity, and other medications.

There was a significant association with rosiglitazone use with an odds ratio of 1.89 (p = 0.02) for malignancy, but not with pioglitazone use (OR = 1.09, p = 0.76).

"We are not aware of a convincing explanation or previous results to support the finding in this study of an association with cancer for rosiglita zone, but not for pioglitazone," the researchers write. "As both are thought to activate PPAR -gamma with similar potency, this finding suggests another mechanism for the association."

Women taking TZDs were more than twice as likely to have cancer as women not taking TZDs (OR = 2.07, p = 0.01), the researchers note, but the association was not significant in men (OR = 1.20, p= 0.63).

The use of sulfonylurea by women was associated with a 51% lower risk of cancer, the report indicates.

"The gender-dependent observation is difficult to explain," the team notes. "We do not know which specific tumors are increased in the TZD users in this population."

The authors acknowledge that the study has several limitations, including its cross-sectional design, lack of confirmation of cancer and absence of information on the temporal relation between TZD use and cancer.

"Our data do not provide strong evidence to change practice at this time," Dr. Ramos-Nino said. "They are disturbing, to be sure, but require further investigation before clinical decisions should be changed."

*BMC Medicine June 21, 2007*

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works extremely well for patients that suffer from Chemotherapy induced Neuropathy. Click here for more info...

<http://www.diabetesincontrol.com/rebuilder/index.php>

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Item 2

**Most Internists Are Switching Patients Off Avandia**

*Though the FDA has yet to advise on the cardiovascular safety of GlaxoSmithKline's Avandia type 2 diabetes drug, some physicians are taking matters into their own hands.*

Internists said they will switch more than half their type 2 diabetes patients currently on Avandia to another therapy, according to research from GfK Market Measures' Event Flash.

This sharply contrasts with general/family practitioners and endocrinologists who expect to switch less than half of their patients.

The news of Avandia's effect on cardiovascular risk has led to a congressional probe, and the FDA plans a hearing to discuss cardiovascular safety of the class and Avandia on July 30. In the meantime, diabetes experts have advised users of the drug to speak with their doctors and not to immediately discontinue use.

But the news of Avandia's effect on cardiovascular risk has prompted some doctors to act. In another finding from the GfK study of 200 physicians who see no fewer than 10 type 2 diabetes patients per week, about a third of internists reported they are reluctant to prescribe Takeda's Actos or any other product containing Actos, which is in the same drug class as Avandia, compared to about a quarter of general/family practitioners and endocrinologists.

Safety concerns have been building since the May 21 release of a New England Journal of Medicine meta-analysis finding that Avandia users are 43% more likely to suffer a heart attack than those taking other diabetes drugs. Since the paper appeared, GSK said prescriptions for Avandia have dropped 15% to 20%.

Reports of Avandia side effects to federal regulators also tripled, according to the Associated Press, due most likely to doctors' low awareness of the drug's possible role in their patients' heart problems in the past.

"Now, patients and their doctors are much more aware of the possible link between Avandia and cardiovascular disease. This is good--this is going to help us going forward to determine whether or not this drug is safe," a Vanderbilt University diabetes specialist stated.

GSK has defended the drug, cautioning against drawing conclusions on adverse event data or on the NEJM meta analysis.

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**DID YOU KNOW:**

**Vitamin C Offers Little Protection Against Colds:** Unless you run marathons, you probably won't get much protection from common colds by taking a daily supplemental dose of vitamin C, according to an updated review of 30 studies. Conducted over several decades and including more than 11,000 people who took daily doses of at least 200 milligrams, the review also shows that vitamin C (ascorbic acid) does little to reduce the length or severity of a cold, according to the researchers at the Australian National University and the University of Helsinki. However, they found that people exposed to periods of high stress – such as marathon runners, skiers and soldiers on sub-arctic exercises – were 50 percent less likely to catch a cold if they took a daily dose of vitamin C. *The review appears in the latest issue of The Cochrane Library*

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You've probably heard the term "low glycemic" bandied about in the media and in discussions about weight loss. You may have even come across some food products labeled as such.

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<http://www.diabetesincontrol.com/ads/atkins/dest.shtml>

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Item 3

**Type 2's Improve Cardiovascular Risk After Switching From Insulin to Pioglitazone/Glimepiride**

*In a poster presentation at the ADA 67<sup>th</sup> Scientific Sessions, Type 2 diabetic patients switched from insulin to a combination of pioglitazone and glimepiride achieved blood glucose control and showed improvement in cardiovascular risk.*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4987>

The researchers switched the 32 women and 66 men enrolled in the study from insulin therapy to pioglitazone/glimepiride after confirming residual beta-cell function using a glucagon stimulation test. The subjects had a mean age of 59 years, disease duration of 5.6 years, mean body mass index (BMI) of 33.9, and hemoglobin A1c (HbA1c) level of 6.9 mg/dL.

Observation parameters at baseline and endpoint included HbA1c, homeostasis model assessment to predict insulin resistance (HOMA-IR), IV glucose tolerance test (GTT), United Kingdom Prospective Diabetes Study cardiovascular risk score (UKPDS), adiponectin, high-sensitivity C-reactive protein (hsCRP), matrix metalloproteinases 9 (MMP9), monocyte chemoattractant protein 1 (MCP-1), and soluble CD40 ligand (sCD40L).

Subjects showing an increase in HbA1c >0.5 % at any timepoint were removed from the study (n = 23, 23%). The remaining 75 patients achieved stable HbA1c values, with a baseline mean of 6.8% and an endpoint mean of 6.7%.

Among the 75 subjects, the researchers found parallel and statistically significant improvements in HOMA-IR, adiponectin, hsCRP, and MCP-1 as well as nonsignificant improvements in the IV GTT sensitivity index, UKPDS risk score, and MMP9. They observed no change in sCD40L.

"The majority of patients switched from insulin to pioglitazone/glimepiride treatment responded not only with a stable glycemic control but also with an improved cardiovascular risk profile after 6 months of therapy," the investigators concluded.

*The study was supported by Takeda Pharma. International Journal of Clinical Practice Vol. 61 Page 1 June 2007 s153, Oral combination therapy with thiazolidinediones and sulfonylureas in type 2 diabetes*

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**Advertisement**

A successful start to insulin therapy is about doing the right thing at the right time. A reusable, digital insulin pen for use with Humalog® (insulin lispro) can offer patients greater flexibility. Humalog® and Humalog® Mixture insulins are available in convenient insulin pens. The new HumaPen® Luxura™ HD -- offered with half unit increments from 1 to 30 -- and HumaPen® MEMOIR both offer greater flexibility. Find progressive dosing guidelines that can help simplify starting insulin in patients new to insulin or those adding Humalog® to basal insulin at [http://ad.doubleclick.net/clk;108162540;16546306;x?http://www.humalog.com/hcp/humapen\\_luxura.jsp?ccd=humdtp17](http://ad.doubleclick.net/clk;108162540;16546306;x?http://www.humalog.com/hcp/humapen_luxura.jsp?ccd=humdtp17)

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Item 4

**New Study Slams Safety of Avandia for Diabetes**

*The safety of the controversial diabetes drug Avandia (rosiglitazone) was attacked in a new analysis by German researchers, who found little evidence that the drug*

improved the quality or length of life and concluded it could actually worsen complications of the disease.

<http://www.diabetesincontrol.com/results.php?storyarticle=4986>

Their conclusions were based on a review of pooled data from 18 past trials involving 8,000 patients.

Dr. Bernd Richter of Duesseldorf's Heinrich-Heine University, who led the research, questioned whether it was ethical to conduct any further clinical tests with Avandia, since "less dangerous" alternative treatments were available.

Drug maker Glaxo dismissed these findings as misleading and said it strongly disagreed with the conclusions, which were published in the Cochrane Library journal.

Avandia has been under a cloud since May, when top U.S. cardiologist Dr. Steven Nissen published a pooled analysis of 42 previous trials that showed it increased the risk of heart attack by 43 percent. Richter said his research was conducted independently of Nissen's, and the timing was a coincidence, though the two teams reached similar conclusions.

The German analysis found that Avandia produced about the same reductions in blood sugar levels as other oral antidiabetic drugs, but patients taking Avandia gained up to 11 pounds and the risk of edema, or swelling, doubled.

Avandia was also linked to heart failure and bone fractures.

Richter noted that even very small risks could be significant for such a widely used medicine. "On a global scale, tiny risks can translate into big effects, because millions of people are taking this drug," he said.

Glaxo said Richter's analysis provided no new evidence about the use of Avandia in clinical practice. "It's looking at a very thin slice of the total available evidence for rosiglitazone and really ignoring a huge amount of research," Ronald Krall, chief medical officer of the world's second-largest drugmaker, said in a telephone interview. Krall said Glaxo has studied Avandia in more than 52,000 patients, and this much larger dataset showed the drug had a similar safety profile to other oral antidiabetic drugs.

The issue will come to a head on July 30, when U.S. Food and Drug Administration advisers meet to discuss the drug's safety. Krall said he is confident Glaxo has a compelling body of evidence to present at the meeting.

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### Start your own walking program



New StepTracker Available at special prices. See the results of the Step Program Study.

<http://www.diabetesincontrol.com/programs/steps/index.shtml>

Purchase your own pedometers and receive the Steps to Health

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### FACT:

**Magic Pill to Eliminate Disease and Add Years to Life:** A molecular compound found in red wine called resveratrol extends the life span of mice by up to 24 percent and up to 59 percent in other animals like flies and fish. The premise behind a formulation of resveratrol is that it activates a gene called SIRT -1,

which may regulate lifespan by being activated by caloric restriction. Mice live longer when they have 30 percent to 40 percent fewer calories than they would normally. Resveratrol may mimic caloric restriction.

**See this week's Item #13**

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Item 5

### **Flavonoids in Orange Juice Make It a Healthy Drink for Diabetics**

*Orange juice, despite its high caloric load of sugars, appears to be a healthy food for diabetics due to its mother lode of flavonoids, a study by endocrinologists.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4985>

Flavonoids suppress destructive oxygen free radicals -- also known as reactive oxygen species, or ROS. An overabundance of free radicals can damage all components of the cell, including proteins, fats and DNA, contributing to the development of many chronic diseases, including heart disease and stroke as well as diabetes.

"Many major diseases are associated with oxidative stress and inflammation in the arterial wall, so the search for foods that are least likely to cause these conditions must be pursued," said Paresh Dandona, MD, PhD, head of the Diabetes - Endocrinology Center of Western New York and senior author on the study.

"Our previous work has shown that 300 calories of glucose induces ROS and other proinflammatory responses," said Dandona, who is Distinguished Professor of Medicine in the UB School of Medicine and Biomedical Sciences.

"We hypothesized that 300 calories-worth of orange juice or of fructose would induce less oxidative stress and inflammation than caused by the same amount of calories from glucose."

The resulting study involved 32 healthy participants between the ages of 20 and 40, who were of normal weight, with a body mass index of 20 -25 kg/m<sup>2</sup>. Participants were assigned randomly and evenly into four groups, who would drink the equivalent of 300 calories-worth of glucose, fructose, orange juice or saccharin-sweetened water.

Fasting blood samples were taken before the test and at 1, 2 and 3 hours after a 10-minute period to consume the drinks. Results showed a significant increase in ROS within 2 hours in samples from the glucose group but not in those from the fructose, orange juice or water group.

"We were intrigued by the fact that there was no increase in ROS or inflammation following orange juice consumption, even though its glucose concentration was the same as in participants in the glucose group," said Dandona. "This raised the question of what in the juice was responsible for suppressing ROS generation: flavonoids and vitamin C or fructose?"

An additional round of test on the samples showed that neither fructose nor vitamin C suppressed the oxygen free radicals. However the two types of flavonoids in orange juice -- hesperetin and naringenin -- inhibited ROS generation by 52% and 77%, respectively.

"Our data are relevant to patients with diabetes," said Dandona, "because stress from ROS and inflammation are increased significantly in this population and may contribute to development of atherosclerosis. Clearly the choice of foods that either don't increase or actually decrease oxidative and inflammatory stress is important.

"The search for safe non-inflammatory foods and diets must continue," Dandona stressed, "especially since obesity, being overweight and type 2 diabetes are associated with oxidative stress and inflammation, and more than 60% of U.S. population is affected by these conditions."

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Item 6

### **Interval Training Workouts Burn More Fat Than Continuous Workouts**

*Taking a break in the middle of your workout may metabolize more fat than exercising without stopping, according to a recent study in Japan.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4984>

Researchers conducted the first known study to compare these two exercise methods—exercising continually in one long bout versus breaking up the same workout with a rest period. The findings could change the way we approach exercise. Who wouldn't want to take a breather for that?

"Many people believe prolonged exercise will be optimal in order to reduce body fat, but our study has shown that repetitions of shorter exercise may cause enhancements of fat mobilization and utilization during and after the exercise. These findings will be informative about the design of [future] exercise regimens," said lead researcher Kazushige Goto, Ph.D. "Most people are reluctant to perform a single bout of prolonged exercise. The repeated exercise with shorter bouts of exercise will be a great help [in keeping up with fitness]."

The researchers used seven healthy (avg. body mass: 66.1, percentage fat: 17.6) men with an average age of 25 who were physically active and familiar with exercise and had them perform three separate trials:

- one single bout of 60-min exercise followed with a 60-min recovery period (Single)
- two bouts of 30-min exercise with a 20-min rest after the first 30-min bout, along with a 60-min recovery period at the end (Repeated)
- one 60-min rest period (Control)

The men performed each trial at the same time of day after fasting overnight. They exercised on a single ergometer (cycling machine) at the commonly recommended exercise prescription of 60% maximum oxygen intake. The recovery and rest periods were conducted while the subjects sat in chairs. Blood samples were taken every 15 minutes during the exercise and every 30 minutes during the recovery period. Their respiratory gas and heart rates were monitored continuously throughout the trial.

The Repeated trial showed a greater amount of lipolysis (fat breakdown) than did the Single trial. This Repeated trial also had a pronounced increase in free fatty acids and glycerol (chemical compounds that are released when stored fat is used) concentrations in the final 15 minutes of exercise, whereas these concentrations only progressively increased throughout the Single trial. Also, the second half of the Repeated trial showed a significantly greater epinephrine response while also having a rapid decrease in insulin concentration as a result of lower plasma glucose. This combination of high epinephrine and low insulin concentration may have also increased the lipolysis. There was also enhanced fat oxidation in the recovery period of the Repeated trial than in the Single trial, but this result may be because the free fatty acids concentration was already high before the recovery period.

The American College of Sports Medicine recommends moderate exercise for the duration of 45 to 60 minutes to ensure a sufficient amount of energy is depleted in obese individuals. This has caused a greater focus on extending exercise sessions in order to burn more fat. However, this study shows that this method may not be the most effective way to enhance fat metabolism, as splitting up a long bout of

exercise with a rest period burns more fat than a continuous bout of exercise. This study could help with the practical application of implementing new exercise methods in order to better manage and control weight in individuals in the future.

*This finding is part of a study entitled Enhancement of fat metabolism by repeated bouts of moderate endurance exercise, found in the June 2007 edition of the Journal of Applied Physiology, which is published by the American Physiological Society.*

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For the diabetic patient, it's not the cholesterol that's the problem. It's the number of LDL particles, especially small LDL particles. To see the real risk, use the NMR LipoProfile(r) test, the only test that directly measures the number of LDL particles and the number of small LDL particles - the particles shown to be more predictive of CHD events than LDL-C. Click here to learn more.  
<http://www.diabetesincontrol.com/ads/liposcience/dest.php>

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#### Item 7

##### **Pumpkin Extract Can Improve Blood Glucose Levels for Diabetics**

*Results from a new study shows that an extract from pumpkin ( Cucurbita ficifolia ) may improve blood glucose levels in diabetics, exert antioxidant effects and prevent the progressive destruction of pancreatic betacells.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4983>

If the research, by scientists from the East China Normal University, can be reproduced in humans, then feeding on a pumpkin extract may promotes regeneration of damaged pancreatic cells in diabetic rats, boosting levels of insulin-producing beta cells and insulin in the blood.

*"The present study provides substantial evidence to demonstrate the hypoglycaemic action of C. ficifolia fruit extract as well as its role as antioxidant agent and thus reveals a mechanism for its cytoprotective action,"* wrote authors Tao Xia and Qin Wang in the *Journal of the Science of Food and Agriculture*.

*"Perhaps this is the first report showing the antioxidant role of C. ficifolia fruit extract and suggesting its utility in the control of diabetes,"* added the authors.

The rats used in this study modelled type-1 diabetes, but the researchers believe the pumpkin extract may also play a role in type-2 diabetes.

Type-1 diabetes occurs when people are not able to produce any insulin after the cells in the pancreas have been damaged, thought to be an autoimmune response.

Tao Xia and Qin Wang divided 12 diabetic rats and 12 normal rats into two groups, one fed a normal diet and the other fed the normal diet supplemented with the pumpkin extract for 30 days. At the end of the study, the researchers report that diabetic rats fed the extract had only five per cent less plasma insulin and eight percent fewer insulin-positive (beta) cells compared to normal healthy rats.

*"Pumpkin extract is potentially a very good product for pre-diabetic persons, as well as those who have already developed diabetes,"* lead author Tao Xia from told *Chemistry & Industry* magazine.

The mechanism behind the potential benefits was proposed to be due to both antioxidants and D-chiro-inositol, a molecule that mediates insulin activity. Boosting insulin levels has the effect of lowering blood sugar levels, which reduces levels of oxidative oxygen species that damage beta-cell membranes, preventing further damage and allowing for some regeneration.

The researchers note however, that beta cells levels in the diabetic rats are unlikely ever to reach that of controls, because some of the cells will have been

damaged beyond repair.

*"Thus our studies support the notion that supplementation of C. ficifolia fruit extract to diabetic patients would help in achieving good glycaemic and metabolic control and prevent long-term complications as a result of the protection offered by its antioxidant action; probably preserving the residual  $\beta$ -cell mass without further loss," they concluded.*

*"The main finding is that feeding pumpkin extract prevents the progressive destruction of pancreatic betacells," he said.*

*Journal of the Science of Food and Agriculture: Volume 87, Issue 9, Pages 1753-1757  
"Hypoglycaemic role of Cucurbita ficifolia (Cucurbitaceae) fruit extract in streptozotocin-induced diabetic rats" Authors: Tao Xia and Qin Wang*

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#### Advertisement

Dr. Philip A. Wood has written a book for healthcare professionals and students of medicine, nursing, pharmacy, and graduate studies, as well lay people interested in understanding the influences of genetics, nutrition, activity level and drugs on diseases associated with excess fat such as obesity, insulin resistance, metabolic syndrome and type 2 diabetes. The book is composed of short, readable chapters with helpful figures to further explain the mechanisms discussed. For further information please click here.

[http://www.amazon.com/exec/obidos/tg/detail/-/0674019474/qid=1132176956/sr=8-1/ref=pd\\_bbs\\_1/002-7853569-1175265?v=glance&s=books&n=507846](http://www.amazon.com/exec/obidos/tg/detail/-/0674019474/qid=1132176956/sr=8-1/ref=pd_bbs_1/002-7853569-1175265?v=glance&s=books&n=507846)

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#### Item 8

#### **Half of Diabetic Patients Not Reaching HbA1c Target**

*Despite significant gains in disease control over the last 6 years, nearly half of patients with diabetes failed to reach national treatment goals in 2006.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4982>

An analysis of 22.7 million hemoglobin A<sub>1c</sub> tests performed on 4.8 million patients with diabetes mellitus at Quest Labs revealed that as of December 2006, 55% of patients had reached the American Diabetes Association (ADA) treatment target of hemoglobin A<sub>1c</sub> levels less than 7%. This compares with 38% of patients in 2001.

Despite these overall gains, the decline in A<sub>1c</sub> values has slowed since 2003, leaving 45% of Americans with diabetes short of ADA targets in 2006. As this study only included those patients getting A<sub>1c</sub> tests regularly at Quest Labs, it is very likely that those patients not getting regular A<sub>1c</sub> tests would bring the numbers higher.

"For this 45%, we are going to need new approaches to control their diabetes," coauthor Dr. Richard W. Furlanetto said at a press briefing. "We'll need new medications, certainly, but I think we'll need intensive education for these people and new ways of allowing them to live with their disease."

Roughly 28% of patients with type 1 diabetes reached an A<sub>1c</sub> level below 7% in 2001, compared with 35% of patients in 2006. In contrast, 45% and 57% of patients with type 2 diabetes reached the target over the same time period, said Dr. Furlanetto, a pediatric endocrinologist and medical director of endocrinology at Quest Diagnostics Nichols Institute, Chantilly, Va.

In patients with type 2 diabetes, the overall mean A<sub>1c</sub> values declined from 7.6% in 2001 to 7.3% in 2003, but then slowed significantly and stabilized at 7.2% in 2006, according to the analysis of data from the Quest Diagnostics Informatics Data Warehouse, a large private reference laboratory database.

The authors suggest that this HbA<sub>1c</sub> plateau mirrors the clinical progression of the disease as well as treatment patterns. Longitudinal analysis indicates that A<sub>1c</sub>

values for individual patients decreased in the first 1-2 years, and then trended slowly upward. This could be a result of aggressive therapy and strict compliance in the early years, followed by worsening of the disease, which limits therapy, and less diligent treatment compliance, Dr. Furlanetto said.

Although the number of tests reported in the study is more than 50 times that of other published reports on diabetes health, reporters asked if the findings apply to the average patient, given that the sample represents a fraction of the roughly 21 million Americans with diabetes.

Presented at the 67<sup>th</sup> ADA Scientific Sessions in Chicago

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**FACT:**

**Next DPP-4 Inhibitor Galvus Delayed Until 2010:** Novartis expected to be in the market this year with Galvus, But the FDA is requiring more studies to determine Galvus's safety, so they will not resubmit until probably mid-2009 Thursday's decision by a committee of experts at the European Medicines Agency comes two days after Novartis said it would not be ready to resubmit Galvus to U.S. regulators until mid-2009, following a request for more safety data. **See this week's Item # 11**

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Item 9

**Superiority Not Proven for Rapid-Acting Insulin Analogues**

*There is currently no evidence available of a superiority of rapid-acting insulin analogues over human insulin in the treatment of adult patients with diabetes mellitus type 1.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4981>

This is the result of the final report of the Institute for Quality and Efficiency in Health Care (IQWiG) which was published in June 2007.

The evidential value and design of studies available so far are inadequate and do not allow conclusions regarding most patient-relevant therapy goals, such as the reduction in long-term complications or overall mortality, according to the report. Due to the lack of data, the benefit of rapid-acting insulin analogues in children and adolescents is unclear. Although one of the manufacturers conducted long-term comparative studies in this group of patients, it is withholding some of the results.

The German Federal Joint Committee commissioned IQWiG to compare the benefit of rapid-acting insulin analogues versus human insulin, as well as to compare the benefit of various rapid-acting insulin analogues with each other. IQWiG assessed all three rapid-acting insulin analogues approved in Germany: insulin aspart (tradenname in Germany: Novorapid), insulin lispro (tradenames in Germany: Humalog, Liprolog), and insulin glulisine (tradenname in Germany: Apidra).

The literature search retrieved a total of 9 published comparative studies, in which patients were observed for at least 24 weeks. Only studies with this minimum duration were included, as they give patients sufficient time to adjust to the new medication, and to observe the treatment effects under stable application. Eight of these studies compared either insulin aspart or insulin lispro with human insulin; no such study was available for glulisine. The only study available that compared two analogues referred to glulisine and lispro.

Regarding insulin pump therapy, no study lasting at least 24 weeks was available. Therefore, it remains unclear whether patients would benefit and which advantage patients would have by using this form of administration. The company Novo Nordisk sponsored 2 completed long-term studies in children and adolescents. However, to date, both studies have only been partially published. In contrast to the manufacturers Sanofi and Lilly, Novo Nordisk was not prepared to provide the information needed for the report.

The conclusions of the 9 studies included in the evaluation are only of limited robustness. None of the studies was blinded, i.e. both the patient and the physician knew which type of insulin was being injected. Without blinding, there is a danger that patients, knowing their type of insulin, behave differently, which would subsequently lead to a bias in the results of the study.

Even though patients have been treated with insulin analogues for 10 years, it is still unclear as to how these types of insulin affect long-term complications of diabetes type 1, mortality, and the necessity of hospital admissions. Regarding the reduction in blood glucose levels (measured by means of HbA1c), patients treated with insulin aspart had, on average, lower levels. However, these statistical differences were so small that an effect on patients' health is not to be expected. Insulin lispro may prevent nocturnal hypoglycaemia better than insulin glulisine. The only study that compared these insulin analogues provided first indications, but no reliable evidence.

The role of rapid-acting insulin analogues in the treatment of diabetes type 2 was assessed in a separate commission; the relevant final report had already been published by IQWiG in December 2005. This report also came to the conclusion that evidence of an additional benefit of insulin analogues has yet to be provided.

*Institute for Quality and Efficiency in Health Care*

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#### Item 10

##### **New Diet Pill Expands 1,000 Times in Your Stomach**

*Italian scientists have invented a new diet pill that swells inside the stomach, giving its users the impression that they have already eaten.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4980>

"The sensation is like eating a nice plate of spaghetti," said Prof Luigi Ambrosio, who led the research.

The pill contains an extremely absorbent powder that expands to more than 1,000 times its initial size when combined with water.

Prof Ambrosio said a 500mg pill, washed down with two glasses of water, would create a tennis ball-sized lump in the stomach, making dieters feel full.

"We had one extremely important investor come to visit and he wanted to try the pill," he said. "He got very excited because he took one at 11 o'clock in the morning and at six o'clock in the afternoon he still couldn't finish an ice cream."

The pill was tested on 20 people for a month last year, and is being tested on a further 90 people at the Policlinico Gemelli hospital in Rome. The results are due in October, but Prof Ambrosio has already won the financing to form a company, Academic Life Science. He hopes to be selling the pill by next May.

"The idea came to us while we were working on a project to design a lining for diapers.

"One of my PhD students came across this particular compound, with incredibly high absorption rates. At the time, scientists were trying to battle obesity with balloons inside the stomach, so we thought this might work."

Prof Ambrosio, of the National Research Council in Naples, said the pill was made from cellulose, the same substance found inside plants. Consequently, he claimed, it also has a beneficial effect on the gut.

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Item 11

#### **Next DPP-4 Inhibitor Galvus Delayed Until 2010**

*Novartis expected to be in the market this year with Galvus, But the FDA is requiring more studies to determine Galvus's safety, so they will not resubmit until probably mid-2009*

<http://www.diabetesincontrol.com/results.php?storyarticle=4979>

The experimental diabetes drug Galvus has been recommended for approval in Europe, lifting prospects for a medicine that faces a lengthy delay in getting to market in the United States.

Thursday's decision by a committee of experts at the European Medicines Agency comes two days after Novartis said it would not be ready to resubmit Galvus to U.S. regulators until mid-2009, following a request for more safety data.

Novartis said the agency's Committee for Medicinal Products for Human Use (CHMP) had also backed its Exelon Patch, which delivers a treatment for Alzheimer's disease through a skin patch, and once-yearly Aclasta for women with postmenopausal osteoporosis.

Recommendations for marketing approval by the agency's Committee for Medicinal Products for Human Use are normally endorsed by the European Commission. Novartis said it expected to get a final decision on Galvus within three months.

Galvus works in a similar way to Merck & Co. Inc. recently launched Januvia product but its path to market has been delayed by worries over skin toxicity.

Both Galvus and Januvia are so-called DPP-4 inhibitors, which are designed to enhance the body's own ability to lower elevated blood sugar and could become an important new way to control type 2 diabetes -- the most common form of the disease.

The drugs' manufacturers and many analysts believe DPP-4 drugs could become blockbusters because they are not associated with weight gain, a major side effect of some established diabetes drugs.

Galvus is being recommended in the European Union for use in combination with other common oral diabetes medicines -- metformin, a thiazolidinedione (TZD) or a sulfonylurea (SU).

"Many type 2 diabetes patients need more than one treatment to bring their blood sugar levels under control, therefore the efficacy and tolerability of Galvus in combination with other medicines is especially significant," Novartis's global head of pharma development, James Shannon, said in a statement.

Galvus is already available in Brazil and Mexico.

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**DID YOU KNOW:**

**Half of Diabetic Patients Not Reaching HbA1c Target:** Despite significant gains in disease control over the last 6 years, nearly half of patients with diabetes failed to reach national treatment goals in 2006. An analysis of 22.7 million hemoglobin A1c tests performed on 4.8 million patients with diabetes mellitus at Quest Labs revealed that as of December 2006, 55% of patients had reached the American Diabetes Association (ADA) treatment target of hemoglobin A1c levels less than 7%. This compares with 38% of patients in 2001. See this week's Item #8

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Item 12

**Food Cravings For Calories Not Carbs, Says Obesity-Related Study**

*People with food cravings want calories, not carbohydrates, says a news study from the US that may have implications for obesity.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4978>

The results could contribute to a deeper understanding of how people develop food and taste preferences and cravings. This may have important implications for the food industry, not just for food formulators and flavor scientists, but also with the growing epidemic of obesity..

With many critics keen to take the blame off a consumer's personal responsibility and heap it purely at the feet of the food industry this research highlights just how multi-faceted and complicated the obesity issue may actually be.

Over 300m adults are obese worldwide, according to latest statistics from the WHO and the International Obesity Task Force. About one-quarter of the US adult population is said to be obese, with rates in Western Europe on the rise although not yet at similar levels.

Roberts and colleagues observed that successful weight loss was related not only to how often people gave in to their cravings, but also to the types of foods they craved. "Participants with a higher percentage of weight loss actually craved foods with higher energy (calorie) density, compared with those who lost a lower percentage of body weight," says Roberts, who is also a professor at the Friedman School of Nutrition Science and Policy at Tufts University. "Energy-dense foods, such as chocolate and some salty snacks, are those that pack the most calories per unit of volume," explains Cheryl Gilhooly, PhD, MPH, research dietitian and first author of the study, "as compared to less energy-dense foods like fruits and vegetables, which have fewer calories per unit of volume."

"These findings suggest," says corresponding author Susan Roberts, PhD, director of the USDA HNRCA's Energy Metabolism Laboratory. Roberts, "that cravings are for calories, not carbohydrate, as is widely assumed. What is commonly called carbohydrate addiction should probably be relabeled as calorie addiction," she added. Some of the most commonly craved foods among study participants were foods that have high sugar plus fat, such as chocolate, and salty snacks, such as chips and French fries. "The craved foods do have carbohydrate, but they also have fat, and some protein, too. The most identifiable thing about the foods people crave is that they are highly dense in calories," Roberts deduces.

The study, which was part of the one-year CALERIE trial, involved 32 overweight but otherwise healthy women, 20 to 42 years of age, who were randomly assigned to two diets that differed in glycemic load, a measurement of how quickly the carbohydrates in a person's diet are converted to blood sugar.

*"The craved foods do have carbohydrate, but they also have fat, and some protein, too. The most identifiable thing about the foods people crave is that they are highly dense in calories,"* she added.

The study, published in the *International Journal of Obesity*, states that food cravings are normal, with 91 per cent of study participants reporting having food cravings. Dieting also seemed to increase cravings.

*"In fact, 94 per cent of the study participants reported cravings after six months of dieting,"* said Roberts. *"However, participants who lost a greater percentage of body weight gave in to their cravings less frequently. Allowing yourself to have the foods you crave, but doing so less frequently may be one of the most important keys to successful weight control."*

The study, which was part of the one-year Comprehensive Assessment of the Long-term Effects of Restricting Intake of Energy (CALERIE) trial, involved 32 overweight but otherwise healthy women, 20 to 42 years of age, who were randomly assigned to two diets that differed in glycemic load.

Participants completed food craving questionnaires assessing the type of foods craved, the frequency and strength of cravings, and how often cravings led to eating the desired food.

*"This is the first study of long-term changes in food cravings in a calorie-restriction program,"* said Roberts and they conclude that cravings for energy-dense foods are common. Although they caution that additional long-term studies are needed to confirm their findings, they write that their results "...suggest that people attempting to lose weight and maintain weight loss may benefit from advice to accept that food cravings may not decrease in frequency." Controlling the frequency of giving in to cravings, rather than suppressing them, they say, may be an important area of emphasis in future weight control programs.

Primary results from the CALERIE study were reported in an earlier issue of *Friedman Nutrition Notes*, available at <http://nutrition.tufts.edu/news/notes/2007-03.html>.

*International Journal of Obesity*- Published on-line ahead of print, doi: 10.1038/sj.ijo.0803672  
*"Food cravings and energy regulation: the characteristics of craved foods and their relationship with eating behaviors and weight change during 6 months of dietary energy restriction."* Authors: C.H. Gilhooly, S.K. Das, J.K. Golden, M.A. McCrory, G.E. Dallal, E. Saltzman, F.M. Kramer, S.B. Roberts

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Item 13

### **Magic Pill to Eliminate Disease and Add Years to Life**

*A molecular compound found in red wine called resveratrol extends the life span of mice by up to 24 percent and up to 59 percent in other animals like flies and fish.*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4977>

David Sinclair, Ph.D., of Harvard Medical School and his colleagues are developing a pill to prevent age-related diseases like cancer, Alzheimer's and heart disease, and add years to a person's life.

Sinclair who discovered the compound has since co-founded a company called Sirtris Pharmaceuticals. Sirtris researchers are beginning to run studies on a formulation of resveratrol in people with diabetes, with the goal to lower blood glucose levels.

Dr. Sinclair stated that, modern medicine is based on treating one disease at a time. But what drugs haven't done is target the natural defense mechanisms of our bodies. He explained, "The body is a pretty clever and complex organism. It's not the molecules themselves that are miraculous. It's the genes that have evolved to protect the body."

The premise behind a formulation of resveratrol is that it activates a gene called SIRT-1, which may regulate lifespan by being activated by caloric restriction. Mice live longer when they have 30 percent to 40 percent fewer calories than they would normally. Resveratrol may mimic caloric restriction.

Dr. Sinclair said he doesn't believe humans will ever live hundreds of years, but with something like resveratrol, we could add on another decade. He said, "The best way to put it is that this is one of the best shots to have a big impact on medicine."

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**FACT:**

**Food Cravings For Calories Not Carbs, Says Obesity-Related Study:** *People with food cravings want calories, not carbohydrates, says a news study from the US that may have implications for obesity.* "These findings suggest," says author Susan Roberts, PhD, director of the USDA HNRCA's Energy Metabolism Laboratory. "That cravings are for calories, not carbohydrate, as is widely assumed. What is commonly called carbohydrate addiction should probably be relabeled as calorie addiction." **See this week's Item #12**

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Item 14

**Low Glycemic Index Diets Better for Weight Loss**

*The review found that dieters focused on eating low GI foods dropped significantly more weight – about 2.2 pounds more – than participants on other diets. Low GI dieters also experienced greater decreases in body fat measurements and body mass index.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4976>

Put aside the white bread and pick up an apple. A diet of foods less likely to spike blood sugar levels helps dieters lose more weight, according to a new systematic review from Australia.

"Losing weight is very difficult and many people are unable to sustain a weight-loss diet. The low glycemic index diet is satisfying and has proven benefits," said review co-author Elizabeth Elliott, Ph.D., professor at the University of Sydney, The Children's Hospital at Westmead.

The glycemic index (GI) ranks carbohydrate-rich foods based on their effect on blood sugar levels. Compared to high GI foods such as white rice and French fries, low GI foods, such as lentils, sweet potatoes and apples produce more consistent blood glucose levels. Previous studies have indicated that keeping blood sugar levels steady throughout the day may stimulate more weight loss in obese people.

Researchers evaluated randomized controlled trials that compared weight loss in people eating foods low on the glycemic index to weight loss in people on higher GI diets or other types of weight loss plans.

Six trials, involving 202 adults from Australia, France, South Africa, Denmark and the United States were included in the review. The diets lasted from five weeks to six months.

None of the studies reported adverse effects associated with consuming a low glycemic index diet. "Compared to other diets, the low GI diet is more satisfying – people are less inclined to feel hungry. One advantage of this type of diet is that it is more likely to be maintained than other strict diets on which people feel hungry," Elliott said.

Low glycemic diets appear to be effective even in obese people who need to lose considerable amounts of weight, the authors said.

In the two studies that evaluated only obese participants, low GI dieters lost about 9.2 pounds, compared with about 2.2 pounds shed by other dieters.

Low glycemic index diets might also benefit heart health.

In the three studies that measured cardiovascular risk factors, people eating low GI foods experienced greater improvements in total blood cholesterol and low-density lipoprotein (LDL) – sometimes called "bad" cholesterol.

Low glycemic index diets can be effective for weight management, Cheskin said, but the success of low glycemic diets lies with an individual's willingness to comply with its nutritional principles. "There aren't many people who need to lose weight who are willing to eat lots of vegetables and whole grains. If they did, they wouldn't have a weight problem in the first place," Cheskin said.

Nevertheless, he said, choosing foods low on the glycemic index does have value for overweight or obese people who want to lose weight.

"It uses a lot of the generally healthful principles, such as eating lots of vegetables and high fiber and avoiding very energy-dense foods that are high in simple sugars and simple carbohydrates," Cheskin said.

*Thomas, DE, Elliott EJ, Baur L. Low glycaemic index or low glycaemic load diets for overweight and obesity. (Review). Cochrane Database of Systematic Reviews 2007, Issue 3. Visit <http://www.cochrane.org> for more information.*

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Item 15

**Less Insulin In the Brain Key to a Long Life**

*Good, old-fashioned diet and exercise might keep you young by reducing the action of insulin in the brain, researchers reported on Thursday.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4975>

The investigators created mutant mice that over-ate, got fat and even had symptoms of diabetes, and yet lived 18 percent longer than normal lab mice. The secret: they lacked a certain key gene that affects insulin, the hormone that regulates glucose.

The genetic engineering mimicked the effects of eating less and exercising, the researchers report in the journal Science.

"This study provides a new explanation of why it's good to exercise and not eat too much," said Dr. Morris White, a Howard Hughes Medical Institute investigator at Children's Hospital in Boston who led the study.

The findings also raise questions about how desirable it is to use insulin to treat type 2 diabetes, said the researchers.

Doctors know that people who exercise regularly live longer on average. Researchers have also learned that putting animals on a strict diet makes them live longer, although this has not yet been shown to work in people.

So White's team sought to see if the two effects were linked. They looked at insulin, because both fasting and exercise make cells more insulin-sensitive, meaning they respond more efficiently to the effects of insulin. They looked at the entire insulin pathway -- a series of actions in the cell that control the body's use of insulin.

White's team engineered mice that had no working copies of one of the genes involved in this pathway, called insulin receptor substrate 2 (Irs2). Mice with no copies of Irs2 had defective brains and diabetes. But mice with one working copy lived 18 percent longer than normal mice.

"What's more, the animals lived longer even though they had characteristics that should shorten their lives such as being overweight and having higher insulin levels in the blood," White said in a statement.

They were also more active than normal mice, and after eating, their brains had higher levels of a compound called superoxide dismutase, an antioxidant that protects cells from damage.

"Diet, exercise and lower weight keep your peripheral tissues sensitive to insulin," White said. That means the body needs to make less insulin. "Since insulin turns on Irs2 in the brain, that means lower Irs2 activity, which we've linked to longer life span in the mouse," he said.

One obvious question is whether drugs can mimic the effects of having less Irs2, perhaps by interfering with its action. The researchers note that people who live to be 100 or more often have reduced insulin levels and their cells show better insulin sensitivity.

New diabetes drugs that increase insulin sensitivity may help, too, White said. But, he added: "The easiest way to keep insulin levels low in the brain is old-fashioned diet and exercise."

Journal Science July 2007

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## **Quote of the Week!**

*“You don't have to let your life be destroyed by diabetes. You can reclaim your life.”*

.....Della Reese

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**Richard K. Bernstein's New Book, Diabetes Solution 2007 is available.** Containing new and revised information, this new book is on special at <http://www.diabetes911.net>. Also Dr. Bernstein's New 5 CD Set "Secrets to Normal Blood Sugars" is available. Recorded Individually For Type 1 and Type 2 Diabetes, These "LIVE" 5 CD Sets Contain The Personal Diabetes Education Program taught by Dr. Bernstein to his patients.

**LIVE WEBCAST:**

Dr. Bernstein will participate in another 60 minute Tele-Seminar on August 8, 2007, at 7:00 PM CST, 8:00 PM EST and 5:00 PM West Coast time, that we invite you to attend, and ask your patients to attend. In addition to calling in, this upcoming call will also be broadcast through a LIVE web-cast on the Internet. Don't miss it. Click here to register for this free teleconference.

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