

# DIABETES IN CONTROL.com Newsletter

The Newsletter for Professionals in Diabetes Care

March 28, 2007 Issue #357

Check out this week's tool on fats from Dr. Phil Woods

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**Top Diabetes Stories:**  
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- Type 2 Diabetes Linked to Higher Dementia Risk\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4672>
- Glucose Level Predicts Hospitalization for Congestive Heart Failure\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4671>
- Dietary Patterns Linked to Type 2 Diabetes Risk\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4669>
- Pesticides Increases Risk of Diabetes in Pregnancy\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4666>
- Just 15 Minutes of Physical Activity Lowers Kids' Risk of Obesity and Diabetes\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4665>
- High Blood Sugar Tied to Increased Cancer Risk\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4664>
- Soft Drinks Associated with Diabetes, New Report\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4663>
- Study Reveals "Missing Link" Between Pre-Diabetes & Type 2 Diabetes\*  
<http://www.diabetesincontrol.com/results.php?storyarticle=4660>

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**From the editor's desk**  
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**This is the last week you can donate to the DiabetesInControl JDRF Walk Team. Show your support for your favorite newsletter by clicking the sneaker to donate**  
<http://walk.jdrf.org/index.cfm?fuseaction=extranet.personalpage&confirmid=86639759>

**Dr. Richard K. Bernstein's** new book is out, **Diabetes Solution New and Revised 2007**, has more info than ever and we have arranged for a special promotion, go to: <http://www.diabetes911.net/12006/promos.php>. This week **Dr. Bernstein** asks the question **WHAT ABOUT THE GLYCEMIC INDEX?**  
<http://www.diabetesincontrol.com/results.php?storyarticle=4673>

Often we see products for weight loss and think, how did that company come up with idea and why do they think they will make money? Well I have been able to secure an industry insider document that helps us understand how these companies come up with these magic bullets. [Click here to read this](http://www.diabetesincontrol.com/results.php?storyarticle=4674)  
<http://www.diabetesincontrol.com/results.php?storyarticle=4674>

Please show your support for Diabetes In Control and register for [www.PresentDiabetes.com](http://www.PresentDiabetes.com)  
[Check it out and Register today!](http://www.diabetesincontrol.com/issues/issue350/presentdiabetes.php)  
<http://www.diabetesincontrol.com/issues/issue350/presentdiabetes.php>

**April 1, 7PM ET dLifeTV on CNBC**

Wired for diabetes control – how technology helps and hinders. Plus, the holy grail of diabetes – the closed loop system. And, a special babysitting service that caters to kids with diabetes. Catch this brand 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.

**We can make a difference!**

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**This week's overview:**  
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- Item #3: Januvia Has 13 Competitors for DPP-IV Inhibitors in Clinical Trials**
- Item #5: Lower Cutoff for Impaired Fasting Glucose Identifies Those Without High CVD Risk**

- Item #6: Diabetic Men Have Lower Risk of Prostate Cancer
- Item #11: Kidney Disease Mortality Increased 52%
- Item #12: SoloStar Lantus & Apidra Insulin Pen to Debut
- Item #14: 'Clean' Children At Greater Risk Of Diabetes
- Item #15: Belly Fat Drives Inflammatory Processes Associated with Diabetes

Check out this weeks **“Test Your Knowledge”** question.  
<http://www.diabetesincontrol.com/results.php?storyarticle=4675>

Dave Joffe, *Editor-in-Chief*

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**NEWS FLASH:**

Dr. Richard K. Bernstein will be doing his 5<sup>th</sup> live conference call, “Ask Dr. Bernstein” this Thursday March 27<sup>th</sup>, at 7PM CST. To register go to <http://www.diabetes911.net/askdrb/index.php>

Get ready to Laugh: **Theresa Garnero, APRN, BC-ADM, MSN, CDE** is back next week with some new cartoons and a new CD both Spanish and English Cartoons

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**Tools for your Practice:**



**Health effects of dietary fats: Replace risks with benefits**

We often talk to our patients about good and bad fats and how to pick the right ones. Dr. Phil Wood has the best handout I have ever seen, [click here to get your copy](http://www.diabetesincontrol.com/results.php?storyarticle=4676)  
<http://www.diabetesincontrol.com/results.php?storyarticle=4676>

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**New Product:**

**Animas 2020 Insulin Pump**



The Animas® 2020 is the first insulin pump to feature an Organic Light-Emitting Diode (OLED) display screen that allows for brighter, clearer images. OLED is the same technology used in today's televisions, digital cameras, PDAs and virtual reality headsets. <http://www.diabetesincontrol.com/forms/animas2020.php>

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**This Week’s Items:**

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2. **Glucose Level Predicts Hospitalization for Congestive Heart Failure\***  
<http://www.diabetesincontrol.com/results.php?storyarticle=4671>
3. **Januvia Has 13 Competitors for DPP-IV Inhibitors in Clinical Trials**  
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4. **Dietary Patterns Linked to Type 2 Diabetes Risk\***  
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**12. SoloStar Lantus & Apidra Insulin Pen to Debut**

<http://www.diabetesincontrol.com/results.php?storyarticle=4661>

**13. Study Reveals "Missing Link" Between Pre-Diabetes & Type 2 Diabetes\***

<http://www.diabetesincontrol.com/results.php?storyarticle=4660>

**14. 'Clean' Children At Greater Risk Of Diabetes**

<http://www.diabetesincontrol.com/results.php?storyarticle=4659>

**15. Belly Fat Drives Inflammatory Processes Associated with Diabetes**

<http://www.diabetesincontrol.com/results.php?storyarticle=4658>

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## This Week's Items:

Item 1

### **Type 2 Diabetes Linked to Higher Dementia Risk**

*Results of a new study suggest that there is a general association between high adiposity and an increased risk of dementia, particularly among the "younger" elderly. In addition to age, other patient factors can confound this association.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4672>

"The few studies exploring the association between adiposity, measured by body mass index (BMI), and dementia in elderly persons were conflicting," Dr. Jose A. Luchsinger and colleagues from Columbia University College of Physicians and Surgeon in New York, write.

The researchers hypothesized that higher adiposity is associated with higher dementia risk, and that this relation is attenuated by age. Their study included 893 subjects with BMI data, 907 with waist circumference data, and 709 with a second weight measurement. At baseline, all subjects were free of dementia.

At 5-year follow-up, evaluations revealed 181 incident dementia cases, 112 Alzheimer's disease cases, and 53 dementia cases associated with stroke. The mean patient age was 77.0 years.

Patients in the third BMI quartile had a lower dementia risk than those in the first BMI quartile, after adjusting for demographics and apolipoprotein E-epsilon-4 status. Patients in the third BMI quartile also had a lower Alzheimer's disease risk. Those in the second BMI quartile had a lower risk of dementia associated with stroke.

"In persons younger than 76 years, the association between BMI quartiles and dementia resembled a U shape," Dr. Luchsinger's team explains. "The second (HR, 0.4) and third (HR, 0.3) quartiles were related to lower risk, while the fourth (HR, 1.0) was similar to the reference," they note. "In older people (at least 76 years), dementia risk decreased with increasing BMI; this association was almost statistically significant (fourth quartile HR, 0.6; p = 0.07 for trend)."

For all of the subjects, an association was observed between those in the fourth BMI quartile of waist circumference and a higher risk of stroke-related dementia. Subjects younger than 76 who were in the fourth quartile of waist circumference had an increased risk of dementia (HR, 2.3; p = 0.03 for trend) and Alzheimer's disease (HR, 5.1; p = 0.04 for trend).

Weight loss was associated with a higher risk of dementia and dementia associated with stroke. Weight gain was related to a higher risk of dementia associated with stroke only.

Arch Neurol 2007;64:392-398.

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Advertisement:

**Breaking News from the American Diabetes Association 66th Scientific Sessions**

Did you miss the ADA Scientific Sessions in Washington, DC? Get up to speed on the latest research and updates to current knowledge on diabetes and dyslipidemia-FREE CME Activities from the ADA Scientific Sessions are now available! Click here to access the interactive CME newsletter summary of several presentations relevant to clinical practice and the CME case-based slide and audio presentations on the real-world management of patients with diabetes and dyslipidemia recorded at the ADA meeting. Don't miss this opportunity to learn the latest clinical updates from one of the year's most critical diabetes events!  
<http://www.cemedicus.com/diabetes>

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Item 2

**Glucose Level Predicts Hospitalization for Congestive Heart Failure**

*In diabetic patients at risk for congestive heart failure (CHF), fasting plasma glucose level is an independent predictor for hospitalization, according to the results of a study.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4671>

"Patients with diabetes mellitus (DM) are at high risk of developing congestive heart failure (CHF)," write C. Held, MD, PhD, from the Karolinska University Hospital in Stockholm, Sweden, and colleagues. "However, the relationships between glucose levels and CHF in people with or without a history of DM have not been well characterized."

The investigators evaluated the associations between fasting plasma glucose level and risk for hospitalization for CHF during follow-up in 31,546 patients at high cardiovascular risk but without CHF who were enrolled in a large-scale clinical trials program. High-risk was defined as the presence of one coronary, peripheral, or cerebrovascular disease or DM with end-organ damage.

Subjects were enrolled in 1 of 2 ongoing parallel trials evaluating the effects of telmisartan, ramipril, or their combination.

At a mean follow-up of 886 days, interim analyses blinded for randomized treatment were performed to compare baseline fasting plasma glucose level with the adjusted CHF event rate. During follow-up, 68 patients were hospitalized for CHF. A 1-mmol/L higher fasting plasma glucose level was associated with a 1.10-fold increased risk for CHF hospitalization after adjustment for age and sex.

"Fasting plasma glucose is an independent predictor of hospitalization for CHF in high-risk subjects," the authors write. "These data provide theoretical support for potential direct beneficial effects of glucose lowering in reducing the risk of CHF and suggest the need for specific studies targeted at this issue."

"The present study represents a large and unique cohort with a relatively long period of follow-up and a large number of CHF events, thus providing a suitable setting and high statistical power to explore the significance of glucose on the development of CHF," the authors conclude. "Although we have shown that FPG [fasting plasma glucose] independently predicts hospitalization for CHF, whether glucose lowering reduces the risk of CHF requires study in prospective, randomized studies designed specifically for this purpose."

*Pearls for your practice:*

- ?? Elevated blood glucose levels may contribute to an increased risk for CHF through increasing left ventricular mass, increasing the risk for coronary artery disease, accelerating endothelial apoptosis, and reducing cardiac output.
- ?? The current study demonstrates that increasing levels of fasting plasma glucose, even among patients without diabetes, increase the risk for incident hospitalization for CHF.

*Circulation. Published online March 5, 2007*

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**DID YOU KNOW:**

**Scientists say exercise strengthens brain:** It boosts brain power by building new brain cells in a brain region linked with memory and memory loss. Researchers have conducted tests on mice and found out exercise affects a part of the brain called dentate gyrus, which is responsible for age-related memory loss. Later they used magnetic resonance images to figure out the effect of exercise on human. They found similar patterns in human.

"Once these findings were established in mice, we were interested in determining how exercise affects the hippocampal cerebral blood volume maps of humans," they wrote. They, however, could not dissect the brains of people to see if new neurons grew, but they could use MRI to have a peek.

Item 3

### **Januvia Has 13 Competitors for DPP-IV Inhibitors in Clinical Trials**

*Never before has there been as much competition for a new class of diabetes drugs.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4670>

Merck & Co posted Q4/2006 sales of US\$ 42 mln with its first-in-class dipeptidyl peptidase IV (DPP-IV) inhibitor Januvia. FDA's recent request for more clinical data to meet conditions set forth in the approvable letter of Novartis' NDA of the DPP-IV inhibitor Galvus will aid Merck to maintain and extend its competitive edge in the field. At least 13 further DPP-IV inhibitors are in clinical development with eight in advanced phase II or III stages. However, the first Big Pharma companies have abandoned the field, partly due to undisclosed safety issues, unsatisfactory clinical results or better alternatives. Available data show differences in duration of action and anticipated dosing frequency.

The high interest of the pharmaceutical industry in DPP-IV inhibitors reflects the market attractivity. The WHO estimates that globally over 170 mln people have diabetes, with type 2 diabetes accounting for 90 % to 95 %. By 2030, the prevalence of diabetes is predicted to double, driven by adverse lifestyle changes. Dipeptidyl peptidase IV is an enzyme that rapidly inactivates the insulinotropic hormone glucagon-like peptide-1 (GLP-1). Inhibition of dipeptidyl peptidase IV by DPP-IV inhibitors enhances the hormone activity of GLP-1 and other bioactive peptides (GIP, PACAP38 and GRP), thereby stimulating the release of insulin and reducing the secretion of glucagon. Both effects contribute to regulation of the elevated blood glucose levels in type 2 diabetic patients as measured by hemoglobin A1c (HbA1c).

Available clinical data suggest that long term treatment with DPP-IV inhibitors was well tolerated with very low rates of hypoglycemia and was not associated with weight gain or gastrointestinal disturbances. The DPP-IV inhibitors are being evaluated as both monotherapy and in combination with other standard antidiabetic drugs, e.g. metformin. The major advantages of DPP-IV inhibitors are the ability to achieve sustainable reductions in HbA1c with an orally administered, well tolerated agent. Other classes of new antidiabetic medications include GLP-1 agonists and dual PPAR agonists. However, GLP-1 agonists require administration by injection and dual PPAR agonists are associated with safety concerns.

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### **Multivitamin Supplements & Diabetes:**

Recent research confirmed that taking a daily multivitamin and mineral supplement has a positive impact on the quality of life for people with diabetes. So regularly taking a multiple is an easy choice, but for most finding the right one to trust with their health proves to be a more difficult matter. alpha betic(r) is uniquely balanced to meet the special dietary needs of people with diabetes and those predisposed to diabetes. alpha betic(r) contains 23 important nutrients in safe and balanced doses, with no copper. For more information: Click Here

<http://www.diabetesincontrol.com/ads/alphabetic/dest.php>

Item 4

### **Dietary Patterns Linked to Type 2 Diabetes Risk**

*Avoiding meats and fatty foods and eating lots of salads and cooked vegetables appears to reduce the risk of developing type 2 diabetes, according to study findings*

<http://www.diabetesincontrol.com/results.php?storyarticle=4669>

Dr. Allison Hodge, of the University of Melbourne, Australia, and colleagues examined the association between dietary patterns and type 2 diabetes in a 4-year study of 36,787 adults in the Melbourne Collaborative Cohort who provided dietary information. During follow-up, 365 new cases of type 2 diabetes were diagnosed.

The researchers defined four eating patterns, based on the predominance of 123 foods and beverages in the diet, which included: olive oil, salad, vegetables, legumes and avoidance of sweet bakery items, margarine and tea (Mediterranean); a variety of salads and vegetables (Salad and Vegetable); meats and fatty fried foods (Meat); and many different fruits (Fruit).

The Mediterranean pattern was associated with country of birth but not with diabetes, according to the authors. There was an inverse association observed between the Salad and Vegetable pattern and diabetes. The Meat pattern was positively associated with diabetes. No association was observed between the Fruit pattern and diabetes risk.

"Our results suggest that avoiding an eating pattern including meat and fatty foods, and favoring a pattern high in salad and cooked vegetables could reduce the risk of developing type 2 diabetes," Hodge said in an interview.

"What is important is that the focus is on eating patterns rather than single foods," she explained. "It may be that these eating patterns contribute to diabetes risk through an impact on body weight; overweight and obesity are still the most important risk factors for type 2 diabetes."

"One interesting thing about our results is that unlike most researchers who have identified eating patterns using factor analysis, we do not find a 'healthy' and an 'unhealthy' pattern," Hodge said. This may be related to the influence of Greek and Italian migrants in Australia, resulting in a wider variety of foods in the diets of the study subjects.

*American Journal of Epidemiology, March 2007.*

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

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## **DID YOU KNOW:**

**Cocoa extract 'targets big four':** Epicatechin, a compound found in cocoa, could target four of the major health problems, it has been claimed today. New research argues that the nutrient helps to target the risk of stroke, heart failure, cancer and diabetes. Norman Hollenberg, professor of medicine at Harvard Medical School, studied the Kuna people in Panama, who drink up to 40 cups of cocoa a week. He found that they have a ten per cent reduction in the risk of the 'big four'. "If these observations predict the future, then we can say without blushing that they are among the most important observations in the history of medicine," Professor Hollenberg said in the journal *Chemistry & Industry*. "We all agree that penicillin and anaesthesia are enormously important. But epicatechin could potentially get rid of four of the five most common diseases in the western world. How important does that make epicatechin? I would say very important." Epicatechin is also found in some fruits and vegetables, teas, wine and chocolate.

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Item 5

### **Lower Cutoff for Impaired Fasting Glucose Identifies Those Without High CVD Risk**

*Risk of CVD mortality among people with IFG largely explained by conversion to diabetes.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4668>

New research found that the current cutoff for impaired fasting glucose set by the American Diabetes Association identifies a group of people who do not have elevated risk of cardiovascular disease. Only those individuals who convert from impaired fasting glucose to diabetes have a higher risk for mortality.

In 1997, the ADA introduced a cutoff value to diagnose IFG. In 2003, this value was lowered from 110mg/dL or 6.1 mmol/L (IFG6.1) to 100mg/dL or 5.6 mmol/L (IFG5.6).

Josina M. Rijkkelijkhuizen, PhD, of the Institute for Research in Extramural Medicine at the VU University Medical Center in Amsterdam, and colleagues conducted a study assessing the effect of lowering the IFG cutoff on the prevalence of IFG and on the associated risk of all-cause and CVD mortality. They also examined whether the link between IFG and mortality is independent of the conversion to diabetes. The study cohort consisted of 1,428

individuals who took part in the Hoorn Study, which began in 1989 in the Netherlands. There was a mean follow-up period of 6.4 years, and patients were followed with respect to mortality.

The prevalence of IFG5.6 at baseline was 33.2% vs. 10.1% for IFG6.1. The mean fasting plasma glucose level of the entire cohort was 100mg/dL or 5.6 mmol/L in 1989 and 112mg/dL or 6.2 mmol/L in 1996; thus, the prevalence of IFG5.6 increased to 55.7% while the prevalence of IFG6.1 increased to 25.6%.

Among those individuals with IFG6.1 in 1989, 42% progressed to diabetes over the course of the study, and the incidence rate was 66.5/1,000 person-years. In contrast, only 21% of the IFG5.6 patients developed diabetes, with an incidence rate of 32.7/1,000 person-years..

During the period from the physical examination in 1996 until Jan. 1, 2005, 192 individuals died; 81 were determined to have died from CVD. For those with IFG6.1, the HR for CVD mortality was 1.87 relative to the reference group with normal glucose levels.

“The HR for CVD mortality for the IFG5.6 group was lower and not statistically significant: 1.37 (95% CI, 0.87-2.16),” the investigators wrote. The two IFG groups both had significantly higher risk for CVD mortality compared with the normal group.

Further analysis showed that individuals with either IFG5.6 or IFG6.1 who did not convert to diabetes did not have significantly higher risk than individuals who had normal fasting glucose levels and did not convert to diabetes.

“Subjects with IFG5.6 or IFG6.1 status who had converted to diabetes during the 6.4 years of follow-up had higher all-cause and CVD mortality risks than subjects who were classified as newly discovered diabetes in 1989 and had significantly (up to 2.5 times) higher all-cause and CVD mortality risks than subjects with normal glucose status at that time,” the investigators wrote.

“The fact that CVD mortality risk is only present in those subjects who will develop diabetes within six years indicates that our focus should lie on treatment of CVD risk factors and early detection of diabetes,” they wrote. Rijkelijhuizen JM, Nijpels G, Heine RJ, et al. High risk of cardiovascular mortality in individuals with impaired fasting glucose is explained by conversion to diabetes.

Diabetes Care. 2007;30:332-336.



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[http://www.diabetesincontrol.com/annodyne/anodyne10\\_31\\_01.php](http://www.diabetesincontrol.com/annodyne/anodyne10_31_01.php)

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Item 6

### **Diabetic Men Have Lower Risk of Prostate Cancer**

*As epidemiologic evidence suggests diabetic men have a slightly lower prostate cancer risk than non-diabetic men.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4667>

Seattle researchers examined this association in a prospective cohort study of 35 239 men, 50–76 years old, in Washington State who completed a baseline questionnaire between 2000 and 2002. Incident prostate cancers as of 31 December 2004 were identified through the SEER registry.

They found that diabetic men had a slightly lower risk of prostate cancer than non-diabetic men (hazard ratio (HR) 0.83). Insulin users overall and insulin users with diabetic complications had decreased risks, compared to non-diabetic men (HR 0.49) and (HR 0.36), respectively. Oral medication use for diabetes was not associated with prostate cancer. Insulin is likely a marker of severity of diabetes.

The researchers concluded: "Future studies of this association should consider diabetes type, treatment, severity, complications and biomarkers"

An interesting association that might be somewhat reassuring for diabetic men.

Diabetes and the risk of prostate cancer: the role of diabetes treatment and complications, C M Velicer, S Dublin and E White. *Category Y. Male Genital System, Breast, U. Urinary System.. Posted on Global Family Doctor 22 March 2007*

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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

### **Pesticides Increases Risk of Diabetes in Pregnancy**

*Exposure to agricultural pesticides in the first-trimester increases a woman's risk of developing diabetes during pregnancy, research shows*

<http://www.diabetesincontrol.com/results.php?storyarticle=4666>

Previous studies have examined the relationship between pesticides and diabetes, the authors explain, but none have focused on pregnancy-related or "gestational" diabetes.

Dr. Tina M. Saldana from the National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina and colleagues assessed the risk of developing gestational diabetes following pesticide exposures among wives of farmers enrolled in the Agricultural Health Study. Of 11,273 women who became pregnant within 25 years after entering the study, 506 (4.5 percent) reported having gestational diabetes.

Overall, 57 percent of women reported having mixed or applied pesticides at some time in their life, and the proportion was similar for those with and without gestational diabetes mellitus, the authors report in the journal *Diabetes Care*.

However, women who mixed or applied pesticides or repaired pesticide-related equipment during the first trimester of pregnancy had a more than twofold increased risk of developing gestational diabetes, the report indicates. In contrast, there was no increased gestational diabetes risk among women with residential exposures to pesticides or indirect exposures during the first trimester.

Similarly, the researchers note, women who had mixed or applied pesticides at any time before enrollment in the study did not face an increased risk of gestational diabetes compared with those who did not. Although much is known about common risk factors for pregnancy-related diabetes, "our understanding of whether and how environmental exposures may affect risk is still limited," the authors conclude.

Understanding any potential effect of environmental exposures on glucose (sugar) tolerance during pregnancy "may have substantial public health importance beyond the direct effects on gestational diabetes."

*Diabetes Care, March 2007.*

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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.

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Item 8

### **Just 15 Minutes of Physical Activity Lowers Kids' Risk of Obesity and Diabetes**

*Even an extra 15 minutes a day of moderate to vigorous running, jumping, or kicking a ball can dramatically cut the risk of childhood obesity, according to researchers.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4665>

In a cross-sectional study of more than 5,000 12-year-olds, a daily quarter-hour of moderate to vigorous exercise was associated with a 50% drop in the risk of obesity for boys, found Andy Ness, Ph.D., of the University of Bristol.

In girls, the decline in risk was lower, at nearly 40%, Dr. Ness and colleagues reported.

"The association between physical activity and obesity we observed was strong," Dr. Ness said. "These associations suggest that modest increases in physical activity could lead to important reductions in childhood obesity."

The study is among the first to use objective measures both of physical activity and lean and fat mass, the researchers said. The study was part of the long-running prospective Avon Longitudinal Study of Parents and Children, which enrolled more than 14,000 pregnant women in England in 1991 and 1992 and has followed the mothers and children in detail since.

For this analysis, the researchers asked children in the larger study to wear an Actigraph, a device containing an accelerometer, for a week, taking it off only to bathe, to swim, or when cycling (because the instrument is not accurate for cycling).

The device registers vertical motion as counts per minute and has been validated as a measure of energy expenditure, Dr. Ness and colleagues said. For this study, the researchers calculated both total physical activity and moderate to vigorous activity, defined as an Actigraph output of more than 3,600 counts per minute. The researchers calculated the body-mass index of the children using standard tools and also measured fat and lean mass using dual energy x-ray absorptiometry scanning.

Of the 6,622 children who agreed to wear an Actigraph, 5,595 wore it at least 10 hours a day for at least three days and were included in the analysis. Absorptiometry scanning was available for 5,500 of them. Analysis found "a strong negative dose-response association between objectively measured physical activity and DXA-derived measures of fat mass and obesity," the researchers said.

Specifically:

- ?? In boys, a difference of 15 minutes of moderate to vigorous activity was associated with between a 55% and 70% reduction in the risk of obesity, depending on which multivariate model was used. Both risk reductions were highly significant at  $P < 0.0001$ .
- ?? In girls, 15 minutes of moderate to vigorous activity led to a risk reduction of between 38% and 39%, depending on the model. Again, the risk reductions were significant, at  $P < 0.0001$  and  $P = 0.002$ , respectively.

When the children were stratified by quintiles of moderate to vigorous activity, there was a highly significant trend -- in both boys and girls -- toward lower obesity risk the higher the activity level.

In the most highly adjusted model, the odds ratio for obesity between top and the bottom quintiles was 0.03 for boys and 0.36 for girls (with the  $P$ -values for the trend at  $P < 0.0001$  and  $P = 0.006$ , respectively). "We know that diet is important," said co-author Chris Riddoch, Ph.D., of Bath University, "but what this research tells us is that we mustn't forget about activity."

"It's been really surprising to us how even small amounts of exercise appear to have dramatic results," he said in a statement.

**Action Points: Explain that diet and exercise both play a role, but that this study suggests that even a small increase in moderate to vigorous physical activity is associated with dramatic reductions in the risk of childhood obesity.**

Online in the open-access journal PLoS Medicine.

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**FACT:**

**The prevalence of chronic kidney disease is on the rise, according to CDC:** In the period from 1999 to 2004, 16.8% of the U.S. population ages 20 and older had chronic kidney disease, up from 14.5% in the period from 1988 to 1994. The difference represents a 15.9% increase based on crude estimates of prevalence. As would be expected, the prevalence of chronic kidney disease was greater among older men and women, and among those with diabetes, cardiovascular disease, and hypertension. In addition, Mexican Americans and non-Hispanic blacks had a greater prevalence of chronic kidney disease, particularly stage 1 disease, than non-Hispanic whites. "The large disparity in prevalence among those with stage 1 chronic kidney disease might be explained, in part, by racial/ethnic differences in microalbuminuria among non-Hispanic blacks and Mexican Americans. According to the CDC, both the incidence and prevalence of end-stage renal disease have increased during the past 30 year, and both are expected to continue increasing through the year 2010.



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Item 9

**High Blood Sugar Tied to Increased Cancer Risk**

*Results of a study involving nearly 65,000 people point to an association between cancer and abnormally high blood sugar levels.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4664>

Dr. Par Stattin from Umea University Medical Center, Sweden noted that, these results "have obvious implications for lifestyle guidance, as it is well known what factors cause blood glucose increases."

By avoiding excessive fat and other dietary risk factors, and by getting regular exercise, "you can decrease your risk of cardiovascular disease, diabetes -- and cancer," he added.

Type 2 diabetes is associated with an increased risk of liver, pancreas, colon cancer, as well as other cancers, Stattin and colleagues note in the journal Diabetes Care. However, less is known about the effect on cancer risk associated with moderately elevated blood sugar levels among non-diabetic subjects.

To investigate further, the researchers examined data from 31,304 men and 33,293 women who participated in a larger study and had glucose (blood sugar) measurements available. In total 2,478 cases of cancer were identified in this group.

In women, the total cancer risk increased with rising blood sugar levels. The relative risk of cancer was 26 percent higher for women with the highest fasting blood sugar compared with women with the lowest fasting blood sugar.

Adjustment for errors in measurement further increased the relative risk of cancer for women with abnormally high blood sugar levels. Overall, there was no significant association between total cancer risk and blood sugar measurements in men. However, for men and women, high fasting glucose was significantly associated with an increased risk of cancer of the pancreas, endometrium, urinary tract and malignant melanoma. These associations were independent of body weight.

These findings, the authors say, provide "further evidence for an association between abnormal glucose metabolism and cancer."

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Item 10

**Soft Drinks Associated with Diabetes, New Report**

*A review of published studies shows a clear and consistent relationship between drinking sugary (non-diet) soft drinks and poor nutrition, increased risk for obesity -- and increased risk for diabetes.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4663>

Dr. Kelly Brownell, director of the Rudd Center for Food Policy and Obesity at Yale University in New Haven, Connecticut, said, "There is no denying that sugar-loaded soft drinks are having "a negative impact on health."

Having analyzed and reviewed 88 studies on the issue, Brownell and his colleagues conclude that recommendations to curb soft drink consumption on a population level are strongly supported by the available scientific evidence.

Results of a study of more than 91,000 women followed for 8 years provides one of the "most striking" links between soft drinks and health outcomes, the investigators note in the American Journal of Public Health.

In the study, women who drank one or more sodas per day -- an amount less than the US national average -- were twice as likely as those who drank less than one soda per month to develop diabetes over the course of the study.

When diet soda replaced regular soda in the analysis, there was no increased risk, "suggesting that the risk was specific to sugar-sweetened soft drinks," note the authors.

"This result alone," they assert, "warrants serious concern about soft drink intake, particularly in light of the unprecedented rise in type 2 diabetes in children."

The data reviewed by Brownell's team also show that higher intake of sugary sodas goes hand-in-hand with lower intake of milk, calcium and other essential nutrients, fruit and fiber, and higher intake of carbohydrates.

Furthermore, there was a "remarkable difference" in results from industry-funded and non-industry-funded studies on soft drink consumption and health outcomes, Brownell said, "with the industry-funded studies much more likely to find the results favorable to industry."

"The bigger issue here, in this arena in particular but in science in general," Brownell said, "is how you can get a distorted view of reality if industry-funded studies are considered in the mix -- and usually they are -- especially, when industry uses these studies in advertising, lobbying, and in talking to the press."

When it comes to soft drink consumption among America's youth, Brownell added, "the decisions parents make are one thing, but the relentless marketing to children is another."

He supports the growing trend towards banning soda sales in schools. "I believe schools should be a commercial-free zone and that beverages that are contributing to ill health should not be sold there," Brownell said.

*American Journal of Public Health, April 2007.*

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Item 11

## **Kidney Disease Mortality Increased 52%**

*The rate of kidney disease mortality in the United States has increased by 52% in the past 16 years and continues to be higher in blacks than whites, according to a study.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4662>

The findings underscore the need for developing additional measures directed at preventing kidney disease, particularly in black communities.

Analysis of Vital Statistics data revealed that the death rate per 100,000 population rose from 10.1% in 1989 to 15.4% in 2005.

Study investigators also reported that the age-adjusted mortality rate was consistently at least twice as high in blacks vs whites in both men (32.6 [95% CI, 27.1 - 38.1] for black men vs 16.5 [95% CI, 15.2 - 17.8] for white men) and women (27.3 [95% CI, 23.3 - 31.3] for black women vs 11.8 [95% CI, 10.9 - 12.7] for white women).

As might be expected, study results also showed that the death rate increased with age, from 1.1 per 100,000 population (95% CI, 0.9 - 1.3) for people younger than 50 years, to 19.0 (95% CI, 17.2 - 20.8) in those aged 50 to 74 years, and to 173.6 (95% CI, 163.5 - 183.7) for those aged 75 years or older.

The increasing kidney disease death rate in Michigan may be explained in part by the increasing prevalence of kidney failure as well as its risk factors, diabetes and hypertension, the authors note.

Interventions aimed at educating black patients about kidney disease and the need for implementing diet and exercise-oriented prevention measures are available in community-based settings such as beauty salons, barber shops, schools, preschools, and Head Start programs.

*March 16 issue of the Morbidity and Mortality Weekly Report. MMWR. 2007;56(10):225-227.*

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## **DID YOU KNOW:**

**Study Reveals “Missing Link” Between Pre-Diabetes & Type 2 Diabetes:** *New research suggests a “missing link” between the pre-diabetes state and the clinical diagnosis of type 2 diabetes mellitus. Both impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are intermediate states in the transition from normal glucose tolerance (NGT) to T2DM and have been termed as “pre-diabetes”. They are associated with a high risk for progression to T2DM. Hepatic glucose production (HGP) is the principal determinant of fasting plasma glucose (FPG). In the current study, the authors have demonstrated that, in the non-diabetic range, the rise in fasting plasma glucose (FPG) concentration is associated with a mild decrease in hepatic glucose production (HGP) and a marked decrease in the glucose clearance rate. “Pinpointing the missing link is quite important,” Dr. Jani said. “It allows us to identify potential future targets in order to develop effective therapies to prevent the progression from pre-diabetes to type 2 diabetes.” For more information see this week’s Item #13*

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Item 12

## **SoloStar Lantus & Apidra Insulin Pen to Debut**

*Sanofi-Aventis is gearing up for the European roll-out of a new disposable insulin pen designed to address a broader spectrum of patient needs than currently available injection devices.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4661>

A SoloStar pen incorporating the French company's 24-hour basal insulin Lantus (insulin glargine) will make its worldwide debut in Germany next month, with an ease of use that will make it a potent competitor against rival products, according to Sanofi.

SoloStar pens for administering Lantus and [Sanofi-Aventis'](#) fast-acting prandial insulin Apidra (insulin glulisine) were approved by the European Commission last September. With Germany as a springboard, the company plans to launch SoloStar into the French market in May and across Europe within 12 months.

The US Food and Drug Administration's review of an approval application for Apidra SoloStar is "ongoing" and

launches in international markets will follow, said Anna Radjanova, spokesperson for Sanofi.

The new product's heightened sensitivity to a combination of user needs should differentiate it from other disposable insulin devices such as Eli Lilly's Humulin/Humalog pen and Novo Nordisk's FlexPen, Sanofi believes.

New features will include simplicity of use, injection force (the amount of pressure needed to inject insulin with a pen), the dial extension (how far the pen extends when a dose is dialled), robustness, the maximum dose deliverable in one injection, and the patient's ability to distinguish between different types of insulin carried in the same pen.

With input from people with diabetes, doctors and nurses, ergonomic tests were run to establish which features would best improve usability. In particular, Sanofi is highlighting the efficiency of SoloStar's drive mechanism, which in comparative tests reduced the necessary injection force by anything from 30% to 50% against FlexPen and the Humulin/Humalog pen.

The injection force and dial extension are important considerations given that up to 58% of people with diabetes have limited joint mobility of the hand and significantly weakened grip strength, often as a result of connective tissue disorders or diabetic neuropathy.

Other key SoloStar features include a dose range of up to 80 units, adjustable in single-unit steps - the highest of any disposable insulin pen, its manufacturer says. SoloStar is also the only disposable insulin pen whose body color identifies the specific insulin used (grey for Lantus, blue for Apidra).

This should aid compliance for, say, patients with Type I diabetes or Type II diabetes with a significant beta-cell deficit who are managed through intensive therapy with a basal insulin plus pre-meal rapid-acting insulin. Many of these patients will need to inject insulin five to seven times a day, Sanofi pointed out.

As Sanofi observed, pens now account for some 56% of all insulin units delivered worldwide, with a volume share of 94% in Japan and 86% in Europe. The exception is the US, where the vial and syringe method predominates and pens account for only around 14% of all units delivered. Within that relatively small segment, however, disposable pens hold a volume share of roughly 73%, while in Europe they make up a more modest 46% of all pen deliveries.

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Item 13

**Study Reveals “Missing Link” Between Pre-Diabetes & Type 2 Diabetes**

*New research suggests a “missing link” between the pre-diabetes state and the clinical diagnosis of type 2 diabetes mellitus.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4660>

Both impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are intermediate states in the transition from normal glucose tolerance (NGT) to T2DM and have been termed as “pre-diabetes”. They are associated with a high risk for progression to T2DM.

Hepatic glucose production (HGP) is the principal determinant of fasting plasma glucose (FPG). In the current study, the authors have demonstrated that, in the non-diabetic range, the rise in fasting plasma glucose (FPG) concentration is associated with a mild decrease in hepatic glucose production (HGP) and a marked decrease in the glucose clearance rate.

“During the fasting state, the decrease in glucose clearance results in an increase in FPG concentration which stimulates basal insulin secretion. The rise in fasting plasma insulin concentration, in turn, inhibits HGP, thus attenuating the rise in FPG,” Rucha Jani, MD, the study’s author said. “The high fasting blood glucose in these subjects can thus be explained by the decrease in glucose clearance. This is an important observation as it provides insight into the pathogenic mechanisms that characterize the ‘pre-diabetic’ stage.”

“Pinpointing the missing link is quite important,” Dr. Jani said. “It allows us to identify potential future targets in order to develop effective therapies to prevent the progression from pre-diabetes to type 2 diabetes.”

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**FACT:**

**Charleston, WV, is the market with the highest incidence of people who purchased medicine for diabetes over the past year.** Scarborough Research, the leading local market research firm for identifying consumer and retail behaviors in the United States, finds that Fifteen percent of consumers in this market are diabetes medication purchasers\*. Knoxville, TN (14 percent), Memphis, TN (11 percent), Columbus, OH (11 percent), and Tulsa, OK (11 percent) round out the top local markets for diabetes medication purchasers. Eight percent of all consumers nationally purchased medication for this disease. The Scarborough analysis also finds that Walgreens is the number one national drug store brand among diabetes medication purchasers. More than 3.1 million, or 18 percent, of these consumers purchased prescription drugs at Walgreens during the past year. CVS (17 percent), Wal-Mart (16 percent), Rite Aid (8 percent), and Eckerd Drug (4 percent) complete the top national drug store brands among diabetes medication purchasers. In Charleston, Wal-Mart is the top store among diabetes medication purchasers, as over one-quarter (27 percent) of these consumers purchased prescription drugs there during the past year. Rite-Aid (20 percent), CVS (14 percent), Fruth Pharmacy (8 percent), and Kroger (5 percent) are other leading stores among diabetes medication purchasers.

Item 14

**'Clean' Children At Greater Risk Of Diabetes**

*Better hygiene and clean environmental living conditions lead to a greater risk of diabetes in children, according to a new study*

<http://www.diabetesincontrol.com/results.php?storyarticle=4659>

Researchers at Bristol University blame better hygiene conditions for the soaring rates of type 1 diabetes in children. The study, involving data from 2.5 million people, says that cases of Type 1 diabetes have increased five-fold in children over the last 20 years.

Professor Polly Bingley from Bristol University added: "The incidence of childhood Type 1 diabetes has been shown to be increasing all over Europe, particularly in the very young.

"The increase is too steep to be put down to genetic factors, so it must be due to changes in our environment. This could either mean that we are being exposed to something new, or that we now have reduced exposure to something that was previously controlling our immune responses. We now need to work to identify what these changes might be."

The results come from researchers at the University of Bristol who were funded by Diabetes UK. The study looked at Oxford's population of 2.6m people between 1985 and 2004.

"It could be a result of people being exposed to fewer infections. Some scientists believe this is why rates of asthma are also rising. The immune system is supposed to fight infection but in asthma and type 1 diabetes it gets misdirected," says researcher Polly Bingley.

"The increase is too steep to be put down to genetic factors, so it must be due to changes in our environment. We now need to work to identify what these changes might be," media reports quoted Bingley as saying.

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Item 15

### **Belly Fat Drives Inflammatory Processes Associated with Diabetes**

*Fat in the belly may promote inflammation leading to diabetes and heart disease, say researchers.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4658>

They report that fat cells inside the abdomen secrete molecules that increase inflammation, establishing a potential mechanistic link between abdominal fat and systemic inflammation.

As scientists learn more about the key role of inflammation in diabetes, heart disease and other disorders, new research from Washington University School of Medicine in St. Louis suggests that fat in the belly may be an important promoter of that inflammation.

Excess fat is known to be associated with disease, but now the researchers have confirmed that fat cells inside the abdomen are secreting molecules that increase inflammation. It's the first evidence of a potential mechanistic link between abdominal fat and systemic inflammation.

For years, scientists have been aware of a relationship between disease risk and excess belly fat. "Apple-shaped" people, who carry fat in the abdomen, have a higher risk of heart disease, diabetes and other problems than "pear-shaped" people, who tend to store fat in the hips and thighs. Too much abdominal fat is associated with a defect in the body's response to insulin. During medical exams, some physicians measure waist circumference to identify patients at increased risk for these problems.

Not just any belly fat will cause inflammation, however. Back in 2004, Washington University investigators found that removing abdominal fat with liposuction did not provide the metabolic benefits normally associated with similar amounts of fat loss induced by dieting or exercising.

"Despite removing large amounts of subcutaneous fat from beneath the skin — about 20 percent of a person's total body fat mass — there were no beneficial medical effects," says Samuel Klein, M.D., the Danforth Professor of Medicine and Nutritional Science and the senior investigator on both studies. "These results demonstrated that decreasing fat mass by surgery, which removes billions of fat cells, does not provide the metabolic benefits seen when fat mass is reduced by lowering calorie intake, which shrinks the size of fat cells and decreases the amount of fat inside the abdomen and other tissues."

In this new study, researchers looked instead at visceral fat — the fat that surrounds the organs in the gut. Unlike subcutaneous fat, visceral fat is not easy to remove surgically because it is very close to the intestines and other internal organs. Since they couldn't just take out the fat, the research team decided to analyze the blood that ran through it to determine whether visceral fat was involved in inflammation or whether, like subcutaneous fat, it was merely a marker of potential problems.

Reporting in the journal *Diabetes*, the research team says visceral fat likely contributes to increases in systemic inflammation and insulin resistance. They sampled blood from the portal vein in obese patients undergoing gastric bypass surgery and found that visceral fat in the abdomen was secreting high levels of an important inflammatory molecule called interleukin-6 (IL-6) into portal vein blood.

"The portal vein is filled with blood that drains visceral fat," says first author Luigi Fontana, M.D., Ph.D., assistant professor of medicine at Washington University in St. Louis and an investigator at the Istituto Superiore di Sanita, Rome, Italy. "Portal vein blood had levels of IL-6 that were 50 percent higher than blood from the periphery."

Increased IL-6 levels in the portal vein correlated with concentrations of an inflammatory substance called C-reactive protein (CRP) in the body. High CRP levels are related to inflammation, and chronic inflammation is associated with insulin resistance, hypertension, type 2 diabetes and atherosclerosis, among other things.

"These data support the notion that visceral fat produces inflammatory cytokines that contribute to insulin resistance and cardiovascular disease," says Klein.

Klein, Fontana and J. Christopher Eagon, M.D., assistant professor of surgery, looked at blood samples from 25 patients. All were extremely obese, and all were undergoing gastric bypass surgery. They took blood from the portal vein and from the radial artery in the arm and found differences in levels of IL-6 between the samples.

Fontana believes the findings help explain how visceral fat can lead to inflammation, insulin resistance and other metabolic problems. And he says by contributing to inflammation, visceral fat cells in the abdomen may be doing even more than that.

"Many years ago, atherosclerosis was thought to be related to lipids and to the excessive deposit of cholesterol in the arteries," Fontana says. "Nowadays, it's clear that atherosclerosis is an inflammatory disease. There also is evidence that inflammation plays a role in cancer, and there is even evidence that it plays a role in aging. Someday we may learn that visceral fat is involved in those things, too."

*Diabetes, March 2007*



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## **Quote of the Week!**

***"We should not let our fears hold us back from pursuing our hopes."***

.....John F. Kennedy

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