

# DIABETES IN CONTROL.com Newsletter

The Newsletter for Professionals in Diabetes Care

July 11, 2007 - Issue #372

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## Top Diabetes Stories:

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**New Lower BP Targets for Diabetics and High-Risk Established CAD Patients\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4953>

**Portion-Control Dishes Helps Obese Diabetics Lose Weight\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4951>

**Vitamin D, Calcium May Prevent, Improve Diabetes\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4950>

**Risk of Stroke is High Within 5 Yrs. of Treatment of Diabetes\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4949>

**Impaired Fasting Glucose Increases Risk Factors for CVD Mortality\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4948>

**Exercise Key in Control of Type 2 Diabetes: 103 Studies\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4946>

**New Definition to Identify Children at Risk of Developing Metabolic Syndrome\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4945>

**Anti-Fat Injection Can Melt Fat Away, Reducing Risk for Metabolic Syndrome\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4942>

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## From the editor's desk

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Nowadays we often take glucose testing, insulin dosing and carb counting for granted. But can you imagine a time when it was not acceptable to use this method of diabetes control. In 1980 after considerable rejections, **Richard K. Bernstein, M.D., F.A.C.E., F.A.C.N., C.W.S.** finally got his own experience in controlling published in Diabetes Care. He had been trying since 1973 and actually went to Medical School at the age of 46, just so he could get published. Remember this was finally published 13 years before, the DCCT trials, where they discovered that tight control was effective in preventing the complications from diabetes. Dr. Bernstein was ahead of his time and still is. [Click here to read that original abstract. \(pdf\)](#)  
[http://www.diabetesincontrol.com/issues/Issue\\_372/DiabetesCare1980Bernstein.pdf](http://www.diabetesincontrol.com/issues/Issue_372/DiabetesCare1980Bernstein.pdf)

The information we learn about diabetes is often fragmented and usually out of order. If you want a natural progression of usable information I recommend you check out [DM EDUCATE? , COMPREHENSIVE ONLINE DIABETES MANAGEMENT COURSE](#) to learn more,  
<http://www.diabetesincontrol.com/results.php?storyarticle=4904>

*Have you ever said why didn't I think of that?* Well for the past 40 years we have been treating hypertension by blocking fluid reuptake in the kidneys. So how come you or I never thought of blocking glucose reuptake? Well someone did and you will want to remember **SGLT2** a renal low-affinity sodium-glucose co-transporter. Current research on Sertigliflozin by GSK show the promise of a whole new class of drugs. While I was at ADA, I spoke with **John Malone, MD, FACE, of the Pediatric Endocrinology Department of the University of South Florida** in Tampa. I asked him what the most interesting thing he saw was. His reply "There is this neat little drug that blocks reuptake of glucose in the kidneys and you just pee off the excess". Stay tuned for more info.

**Would you be interested in going on a diabetes cruise?** We are planning a 9 day Diabetes Education Cruise with Dr. Richard K. Bernstein for next spring or fall. We will provide 16-20 Hours of CME and CE for medical professionals to learn Dr. Bernstein's treatment methods and education for patients with diabetes. Medical professionals who attend will be offered the opportunity to become part of the referral list for patients. If you might be interested, just send us an email with "Diabetes Cruise" in the subject line. **THIS IS A ONCE IN A LIFETIME OPPORTUNITY!** We will need a least 100 participants to make this happen. Send to [publisher@diabetesincontrol.com](mailto:publisher@diabetesincontrol.com)

## July 15, 7PM ET on CNBC – SUMMER SEASON PREMIERE!

It's "Diabetes Hardball" when Nicole Johnson turns the tables on MSNBC's Chris Matthews; Dr. Aaron Vinik talks about advances in treating diabetic neuropathy; and in Real People, Real Stories, a Connecticut woman who uses yoga to lower her blood sugar and stress. Tune in for the exciting season premiere of dLifeTV: Sundays on CNBC at 7 PM ET, 6 PM CT, and 4 PM PT Check your local listings for details.

We can make a difference!

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**This week's overview:**

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- Item #2: 14.5 Billion of Potential Savings by Using Technology in Diabetes Management
- Item #7: Yogurt Can Help Delay Diabetes
- Item #10: ADA: Lipid Effects of Diabetes Agents May Protect Arterial Function
- Item #11: Scientists Working On A New Insulin Pill
- Item #13: It's Official - Stress Makes You Fat
- Item #14: Beta-Blockers Exert Anti-Atherosclerotic Effects
- Item #15: ADA: New Drug Alogliptin Controls Glucose Without Risk of Hypoglycemia

Check out this weeks **“Test Your Knowledge”** question. This week’s question deals with CGMS.  
<http://www.diabetesincontrol.com/results.php?storyarticle=4954>

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

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**Tools for your Practice:**  
**USING HUMOR IN DIABETES EDUCATION**

Healthcare is a serious business, so using humor as a therapeutic tool to assist people may not be in the forefront of your mind. **Theresa L. Garner** has prepared a handout to help us overcome our sometimes over serious manners and learn the necessary skills to use humor.  
<http://www.diabetesincontrol.com/results.php?storyarticle=4955>

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**New Product:**

**Portion Control Plates:** A plate and cereal bowl with markers for proper portion sizes appear to help obese patients with diabetes lose weight and decrease their use of glucose-controlling medications, according to a report in the June 25 issue of *Archives of Internal Medicine*, one of the *JAMA/Archives* journals. The plates were divided into sections for carbohydrates, proteins, cheese and sauce, with the rest left open for vegetables. The sections approximately totaled an 800-calorie meal for men and a 650-calorie meal for women. The cereal bowl is designed to allow a 200-calorie meal of cereal and milk. More info at [www.portiondoctor.com](http://www.portiondoctor.com)  
See this week’s Item #3



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**This Week’s Items:**

- 1. **New Lower BP Targets for Diabetics and High-Risk Established CAD Patients\***  
<http://www.diabetesincontrol.com/results.php?storyarticle=4953>

## **2. 14.5 Billion of Potential Savings by Using Technology in Diabetes Management**

<http://www.diabetesincontrol.com/results.php?storyarticle=4952>

## **3. Portion-Control Dishes Helps Obese Diabetics Lose Weight\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4951>

## **4. Vitamin D, Calcium May Prevent, Improve Diabetes\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4950>

## **5. Risk of Stroke is High Within 5 Yrs. of Treatment of Diabetes\***

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## **10. ADA: Lipid Effects of Diabetes Agents May Protect Arterial Function**

<http://www.diabetesincontrol.com/results.php?storyarticle=4944>

## **11. Scientists Working On A New Insulin Pill**

<http://www.diabetesincontrol.com/results.php?storyarticle=4943>

## **12. Anti-Fat Injection Can Melt Fat Away, Reducing Risk for Metabolic Syndrome\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4942>

## **13. It's Official - Stress Makes You Fat**

<http://www.diabetesincontrol.com/results.php?storyarticle=4941>

## **14. Beta-Blockers Exert Anti-Atherosclerotic Effects**

<http://www.diabetesincontrol.com/results.php?storyarticle=4940>

## **15. ADA: New Drug Alogliptin Controls Glucose Without Risk of Hypoglycemia**

<http://www.diabetesincontrol.com/results.php?storyarticle=4939>

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## **ITEMS For The Week:**

Item 1

### **New Lower BP Targets for Diabetics and High-Risk Established CAD Patients**

*It has changed from 140/90 mm Hg to 130/80*

<http://www.diabetesincontrol.com/results.php?storyarticle=4953>

Blood pressure (BP) targets in men and women with established coronary artery disease (CAD), or who are at high risk of developing CAD should be 130/80 mm Hg; lower than those specified in the Joint National Committee (JNC) 7th report of 140/90 mm Hg, a new American Heart Association Scientific Statement specifies.

The BP target of 140/90 remains appropriate for general CAD prevention, the writing group, led by Dr Clive Rosendorff (Mount Sinai School of Medicine, New York, NY), says.

The JNC 7th report currently recommends that the lower target of 130/80 mm Hg be used in patients with diabetes or chronic kidney disease (CKD); the new statement suggests this group should be broadened. "When people walk into their doctors' offices with systolic pressures between 130 and 140, most primary care doctors and many cardiologists would believe that patient had normal blood pressure and wouldn't require additional treatment," Rosendorff said that, "We have tried to show that in fact there is a great deal to be gained by treating those patients to lower levels."

The statement deals both with primary prevention patients — divided into "general" prevention or high CAD risk — as well as patients with pre-existing CAD in different forms: stable angina; unstable angina/non-ST elevation MI; ST-elevation MI; heart failure secondary to CAD. Patients in the high-risk category are defined as patients who also have diabetes, CKD, known CAD, a CAD-risk equivalent (carotid disease, peripheral artery disease, or abdominal aortic aneurysm), or a ten-year Framingham risk score = 10%; these patients should all have their BP lowered to < 130/80 mm Hg, as would patients with pre-existing CAD. In patients with heart failure, physicians should consider a target even lower, the authors suggest, < 120/80 mm Hg, although blood pressure lowering should be slow, they caution.

Authors of the statement also provide recommendations for drug therapy, according to CAD status. In keeping with recent European guidelines, beta-blockers are no longer recommended for blood pressure control in the primary prevention group.

"There have been lots of comparative clinical trials to show that for preventing both stroke and CAD complications, beta-blockers are inferior to newer classes of drugs like ACE inhibitors, angiotensin-receptor blockers, or calcium channel blockers, so we have dropped beta-blockers right out of the picture for prevention," Rosendorff explained. "However, once there is established, occlusive CAD, with symptoms like angina or acute MI, then beta-blockers come right back to center stage."

### Practice Pearls

- ?? Approximately one quarter of US adults have prehypertension and one quarter have hypertension, respectively. Systolic BP increases gradually as adults grow older, and it is a stronger predictor of ischemic heart disease than diastolic BP among adults older than 60 years.
- ?? The current guidelines recommend that initial treatment of hypertension among patients without known heart disease or diabetes may include ACE inhibitors, ARBs, calcium channel blockers, or thiazide diuretics.

*Circulation. 2007;115:2761-2788.*

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

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#### Item 2

### 14.5 Billion of Potential Savings by Using Technology in Diabetes Management

*A recent report funded by The Robert Wood Johnson Foundation identified this information technology-enabled diabetes management.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4952>

This is significant since diabetes tallies \$132 billion in annual health care costs. The study found that all forms of information technology-enabled diabetes management (ITDM) can improve care processes, delay complications and save health care costs. Examples of ITDM include:

- ?? diabetes registries
- ?? clinical decision support systems
- ?? remote monitoring

However, after simulating a decade of ITDM, researchers discovered that electronic diabetes registries saved the most—**\$14.5 billion**. Furthermore, when implemented nationally, only diabetes registries were shown to be cost beneficial.

The findings underscore the importance of combining chronic disease management and information technology into the current health care system. The current system tends to focus on acute care, even though chronic illnesses such as diabetes account for the majority of health care costs.

The full report is accessible at: . <http://www.citl.org/research/ITDM.htm>

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## DID YOU KNOW:

**Men with diabetes talk as much as women with diabetes:** Turns out, when you actually count the words, there isn't much difference between the sexes when it comes to talking. A team led by Matthias R. Mehl, an assistant professor of psychology at the University of Arizona, came up with the finding, which is published in Friday's issue of the journal *Science*. The researchers placed microphones on 396 college students for periods ranging from two to 10 days, sampled their conversations and calculated how many words they used in the course of a day. The score: Women, 16,215. Men, 15,669. The difference: 546 words: "Not statistically significant," say the researchers. "What's a 500-word difference, compared with the 45,000-word difference between the most and the least talkative persons" in the study, said Mehl.

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Item 3

### **Portion-Control Dishes Helps Obese Diabetics Lose Weight**

*A plate and cereal bowl with markers for proper portion sizes appear to help obese patients with diabetes lose weight and decrease their use of glucose-controlling medications, according to a new report.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4951>

Between 1960 and 2000, the proportion of U.S. adults who were obese increased from 13.4 percent to 30.9 percent, according to background information in the article. Most cases of type 2 diabetes can be attributed directly to obesity. Restricting calories has been shown to improve blood sugar control in diabetics, partially by contributing to weight loss. "The increasing prevalence of obesity is paralleled by increasing portion sizes in the marketplace," the authors write. "Portion sizes are an important determinant of energy intake; the number of calories ingested by subjects at a meal has been directly correlated with the serving size offered."

Sue D. Pedersen, M.D., F.R.C.P.C., and colleagues at the University of Calgary, Alberta, Canada, conducted a six-month controlled trial of commercially available portion control plates and bowls in 2004. The plates were divided into sections for carbohydrates, proteins, cheese and sauce, with the rest left open for vegetables. The sections approximately totaled an 800-calorie meal for men and a 650-calorie meal for women. The cereal bowl is designed to allow a 200-calorie meal of cereal and milk. Half of 130 obese patients with diabetes (average age 56) were randomly assigned to use the plate for their largest meal and the bowl when they ate cereal for breakfast. The other half of the participants received usual care, which consisted of dietary assessment and teaching by dietitians.

At the end of the six-month follow-up, 122 patients remained in the study. Individuals using the portion-control dishes lost an average of 1.8 percent of their body weight, while those receiving usual care lost an average of 0.1 percent. A significantly larger proportion of those using the dishes—16.9 percent vs. 4.6 percent—lost at least 5 percent of their body weight. "This is important, as a 5 percent weight loss has been shown to be clinically significant in terms of decreasing morbidity and mortality associated with obesity-linked disorders such as cancer and myocardial infarction [heart attack]," the authors write.

In addition, more of those in the intervention group vs. the regular care group experienced a decrease in their use of diabetes medications after six months (26.2 percent vs. 10.8 percent).

"In conclusion, the portion control tool studied in this trial was effective in inducing weight loss in obese persons with type 2 diabetes mellitus comparable to that seen in investigations of weight loss pharmacotherapy," the authors write. "This simple, inexpensive tool also enabled obese patients with diabetes mellitus to decrease their hypoglycemic medication requirements. This intervention holds promise for use in overweight populations with and without diabetes mellitus."

See this week's New Product for information on the portion control plates.

*Arch Intern Med.* 2007;167:1277-1283.

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Do you have patients who could benefit from an insulin pen with memory? HumaPen® MEMOIR for use with Humalog® (insulin lispro) is the first insulin pen with a memory that records date, time, and amount of the last 16 doses, including priming doses. As part of a multiple-daily injection regimen, your patients can gain greater flexibility. Depending on your patients' lifestyles, a Humalog® or Humalog® Mixture insulin may be prescribed. Find important safety and prescribing information on Humalog® and Humalog® Mixture insulins at

Item 4

### **Vitamin D, Calcium May Prevent, Improve Diabetes**

*Combined supplementation with vitamin D and calcium may improve blood sugar and insulin levels and prevent diabetes by 64%, suggests a new meta-analysis and review.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4950>

*Although the evidence to date suggests that vitamin D and calcium deficiency influences post-prandial glycemia and insulin response while supplementation may be beneficial in optimizing these processes, our understanding of the exact mechanisms by which vitamin D and calcium may promote beta cell function, or ameliorate insulin resistance and systemic inflammation is incomplete," wrote lead author Anastassios Pittas.*

*"It is also not clear whether the effects are additive or synergistic," he added.*

Vitamin D refers to two biologically inactive precursors - D3, also known as cholecalciferol, and D2, also known as ergocalciferol. The former, produced in the skin on exposure to UVB radiation (290 to 320 nm), is said to be more bioactive. The latter is derived from plants and only enters the body via the diet, from consumption of foods such as oily fish, egg yolk and liver.

Both D3 and D2 precursors are hydroxylated in the liver and kidneys to form 25- hydroxyvitamin D (25(OH)D), the non-active 'storage' form, and 1,25-dihydroxyvitamin D (1,25(OH)2D), the biologically active form that is tightly controlled by the body

Writing in the *Journal of Clinical Endocrinology & Metabolism*, Pittas and co-workers reviewed data from observational studies and clinical trials in adults with results related to the control of glucose. The data from observational studies showed a "relatively consistent association" between low intakes of calcium, vitamin D, or dairy intake and type-2 diabetes, with highest levels associated with a 64 per cent lower prevalence of the disease, and a 29 per cent lower prevalence of metabolic syndrome among non-blacks.

When intake of calcium and vitamin D was combined, the inverse associations were still observed, with the highest versus lowest combined intake being associated with an 18 per cent lower incidence of diabetes.

*"Evidence from trials with vitamin D and/or calcium supplementation suggests that combined vitamin D and calcium supplementation may have a role in the prevention of type-2 diabetes only in populations at high risk (i.e. glucose intolerance)," wrote the reviewers from Tufts-New England Medical Center.*

They noted that research into this area remains limited and called for future research to focus on clarifying and quantifying the link between calcium intake and 25(OH)D levels and the incidence of type-2 diabetes.

*Journal of Clinical Endocrinology & Metabolism- June 2007, Volume 92, Number 6, Pages 2017-2029. doi:10.1210/jc.2007-0298 "The Role of Vitamin D and Calcium in type 2 diabetes. A systematic Review and Meta-Analysis" Authors: A.G. Pittas, J. Lau, F. Hu, B. Dawson-Hughes*

### **Start your own walking program**



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### **FACT:**

**Women Who Drink a Little May Lower Heart-Attack Risk:** Researchers studied 320 women ages 35 to 69 who had had heart attacks, comparing them with 1,565 healthy women matched for age. After adjusting for

age, race, education, smoking and body mass index, women who had a daily alcoholic drink had a 31 percent reduced risk of a nonfatal heart attack compared with those who drink less than one drink a day. But among those who drank at all, becoming drunk even once a month — and by that the researchers mean drinking enough to cause slurred speech or unsteady gait — led to an almost sixfold increase in the likelihood of a heart attack. The message is that a small amount is O.K., and drinking to intoxication can be harmful.” *the journal Addiction, May 2007*

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Item 5

**Risk of Stroke is High Within 5 Yrs. of Treatment of Diabetes**

*Risk of stroke is high within 5 years of treatment for type 2 diabetes and more than double that for the general population. More Reason to recommend an aspirin a day*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4949>

Cardiovascular risk factors are suboptimally treated in diabetes, possibly because of the impression that there is a long delay between diagnosis and the development of macrovascular complications such as stroke. The researchers from Canada determined the incidence of stroke in people newly treated for type 2 diabetes. They conducted an inception cohort study with the use of linked administrative databases from Saskatchewan Health. Subjects entered the type 2 diabetes cohort on receipt of their first prescription for an oral antidiabetic drug. They defined incident stroke as any hospital admission with International Classification of Diseases, Ninth Revision, codes 430 to 438 inclusive. Age-standardized incidence rates were compared between the diabetes cohort and the general population. There were 12 272 subjects in the diabetes cohort, the mean age was 64 years, and 55% were male.

They found that during a mean 5-year follow-up, 9.1% of the diabetes cohort had a stroke. The age-standardized incidence rate for stroke was 642 per 100 000 person-years in subjects with diabetes, compared with 313 per 100 000 person-years in the general population (rate ratio=2.1). The relative short-term risk for stroke in the diabetes cohort compared with the general population ranged from 1.8 in persons >75 years to 5.6 in the 30 to 44-year category.

The researchers concluded: "The risk of stroke is high within 5 years of treatment for type 2 diabetes and more than double the rate for the general population. This further supports the need for aggressive early cardiovascular risk factor management in type 2 diabetes."

These figures are of concern and do not include those not commenced on an oral hypoglycemic.

**Stroke 2007;38:1739. June 2007.** *Short-Term Risk for Stroke Is Doubled in Persons With Newly Treated Type 2 Diabetes Compared With Persons Without Diabetes: A Population-Based Cohort Study, Thomas Jeerakathil, MD, Msc, Jeffrey A. Johnson, PhD, Scot H. Simpson, PharmD, MSc and Sumit R. Majumdar, MD, MPH. Correspondence to Dr Thomas Jeerakathil*

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Do you have patients in pain? Over 5,000 Anodyne Therapy Care Providers in 35 countries worldwide are helping thousands of patients per month with painful, circulatory problems get relief. To learn how you can help your patients get back to life, click here.  
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Item 6

**Impaired Fasting Glucose Increases Risk Factors for CVD Mortality**

*New studies are showing that we must treat impaired fasting glucose more aggressively.*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4948>

Diabetes mellitus is a well-established risk factor for cardiovascular disease (CVD) and all-cause mortality. These Australian investigators sought to compare the mortality risks of diabetes with those of less marked levels of hyperglycemia, impaired fasting glucose and impaired glucose tolerance while adjusting for concomitant CVD risk factors. The population-based sample of more than 11,000 people 25 years and older included demographic, health history, anthropomorphic, and laboratory data collected on enrollment in 1999-2000. Categories of abnormal glucose metabolism were determined based on 1999 World Health Organization criteria. These data were linked to the Australian National Death Index through June 2005. Persons not appearing in the death index were assumed to be alive.

Follow-up was a median of 5.2 years. Deaths in persons 25-44 were too low for meaningful analysis. For those 65 or over deaths were higher in diabetics, but otherwise there was not a consistent picture. After adjusting for age, sex and other established CVD risk factors, diabetes and impaired fasting glucose were both independent risk factors for CVD mortality with similar hazard ratios, but impaired glucose tolerance was not.

The authors concluded: "This study emphasizes the strong association between abnormal glucose metabolism and mortality, and it suggests that this condition contributes to a large number of CVD deaths in the general population. CVD prevention may be warranted in people with all categories of abnormal glucose metabolism."

*This study demonstrates the need for intervention trials to prevent CVD mortality in patients with impaired fasting glucose.*

*Circulation. 2007;116: June 2007. Risk of Cardiovascular and All-Cause Mortality in Individuals With Diabetes Mellitus, Impaired Fasting Glucose, and Impaired Glucose Tolerance. The Australian Diabetes, Obesity, and Lifestyle Study (AusDiab), E.L.M. Barr MPH, P.Z. Zimmet PhD, T.A. Welborn PhD, D. Jolley MSc, D.J. Magliano PhD, D.W. Dunstan PhD, A.J. Cameron MPH, T. Dwyer MD, H.R. Taylor MD, A.M. Tonkin MD, T.Y. Wong PhD, J. McNeil PhD, and J.E. Shaw MD*

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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

**Yogurt Can Help Delay Diabetes**

*Homemade curd delays onset of diabetes, slowing down the progression of diabetes, lowering bad cholesterol and raising heart-protective good cholesterol. The findings have been reported in the latest issue of international journal Nutrition.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4947>

The study, conducted by the National Dairy Research Institute in Karnal, Haryana, examined the effect of bacteria found in homemade yoghurt — made from skimmed, cow or buffalo milk — on blood glucose, insulin, lipid levels and liver glycogen on a group of rats. Yoghurt came out the winner on all fronts.

"The results confirmed that curd containing probiotic bacteria, Lactobacillus acidophilus and Lactobacillus casei, exhibited a significant delaying effect on the progression of diabetes induced by high fructose administration in rats," says lead author Hariom Yadav with the Animal Biochemistry Division at the National Dairy Research Institute.

For the research, rats were divided into three groups. One group was fed a normal diet, the second was given a diet with fructose solution and the third was put on a diet with the fructose solution and supplemented with curd.

After eight weeks, researchers reported that fasting blood glucose levels had increased in both fructose-fed groups, but the rate was significantly less in the curd group.

"Yoghurt is a staple of Indian diet. Studies have earlier linked yoghurt with improved lipids but this is the first time a protective benefit has been established for diabetes," says Dr Anoop Misra, department of diabetes and metabolic diseases, Fortis Group of Hospitals.

The study has yet to be duplicated in humans but the obvious question is how much yogurt should one consume?

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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

### **Exercise Key in Control of Type 2 Diabetes: 103 Studies**

*The review found, studies that focused only on boosting exercise levels yielded greater benefits than those that tried to change patients' diets, exercise habits and medication adherence all at once.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4946>

People with type 2 diabetes may go a long way in managing their condition if they take up regular exercise, a new research review shows.

Researchers found that when they combined the results from 103 studies, there was clear evidence that lifestyle changes helped people with type 2 diabetes gain better control over their blood sugar.

But while diet, exercise and medication are all vital to diabetes management, exercise alone was effective in these studies.

In fact, the review found, studies that focused only on boosting exercise levels yielded greater benefits than those that tried to change patients' diets, exercise habits and medication adherence all at once.

The findings "could mean that it is easier for people to focus on one thing at a time," lead study author Dr. Vicki Conn said in a statement. "It is easy for people to get overwhelmed when asked to make too many changes."

For their study, the researchers combined the results of 103 studies that involved a total of 10,455 adults with type 2 diabetes, a disorder in which the body cannot properly use the blood-sugar-regulating hormone insulin.

Type 2 diabetes is closely linked to obesity, and diet, exercise and adherence to medication are the cornerstones of managing the disease. But Conn's team found that blood sugar improvements were twice as great in studies that focused on exercise alone than in those that tried to improve diet, exercise and medication adherence.

Importantly, the researchers point out, exercise helped study participants regardless of their weight or how poor their blood sugar control had been in the past.

"The improvements from exercise," Conn said, "were equal across the board."

*Diabetologia May 2007.*

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## **FACT:**

**Insulin's 85<sup>th</sup> anniversary:** On 23 January 1922, the first injection of a pancreatic extract into a human patient was carried out at Toronto General Hospital, Canada. The 14-year-old patient, Leonard Thomson, had been diagnosed with diabetes two-and-a-half years earlier. He was emaciated, pale, and exhausted by the disease and the diet of just 450 calories per day. However after the treatment with the purified pancreatic extract, Thomson achieved significant improvements in his general health and well-being after only few days.

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Item 9

### **New Definition to Identify Children at Risk of Developing Metabolic Syndrome**

*The International Diabetes Federation (IDF) has developed a new definition of metabolic syndrome to help identify children at risk of developing the syndrome.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4945>

"The metabolic syndrome in adults is defined as a cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus, which include abdominal obesity, dyslipidemia, glucose intolerance, and hypertension," write Paul Zimmet, MD, PhD, from the International Diabetes Institute in Melbourne, Victoria, Australia, and colleagues from the IDF Task Force on Epidemiology and Prevention of Diabetes. "In 2005, the [IDF] published its definition of the metabolic syndrome in adults. However, to date no unified definition exists to assess risk or outcomes in children and adolescents."

To meet the need for an easy-to-use, clinically accessible diagnostic tool to identify metabolic syndrome in children and adolescents, the IDF developed a new, simple definition, extending previous studies using modified adult criteria to investigate prevalence in young people.

Because of insufficient data in children younger than 6 years, this age group was excluded from the definition.

In children aged 6 to younger than 10 years, the IDF definition of the at-risk group for later development of metabolic syndrome consists of obesity (waist circumference = 90th percentile). Although metabolic syndrome should not be diagnosed in this age group, a strong message for weight reduction should be delivered for those with abdominal obesity, and further measurements should be made if there is a family history of metabolic syndrome, type 2 diabetes, dyslipidemia, cardiovascular disease, hypertension, or obesity.

In adolescents aged 10 to younger than 16 years, metabolic syndrome can be diagnosed by abdominal obesity (waist circumference = 90th percentile, or adult cutoff if lower) and the presence of 2 or more other clinical features (triglycerides = 1.7 mmol/L; high-density lipoprotein cholesterol < 1.03 mmol/L; blood pressure = 130 mm Hg systolic or = 85 mm Hg diastolic; glucose = 100mg/dL ( 5.6 mmol/L) [oral glucose tolerance test recommended]; or known type 2 diabetes).

For adolescents older than 16 years, existing IDF criteria for adults should be used.

"Early identification of children who are at risk of developing the syndrome, type 2 diabetes mellitus, and cardiovascular disease in later life is important," the authors write. "Circumstances in utero and in early childhood predispose a child to disorders such as obesity, dysglycemia, and the metabolic syndrome. Furthermore, urbanization, unhealthy diet, and sedentary lifestyle are major contributors to such disorders."

"Early detection followed by treatment — particularly lifestyle intervention — is vital to halt the progression of the metabolic syndrome in children and adolescents," the authors conclude. "Such action should reduce morbidity and mortality in adulthood and help keep to a minimum the global burden of cardiovascular disease and type 2 diabetes mellitus. Governments and society must be made more aware of the problems associated with obesity and the likelihood of progression to the metabolic syndrome in children and adolescents."

*Lancet. 2007;369:2059-2061.*

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Item 10

**ADA: Lipid Effects of Diabetes Agents May Protect Arterial Function**

*Lipoprotein subfraction changes may be at the root of the dyslipidemia accompanying type 2 diabetes and help explain how thiazolidinediones improve carotid intima-media thickness.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4944>

High-density and low-density lipoprotein particle size and concentration were significantly improved with pioglitazone (Actos) compared with glimepiride (Amaryl), found Peter M. Meyer, Ph.D., of Chicago's Rush Medical Center.

This was revealed in their lipoprotein subfraction subanalysis of the CHICAGO (Carotid Intima-Media Thickness in Atherosclerosis Using Pioglitazone) trial, which was presented at ADA, last week.

The results were "consistent with a reversal of the pattern of change associated with the transition from insulin sensitivity to insulin resistance or diabetes," they said, and "may explain some of the observed decrease in carotid-intima media thickness progression in the pioglitazone group."

This prospective, double-blind study compared the two drugs in a multiracial and multiethnic population in Chicago. Participants had newly diagnosed type 2 diabetes, which was controlled by diet, or any combination of sulfonylurea, metformin, and insulin.

The 462 patients were randomized to 72 weeks of treatment with pioglitazone at a dose of 15 to 45 mg/d or glimepiride at a dose of 1 to 4 mg/d.

Among the main findings published in the *Journal of the American Medical Association* in 2006, the researchers reported that pioglitazone significantly slowed progression of carotid-intima media thickness compared with glimepiride ( $P=0.008$ ).

The subanalysis focused on lipoprotein subfractions measured with NMR spectroscopy done on blood samples taken at baseline and periodically through the study.

"Patients with type 2 diabetes manifest a form of dyslipidemia typified by high LDL particle concentration, small LDL particle size, and high triglyceride and low HDL cholesterol levels," they said. At 72 weeks there were significant differences favoring pioglitazone in reversing these trends although the baseline lipoprotein parameters were similar between groups.

Total LDL particle concentration was significantly improved by pioglitazone compared with glimepiride (-209.7 versus -109.3 nmol/L,  $P=0.01$ ). LDL particle size was likewise improved with pioglitazone (0.59 versus 0.17 nm,  $P=0.001$ ). This was achieved by increasing large LDL particle concentrations and significantly reducing those of medium-small and small LDL particles ( $P=0.001$  for all).

The VLDL particle size decreased significantly with pioglitazone compared with glimepiride (-5.01 versus -0.69 nm,  $P=0.001$ ). This was primarily by increasing small VLDL particle concentration (7.11 versus -1.4 nmol/L,  $P=0.001$ ) while also modestly decreasing large and medium-intermediate VLDL concentrations.

Total HDL particle concentrations increased slightly with pioglitazone but decreased with glimepiride (0.21 versus -1.05 nmol/L,  $P=0.001$ ).

HDL particle size followed the same pattern (0.14 versus -0.01 nm,  $P=0.001$ ). Large and medium HDL particle concentrations increased while that of small particles decreased (all  $P=0.01$ ).

The researchers noted that the study was underpowered to compare cardiovascular event rates between groups, so it is not known whether the differences seen in carotid intima-media thickness and lipoprotein subfractions would impact outcomes.

However, "in aggregate, the changes in lipoprotein subfraction distribution would be predicted to produce a reduction in cardiovascular disease risk with pioglitazone versus glimepiride," they concluded.

Practice Pearls: Explain to interested patients that this study suggests pioglitazone may have beneficial effects upon lipoprotein subfractions in patients with type 2 diabetes

*American Diabetes Association 2007 meeting: Meyer PM, et al "Comparative Effects of Pioglitazone and Glimepiride on Lipoprotein Subfractions: Abstract 906-P.*

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Item 11

### Scientists Working On A New Insulin Pill

*Insulin injections may soon be a thing of the past.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4943>

A British company has developed a form of the protein that can be taken orally. Scientists at Diabetology, a small research and development company that has spent many years trying to develop oral insulin, believe that it will better control of symptoms. The company has successfully enclosed the insulin in a capsule that prevents it from being digested by stomach acids, and carries it intact into the small intestine. Once the capsule has reached the small intestine, it is dissolved and releases a mixture of insulin and other materials that enhance the absorption of the insulin through the intestinal wall. Thereafter, the insulin is transported to the liver, where it creates a store that can be drawn on by the body.

The researchers say that the mechanism by which the capsule carries insulin into the body approximates the behavior of the pancreas, the source of insulin in healthy people that releases it as it is needed. Diabetology has already carried out a small trial of 16 patients with type 2 diabetes, the commoner type that usually develops in middle age, led by Cardiff University Professor David Owens. Dr Steve Luzio, another researcher at the university, presented the results of the trial at the American Diabetes Association meeting in Chicago. He announced that the oral dose taken twice daily before breakfast and before dinner, controlled glucose levels successfully in the patients treated. Glen Travers, the Executive Chairman of Diabetology, hopes that the product will enable better control of the disease to be achieved, without the increased risk of heart attack that has been linked to the widely used diabetes drug rosiglitazone.

*ADA Scientific Sessions June 2007*

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## DID YOU KNOW:

**Yogurt delays onset of diabetes:** Eating yogurt with probiotic bacteria, *Lactobacillus acidophilus* and *Lactobacillus casei*, exhibited a significant delaying effect on the progression of diabetes induced by high fructose administration in rats. "Studies have earlier linked yoghurt with improved lipids but this is the first time a protective benefit has been established for diabetes," says Dr Anoop Misra, department of diabetes and metabolic diseases, Fortis Group of Hospitals. The findings have been reported in the latest issue of international journal Nutrition. See this week's Item #9

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Item 12

### **Anti-Fat Injection Can Melt Fat Away, Reducing Risk for Metabolic Syndrome**

*For those who eat to combat stress, researchers here may have made a dream come true -- an injection that inhibits a well-know peptide, that makes fat melt away, at least in mice.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4942>

In mice subjected to the equivalent of eating a pound of ice cream to get over some murine vicissitudes, blocking a well-known neuropeptide caused excess visceral fat to vanish, according to Zofia Zukowska, M.D., Ph.D., of Georgetown, and colleagues.

They indicated that in a series of experiments, stress led to the release of Neuropeptide Y (NPY) from sympathetic nerves, which in turn upregulated NPY and its Y2 receptors (NPY2R) in a process dependent on the presence of glucocorticoids in the abdominal fat, the researchers reported online in *Nature Medicine*.

This positive feedback response by NPY led to the growth of abdominal fat, resulting in an increase in angiogenesis in white fat tissue, infiltration by macrophages, and proliferation of new adipocytes.

Over time, a feedback loop resulted in abdominal obesity and a metabolic syndrome-like condition in the animals, they said.

But injecting the new fat tissue with a compound that blocks the peptide's Y2 receptors (known as NPY2R) stopped the process and caused established visceral fat to disappear, Dr. Zukowska and colleagues said.

"We couldn't believe such fat remodeling was possible, but the numerous different experiments conducted over four years demonstrated that it is, at least in mice," Dr. Zukowska said.

She added that pilot studies show a similar mechanism exists in monkeys, but noted that a great deal of research remains to be done before the approach can be evaluated in humans. In the long run, "we are hopeful that these findings might eventually lead to control of metabolic syndrome, which is a huge health issue for many Americans," she said.

"Decreasing fat in the abdomen of the mice we studied reduced the fat in their liver and skeletal muscles, and also helped to control insulin resistance, glucose intolerance, blood pressure and inflammation."

Interestingly, reversing the process - adding Neuropeptide Y to certain areas of the mice - increased fat tissue locally, noted co-author Stephen Baker, M.D., D.D.S, of Georgetown University Hospital. The findings could open to the door to adding fat grafts for cosmetic purposes, such as facial rejuvenation, buttock and lip enhancement, and facial reconstruction, or to removing fat.

"This is the first well-described mechanism found that can effectively eliminate fat without using surgery," he said. "A safe, effective, non-surgical means to eliminate undesirable body fat would be of great benefit to our patients."

While it's hard to duplicate office politics or an ill-starred love life in mice, the researchers did the next best thing. In separate experiments they made the animals stand in cold water for long periods of time or put them in a cage with an aggressive alpha mouse. In both cases, the animals produced more Neuropeptide Y because of the stress but they didn't gain excessive weight unless they were also fed a high-fat, high-sugar diet.

Then they packed it on. Within two weeks, they had abdominal obesity and within three months had a metabolic syndrome-like condition. In contrast, control mice fed a normal diet - but still subjected to the stress - gained significantly less weight (at  $P < 0.05$ ).

But among the chubby mice either an implanted slow-release pellet of an NPY2R blocker or daily injections caused a 40% reduction in visceral fat within two weeks, the researchers found.

Also, mice genetically modified not to have the receptors in the first place didn't gain weight in response to stress and the high-fat, high-sugar diet.

Lydia Kuo, Ph.D., a co-author, said one key take-home message is that stress has a direct physiological effect on fat tissue, rather than being mediated through the brain.

"This is the first study to show that stress has a direct effect on fat accumulation, body weight and metabolism," Dr. Kuo said. "In humans, this kind of stress-mediated fat gain may have nothing to do with the brain, and is actually just a physiological response of their fat tissue."

Co-author Herbert Herzog, Ph.D., of Sydney, Australia's Garvan Institute of Medical Research said the findings should change how we deal with obesity.

"There are millions of people around the world who have lived with high levels of stress for so long their bodies think it's 'normal'," he said. "If these people also eat a high fat and high sugar diet, which is what many do as a way to reduce their stress, they will become obese."

But pharmaceutical interventions to block the Neuropeptide Y receptor could change all that, he said.

*Naturez : Kuo LE et al. "Neuropeptide Y acts directly in the periphery on fat tissue and mediates stress-induced obesity and metabolic syndrome." Nature Med 2007; doi:10.1038/nm1611.*

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### Item 13

#### **It's Official - Stress Makes You Fat**

*Australian scientists have discovered why stress can make us fat. New research published in an international journal has revealed that chronic stress triggers the body's fat cells to grow and multiply.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4941>

The link between stress and obesity has been known for more than a decade but these findings are the first to explain how exactly the connection works.

The research by Australian, US and Slovakian scientists could lead to new therapies that shrink fat cells or make them die.

Professor Herbert Herzog, director of neuroscience at the Sydney's Garvan Institute of Medical Research, said he expected the findings to have a profound effect on the way society deals with the obesity epidemic.

The research team made its discovery by feeding stressed and unstressed mice a "comfort food" diet high in fat and sugar.

The stressed mice gained twice as much fat as unstressed mice, because the stress caused fat to be stored differently.

Prof Herzog said a molecule called neuropeptide Y, released by the body when stressed, appeared to unlock receptors in the body's fat cells, stimulating the cells to grow in size and number. This same mechanism was expected in humans.

While the stress reaction was normal and unavoidable, scientists are working to block the dangerous knock-on fat reaction that it triggers.

"If we can interfere before it causes fat to amass, it could have a major impact on cardiovascular disease, diabetes, and cancer which all have links with obesity," Prof Herzog said.

Study leader Professor Zofia Zukowska, of Georgetown University, said they also hoped to be able to target obesity directly.

"We may be able to reverse or prevent obesity caused by stress and diet, including the worst kind of obesity - the apple-shaped type," Prof Zukowska said.

*the journal Nature Medicine. July 2, 2007*

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## FACT:

**Soaring diabetes rates causes highest level of amputees since the Civil War.** Business is booming largely because of amputations related to diabetes. As more Americans become obese and 1.5 million of them are diagnosed with diabetes each year, a growing number are confronting one of the most brutal consequences of the disease: suffering amputation of a limb or two. The number of amputees in the U.S. has grown to 1.9 million, up nearly three-quarters of a million people over the last decade, according to federal statistics. About 60% of those are diabetes-related. While public health experts are ramping up efforts nationwide to reverse the trend, it is leading to a boom in the long-sleepy prosthetics industry, which experts say hasn't seen a sales increase like this since its modern inception on the Civil War battlefields. Sales of prosthetics have jumped from \$340 million in 1996 to nearly \$600 million last year, according to estimates based on federal data.

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Item 14

### **Beta-Blockers Exert Anti-Atherosclerotic Effects**

*Beta-blocker therapy can provide statistically significant regression of coronary artery plaque, and slow the progression to coronary atherosclerosis.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4940>

Atheroma volume decreased by an average of 2.4 mm<sup>3</sup>/y among beta blocker-treated patients, compared with 0.4 mm<sup>3</sup>/y among those who did not receive beta-blockers ( $P=0.034$ ), reported Steven E. Nissen, M.D., of the Cleveland Clinic, and colleagues.

The volume of coronary plaque decreased significantly from baseline to the end of the evaluation period in patients who received beta-blockers ( $P<0.001$ ) but not in patients whose therapy did not include beta-blockers ( $P=0.86$ ).

"The analysis demonstrates that beta-blockers can slow progression of coronary atherosclerosis," concluded Dr. Nissen and colleagues. "The findings provide additional support for the current clinical guidelines advocating long-term use of beta-blockers to treat most forms of coronary artery disease."

The authors pointed out that beneficial effects on recurrent myocardial infarction, sudden cardiac death, and total mortality in MI patients emerged primarily from studies done two decades ago. Whether beta-blockers provide the same benefits in the current era of aggressive reperfusion for MI had not been clear.

To examine the effects of beta-blockers in contemporary patients, the investigators reviewed data from four clinical trials that used IVUS to evaluate the impact of medical interventions on coronary atherosclerosis volume. The four studies analyzed were:

- ?? REVERSAL, a randomized comparison of moderate versus aggressive lipid-lowering therapy with statin drugs
- ?? CAMELOT IVUS, a randomized comparison of a calcium-channel blocker and an ACE inhibitor
- ?? ACTIVATE, which evaluated lipid modification with a CoA-cholesterol acyltransferase inhibitor
- ?? ASTEROID, a trial of high-intensity lipid-lowering therapy with a statin

The same IVUS technique was used in all four trials, and patients in each trial had IVUS at baseline and at the study's end.

The trials involved a total of 1,515 patients with coronary artery disease, including 1,154 who received beta-blockers as a component of their treatment. On average, patients treated with beta-blockers received the agents for 91% of the trials' duration. More patients in the beta-blocker group had a history of MI, angina, and hypertension.

Patients treated with beta-blockers had a significantly greater reduction in atheroma volume in a univariate analysis and a multivariate analysis that controlled for MI, angina, and hypertension. Adjustments for LDL-cholesterol level, concomitant medications, and clinical trial did not change the results.

The investigators said that antiatherosclerotic effects of beta-blockers have been demonstrated in multiple animal models but not in human coronary arteries. However, a meta-analysis of randomized controlled trials last year found that long-term beta-blocker therapy was associated with a significant slowing of carotid intima-media thickening in hypertensive patients with diabetes or coronary heart disease and asymptomatic carotid artery disease.

Dr. Nissen and colleagues pointed out that beta-blockers reduce heart rate and slow blood velocity, leading to less turbulent blood flow and less intramural stress. However, adjustment for average heart rate during therapy did not change the results. The investigators also cited evidence that beta-blockers may reduce the affinity of LDL cholesterol for vessel wall proteoglycans and blunt catecholamine-induced endothelial permeability to lipoproteins.

*Annals of Internal Medicine: Sipahi I et al. "Beta-blockers and coronary atherosclerosis: Pooled analysis of 4 intravascular ultrasonography trials." Ann Intern Med. 2007;147:10-18.*

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Item 15

**ADA: New Drug Alogliptin Controls Glucose Without Risk of Hypoglycemia**

*An investigational new agent, a highly selective dipeptidyl peptidase-IV (DPP-4) inhibitor, has shown good efficacy and safety in the treatment of type 2 diabetes mellitus, according to results of a phase 1 study.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4939>

Dr. Qais A. Mekki, of Takeda Global Research and Development, presented findings of a randomized study of the drug, Takeda's alogliptin, in 36 healthy men. They were given 25, 50, 100, 200, 400, or 800 mg or placebo.

Alogliptin was absorbed within 1-2 hours with all doses, with nearly complete inhibition of DPP-4. Inhibition ranged from 74.3% to 97.0% at 24 hours and from 47.5% to 83.0% at 72 hours.

Mean area under the curve (AUC) increased with increasing doses. Half-life was 12.4-21 hours. All doses were well-tolerated.

"DPP-4 enables the body to provide the body with insulin on demand," Dr. Mekki told Reuters Health. He added that because the drug's target is very specific, it "has no off-target effects."

"We can see efficacy even in this short time period," Dr. Mekki said of the two-week observational period. "We have seen no cases of toxicity...It will not cause hypoglycemia, because it acts on demand. It is not active in normoglycemia."

"We are currently in phase 3 studies and have had no concerns. We plan to file a NDA in mid-2008," he said.

*Presented at the 67th Scientific Session of the American Diabetes Association in Chicago.*

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**Quote of the Week!**

.....*time flies like an arrow and fruit  
flies like bananas*

**Linda Savitz**

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