

DIABETES IN CONTROL.com Newsletter

The Newsletter for Professionals in Diabetes Care

May 23, 2007 - Issue #365

Do you or your patients use a shallow angle set for your pump? Please Click here to learn about a new set with a built in self-injector.

<http://www.diabetesincontrol.com/studies/inset.php>

Top Diabetes Stories:

Insulin Levels Can Predict Weight Loss on Certain Diets*

<http://www.diabetesincontrol.com/results.php?storyarticle=4826>

Avandia Tied To 43% Increased Heart Attack Risk In Study*

<http://www.diabetesincontrol.com/results.php?storyarticle=4825>

Women With Heart Disease And Diabetes Less Likely To Receive Proper Care*

<http://www.diabetesincontrol.com/results.php?storyarticle=4823>

Headache Linked to Increased Prevalence of Retinopathy in Midlife*

<http://www.diabetesincontrol.com/results.php?storyarticle=4821>

Diabetes Drug Costs Soar 70%*

<http://www.diabetesincontrol.com/results.php?storyarticle=4819>

Initial Serum Glucose Level Points to Outcome After MI*

<http://www.diabetesincontrol.com/results.php?storyarticle=4818>

New Finding Discovers How Embryos Create Beta-Cells*

<http://www.diabetesincontrol.com/results.php?storyarticle=4817>

Comparison of Insulin Detemir and Insulin Glargine in Type 1 Diabetes*

<http://www.diabetesincontrol.com/results.php?storyarticle=4813>

From the editor's desk

Use of the insulin analogues glargine and detemir can result in better glucose control. However, because glargine and detemir differ from one another, further clinical experience may identify which patient groups will do better on each drug. **Dr Matthew C. Riddle** recently spoke at an American Diabetes Association meeting and explained what this means for our patients.

<http://www.diabetesincontrol.com/results.php?storyarticle=4827>

Richard K. Bernstein, M.D., F.A.C.E., F.A.C.N., C.W.S. has prepared an update on Recent Developments Regarding Risk Factors For Heart Disease. Also don't miss Dr. Bernstein on CBS Radio Nationwide from 10:00-10:30 a.m. CST Wednesday, May 23.

<http://www.diabetesincontrol.com/results.php?storyarticle=4828>

Would you be interested in going on a diabetes cruise? We are planning a 7-9 day Diabetes Education Cruise with Dr. Richard K. Bernstein for next spring or fall. We will provide CME for medical professionals to learn Dr. Bernstein's treatment methods and education for patients with diabetes. If you might be interested, just send us an email with "Diabetes Cruise" in the subject line. Send to publisher@diabetesincontrol.com

We need a few more people for a new study for patients who use a shallow angle set with their pump. Please [click here](#) to find out more.

<http://www.diabetesincontrol.com/studies/inset.php>

May 27, 7PM ET on CNBC

dLife takes an in-depth look at the breakthrough diabetes products Exubera and Byetta; cutting risk and improving care in San Antonio; and one man's quest to climb mountains with diabetes. Watch this exciting 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!

This week's overview:

Item #3: Lower Risk For Diabetes Associated With Cereal Fiber And Magnesium Intake

- Item #5: Vildagliptin Inhibits Glucagon Release and Increases Insulin Secretion
- Item #7: Enzymes and Exercise Curb Insulin Resistance
- Item #11: Diabetes Drug Use Triples for Girls
- Item #12: Study Links Premature Birth to Blood Sugar Problems in Young Adults
- Item #13: Urine Test Predicts Diabetic Kidney Disease
- Item #15: Study Links Obesity to Protein in Infant Formula

Check out this weeks **“Test Your Knowledge”** question.
<http://www.diabetesincontrol.com/results.php?storyarticle=4829>

Dave Joffe, *Editor-in-Chief*

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NEWS FLASH:

Avandia Tied To 43% Increased Heart Attack Risk In Study

Analysis Reveals Avandia Linked To 43 Percent Increased Risk For Heart Attack And a 64 Percent Greater Risk of Cardiovascular Death, according to the review published by the New England Journal of Medicine. [See this week’s Item #2](#)

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Tools for your Practice:

The Charcot Foot in Diabetes: Six Key Points According to information from the Diabetes U.K. Annual Professional Conference in Glasgow, Scotland, Charcots often goes undiagnosed until to late. We have gotten a handout from the AAFP that explains common mistakes that often postpone diagnosis.

<http://www.diabetesincontrol.com/results.php?storyarticle=4830>

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New Product:



Protective Pouch To Enhance Beta-Cell Therapy

The student-designed cell therapy pouch is formed by two concentric stents, similar to the ones used to keep clogged blood vessels open. A band of nylon mesh surrounds the inner stent and holds the microcapsules containing helpful cells. The tiny openings in the mesh, each about 250 microns in diameter, would allow blood to pass through to nourish the cells and disperse helpful proteins. But the openings are too small to allow the microcapsules to escape. [More](#)

Information

<http://www.diabetesincontrol.com/results.php?storyarticle=4831>

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This Week’s Items:

1. **Insulin Levels Can Predict Weight Loss on Certain Diets***
<http://www.diabetesincontrol.com/results.php?storyarticle=4826>
2. **Avandia Tied To 43% Increased Heart Attack Risk In Study***
<http://www.diabetesincontrol.com/results.php?storyarticle=4825>
3. **Lower Risk For Diabetes Associated With Cereal Fiber And Magnesium Intake**
<http://www.diabetesincontrol.com/results.php?storyarticle=4824>
4. **Women With Heart Disease And Diabetes Less Likely To Receive Proper Care***
<http://www.diabetesincontrol.com/results.php?storyarticle=4823>

5. Vildagliptin Inhibits Glucagon Release and Increases Insulin Secretion

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6. Headache Linked to Increased Prevalence of Retinopathy in Midlife*

<http://www.diabetesincontrol.com/results.php?storyarticle=4821>

7. Enzymes and Exercise Curb Insulin Resistance

<http://www.diabetesincontrol.com/results.php?storyarticle=4820>

8. Diabetes Drug Costs Soar 70%*

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9. Initial Serum Glucose Level Points to Outcome After MI*

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10. New Finding Discovers How Embryos Create Beta-Cells*

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11. Diabetes Drug Use Triples for Girls

<http://www.diabetesincontrol.com/results.php?storyarticle=4816>

12. Study Links Premature Birth to Blood Sugar Problems in Young Adults

<http://www.diabetesincontrol.com/results.php?storyarticle=4815>

13. Urine Test Predicts Diabetic Kidney Disease

<http://www.diabetesincontrol.com/results.php?storyarticle=4814>

14. Comparison of Insulin Detemir and Insulin Glargine in Type 1 Diabetes*

<http://www.diabetesincontrol.com/results.php?storyarticle=4813>

15. Study Links Obesity to Protein in Infant Formula

<http://www.diabetesincontrol.com/results.php?storyarticle=4812>

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ITEMS For The Week:

Item 1

Insulin Levels Can Predict Weight Loss on Certain Diets

Individual differences in insulin secretion may explain why some individuals respond well to either a low-fat diet or low-glycemic-load diet, whereas others do not, a randomized study suggests.

<http://www.diabetesincontrol.com/results.php?storyarticle=4826>

The findings imply that a simple, baseline oral glucose tolerance test to assess serum insulin concentration may help clinicians and dieticians choose weight-loss strategies for obese subjects.

Dr. Ebbeling stated that, "We often ask, why do people succeed with a conventional low-fat diet while others who are following the exact same diet can't keep weight off?" "Usually we answer this question with something like: 'the ones who succeed are more motivated, or have more willpower, or they're more able to stick with a diet while others are not as motivated.' But this really is not a complete answer to the question. So we sought to determine if biology had something to do with it."

Ebbeling and colleagues randomized 73 obese young adults (aged 18 - 35 years) to a 6-month dietary intervention: either a low-glycemic-load diet (40% carbohydrate, 35% fat, and rich in low-glycemic index foods), or a low-fat diet (55% carbohydrate and 20% fat). At baseline, all subjects were given an oral glucose tolerance test to check for insulin concentration after 75 g of dextrose. Subjects adhered "intensively" to diets for 6 months, then were followed up for an additional 12 months.

For the group as a whole, changes in body weight and body fat percentage at 18 months did not differ between the 2 diet groups; however, when stratified according to baseline glucose tolerance test, subjects with above-median insulin concentration (> 57.5 µIU/mL) lost significantly more weight on the low-glycemic-load diet than they did on the low-fat diet by 18 months. In contrast, subjects with insulin concentrations below median levels (= 57.5 µIU/mL) during the baseline glucose tolerance test had similar outcomes, regardless of to which diet they had been randomized.

Differences between the diets were seen in effects of the different diets on lipid parameters, regardless of baseline glucose tolerance tests. The low-glycemic-load diet produced significant improvements in high-density lipoprotein (HDL) cholesterol and triglyceride profiles, whereas the low-fat diet produced significantly greater reductions in low-density lipoprotein (LDL) cholesterol levels.

"Regardless of insulin secretion at baseline, the LGL [low-glycemic-load] diet has beneficial effects on HDL cholesterol and triglycerides that were not seen on the LF [low-fat] diet, while LDL cholesterol decreased in the participants in the LF diet, but not the LGL diet," Dr. Ebbeling said. "This is just speculation on our part, but an

LGL diet that also substitutes unsaturated fats for fats may be even more beneficial for everyone, since the beneficial effects on insulin, cholesterol, and triglycerides with the LGL diet were seen regardless of insulin secretion."

"Spikes in insulin concentration after a meal are believed to promote feelings of hunger and can lead to overeating," and "people who are 'high insulin secreters' may be particularly susceptible to weight gain with conventional low fat diets that are higher in carbohydrates," says Dr. Ebbeling. By contrast, low insulin secreters seem to do the same on either the low-fat diet or the low-glycemic-load diet, she continued. "It seems that people who are high insulin secreters may be particularly susceptible to weight gain and may be more challenged to lose weight with a conventional low fat diet."

Dr. Ebbeling states that, "From a clinical perspective, our findings provide rationale for individualizing weight loss diets or diet prescription based on an oral glucose tolerance test."

JAMA. 2007;297:2092-2102.

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Item 2

Avandia Tied To 43% Increased Heart Attack Risk In Study

Analysis Reveals Avandia Linked To 43 Percent Increased Risk For Heart Attack And 64 percent greater risk of Cardiovascular Death.

<http://www.diabetesincontrol.com/results.php?storyarticle=4825>

Avandia, the biggest-selling diabetes drug in the world, is linked to a greater risk of heart attack and possibly death, says a new scientific analysis published online Monday.

More than 6 million people worldwide have taken the drug sold by London-based GlaxoSmithKline PLC since it came on the market eight years ago. Pooled results of dozens of studies revealed a 43 percent higher risk of heart attack and a 64 percent greater risk of cardiovascular death, according to the review published by the New England Journal of Medicine.

Experts said the overall risk was small and cautioned people not to stop taking the drug on their own but to talk to their doctors.

"There are more heart attacks, more strokes, deaths, et cetera," one of the study's researchers, Dr. Steven Nissen, said. "It is most urgent that both the FDA and the company look at the original source data and do careful analysis."

The company downplayed the report of heart risks, saying the analysis by Dr. Nissen and statistician Kathy Wolski at the Cleveland Clinic is not definitive scientific proof. In a conference call Monday, Dr. Lawson McCartney, who leads Glaxo's diabetes drug development, said the company is not seeing "anything like" the problems reported in the medical journal.

"We remain very confident in the safety and of course in the efficacy of Avandia as an important diabetic medicine," McCartney said.

GlaxoSmithKline earns \$3 billion a year from the drug, the biggest-selling diabetes drug in the world, according to Forbes magazine.

The government will take no immediate action on a label change or other measures regarding the drug, said Dr. Robert J. Meyer of the U.S. Food and Drug Administration's Center for Drug Evaluation and Research.

FDA officials acknowledged that Glaxo submitted information last August indicating some increased risk from the drug but that other studies were contradictory.

FDA said it has studied the same data as Dr. Nissen, but that "unpublished data" suggests "contradictory evidence about (Avandia's) risks" — which essentially means the FDA doesn't have enough evidence to pull the

drug off the market.

However, several members of Congress expressed alarm at the report and said they would hold hearings on the safety issues.

In a strongly-worded editorial accompanying the study, patients were warned not to quit Avandia on their own without discussing their concerns with their doctors, wrote Drs. Bruce Psaty and Curt Furberg. To the extent that the new analysis shows valid risks, the drug "represents a major failure of the drug-use and drug-approval processes in the United States," they said.

Psaty, a researcher at the University of Washington in Seattle, said the Nissen study means there's no good reason for most patients to take Avandia.

When the drug was approved, "evidence was at best mixed" on its benefit, wrote the two doctors. Both have been frequent critics of the FDA's failure to spot dangers in the drug approval process and its conduct in the case involving Vioxx. The popular arthritis medicine sold by Merck & Co. was taken off the market in 2004 when heart problems came to light after it had been taken by millions of people

Several experts said Avandia was another example of the FDA failing to detect a safety problem early enough.

In a study published last September, the drug rosiglitazone (Avandia) appeared to cut the risk of developing diabetes or dying by more than half. It also helped restore normal blood-sugar function in many participants. That study involved about 5,000 people with "pre-diabetes," or blood-sugar abnormalities.

But even that study's researchers acknowledged that a small percentage of those on Avandia developed heart failure.

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DID YOU KNOW:

Study links regular exercise to a 41% reduction in ED: All it took was about 30 minutes of walking a day. Although erectile dysfunction is not life-threatening, it can surely impair quality of life. A Harvard study linked regular exercise to a 41% reduction in the risk of erectile dysfunction -- And in 2004, a randomized clinical trial reported that moderate exercise (averaging less than 28 minutes a day) can help restore sexual performance in obese, middle-aged men with erectile dysfunction. *Harvard Men's Health May 2007*

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Item 3

Lower Risk For Diabetes Associated With Cereal Fiber And Magnesium Intake

Higher dietary intake of fiber from grains and cereals and of magnesium may each be associated with a lower risk of type 2 diabetes, according to a report and meta-analysis.

<http://www.diabetesincontrol.com/results.php?storyarticle=4824>

Projections indicate that the number of people diagnosed with diabetes worldwide may increase from 171 million in 2000 to 370 million by 2030, according to background information in the article. The associated illness, death and health care costs emphasize the need for effective prevention, the authors write. Fiber may help reduce the risk of diabetes by increasing the amount of nutrients absorbed by the body and reducing blood sugar spikes after eating, among other mechanisms. Current American Diabetes Association guidelines include goals for total fiber intake, but research suggests that some types of fiber may be more beneficial than others. Findings regarding magnesium and diabetes risk remain unclear.

Matthias B. Schulze, Dr.P.H., and colleagues at the German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, conducted a study of 9,702 men and 15,365 women age 35 to 65 years. Participants completed a food questionnaire when they enrolled in the study between 1994 and 1998, then were followed up through 2005 - an average of seven years - to see if they developed diabetes. In addition, the researchers performed a meta-analysis of previously published work related to intake of fiber or magnesium and risk of diabetes.

During the follow-up period, 844 individuals in the study developed type 2 diabetes. Those who consumed more fiber through cereal, bread and other grain products (cereal fiber) were less likely to develop diabetes than those who ate less fiber. When the participants were split into five groups based on cereal fiber intake, those who ate the most (an average of 17 grams per day) had a 27 percent lower risk of developing diabetes than those in the

group that ate the least (an average of 7 grams per day). Eating more fiber overall or from fruits and vegetables was not associated with diabetes risk, nor was magnesium intake.

In the meta-analysis, the researchers identified nine studies of fiber and eight studies of magnesium intake. Based on the results of all the studies, in which participants were classified into either four or five groups according to their intake of fiber or magnesium, those who consumed the most cereal fiber had a 33 percent lower risk of developing diabetes than those who took in the least, while those who consumed the most magnesium had a 23 percent lower risk than those who consumed the least. There was no association between fruit or vegetable fiber and diabetes risk.

"In conclusion, the evidence from our study and previous studies, summarized by means of meta-analysis, strongly supports that higher cereal fiber and magnesium intake may decrease diabetes risk," the authors conclude. "Whole-grain foods are therefore important in diabetes prevention."

Arch Intern Med. 2007;167:956-965

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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
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Item 4

Women With Heart Disease And Diabetes Less Likely To Receive Proper Care

Women with heart disease and diabetes are less likely to receive several types of routine outpatient medical care than men who have similar health problems, according to a RAND Corporation study.
<http://www.diabetesincontrol.com/results.php?storyarticle=4823>

While previous research has shown that women less frequently receive expensive medical care such as angioplasty for heart disease, few studies have evaluated gender disparities in managed care settings.

All the patients in the RAND Health study had either private insurance or were enrolled in Medicare managed care plans, had been diagnosed with heart disease and/or diabetes, and had visited health providers to receive care.

Chloe Bird, the study's lead author and a sociologist at RAND said that, "sound that the routine medical care received by women for their heart disease and diabetes was not as good as the care received by men," said, a nonprofit research organization. "These are low-cost treatments that can forestall serious health problems in the future -- and women with diabetes and heart disease are not receiving them as often as men with similar problems."

Researchers studied more than 50,000 men and women and examined 11 different screening tests, treatments or measurements of health status shown to be important to all people diagnosed with heart disease or diabetes.

Among people enrolled in commercial health plans, women were significantly less likely than men to receive the care evaluated in six of the 11 measures, while women enrolled in the Medicare plans were less likely to receive the care evaluated in four of the 11 measures.

The largest disparity found by researchers was that women were less likely to lower their cholesterol to recommended levels after suffering a heart attack or other acute cardiac event, or if they had diabetes.

For example, women with diabetes were 19 percent less likely than men to have their cholesterol within recommended ranges if they were enrolled in Medicare and 16 percent less likely than men to have cholesterol with recommended ranges if enrolled in commercial health plans.

Other types of care women received less often than men included being prescribed ACE inhibitor drugs for chronic heart failure and receiving prescriptions for beta blocker drugs following a heart attack.

The disparities were found among women even though they generally see a doctor or other health care provider more often than men. The disparities also remained after researchers accounted for socioeconomic factors that may influence care.

"These were all insured people. They all had access to medical care and they were all diagnosed with these diseases," Bird said. "The disparities cannot be explained by a lack of patient reporting or not recognizing the symptoms of a disease."

journal Women's Health Issues. May/June edition

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FACT:

More than 1.6 million people with diabetes don't have health insurance: This comes from the Centers for Disease Control and Prevention. Almost 4.5 million — nearly one-quarter of all patients diagnosed with the disease — are poor or close to it, but fewer than two million are covered by Medicaid. The situation adds to an already bleak picture of an American epidemic. The number of people with diabetes grows by eight percent each year. Under the current system, their future won't even include test strips, medication, or nutrition counseling, let alone continuous glucose monitors or inhaled insulin. Health care providers and advocates interviewed for this story said that only a health care policy that increases access to health insurance and emphasizes education and prevention can turn the tide. *CDC*

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Item 5

Vildagliptin Inhibits Glucagon Release and Increases Insulin Secretion

The selective inhibitor of dipeptidyl peptidase IV (DPP-4), vildagliptin, promotes reduction of plasma glucose levels in patients with type 2 diabetes by suppressing endogenous glucose production and augmenting insulin secretion.

<http://www.diabetesincontrol.com/results.php?storyarticle=4822>

Dr. Bogdan Balas from University of Texas Health Science Center says that "DPP-4 inhibitors work by restoring the entero-insular axis (small intestine-pancreas-liver crosstalk) and therefore correcting a very important physiologic defect in type 2 diabetes."

Dr. Balas and associates investigated the mechanisms by which vildagliptin reduces postmeal plasma glucose concentrations in type 2 diabetic patients by examining the response to a single dose of vildagliptin in patients not previously exposed to a DPP-4 inhibitor.

Vildagliptin completely suppressed plasma DPP-4 activity for more than 14 hours, during which meal-stimulated plasma insulin and C-peptide concentrations increased significantly and plasma glucagon decreased significantly, the authors report.

These changes produced significant reductions in postmeal plasma glucose concentration throughout the overnight period, the results indicate, and fasting plasma glucose was 14 mg/dL lower than baseline on the morning after evening administration of vildagliptin. Insulin secretion increased within 30 minutes after ingestion of vildagliptin and remained elevated after the meal and throughout the sleeping hours, the researchers note.

Within 60 minutes after vildagliptin administration and for all time periods in the ensuing 12 hours, suppression of endogenous glucose production was significantly greater than after placebo administration, the report indicates.

"Due to the fact they might preserve beta cell function (and number), one should think of starting DPP-4 inhibitor or an incretin-mimetic as soon as type 2 diabetes is diagnosed." "I think DPP-4 inhibitors will soon find their place as first and second-choice therapy," Dr. Balas said.

Dr. Balas explained that, because DPP-4 inhibitors "don't seem very effective when they are administered as single-therapy, it is likely that their first indication will be as add-on therapy to metformin or a thiazolidinedione." "If the safety profile proves excellent in long-term studies (as it did in short- and medium-term ones), most likely DPP-4 inhibitors will replace sulfonylureas in current practice."

J Clin Endocrinol Metab 2007;92:1249-1255.

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Item 6

Headache Linked to Increased Prevalence of Retinopathy in Midlife

A history of migraine and other headache types has been linked to an increased prevalence of retinopathy in middle-aged individuals, supporting the hypothesis that neurovascular dysfunction underlies vascular headaches.

<http://www.diabetesincontrol.com/results.php?storyarticle=4821>

Investigators at the University of North Carolina at Chapel Hill found that, among a biracial cohort of individuals aged 51 to 71 years, those with headache were between 1.3 and 1.5 times more likely to have retinopathy than those without headaches.

"Middle-aged people with a history of migraine and other headaches are more likely to have retinopathy," the study's lead author Kathryn M. Rose, PhD, said in a statement from the American Academy of Neurology.

She added this association persisted even after controlling for diabetes, blood glucose levels, pack-years of smoking, average mean arterial pressure, or use of antihypertensive medications.

According to the authors, migraine has been consistently linked with stroke, but research findings into the relationship between hypertension and coronary heart disease have been inconsistent.

Furthermore, recent research has shown retinal microvascular abnormalities can predict clinical and subclinical stroke as well as other cardiovascular outcomes. "Because the retinal and cerebral microcirculations share similar anatomy, embryology, and physiology, and because neurovascular mechanisms may underlie both migraine and retinal microvascular abnormalities, an association between the two is biologically plausible," they write.

The cross-sectional study included 10,902 participants enrolled in the Atherosclerosis Risk in Communities (ARIC) Study, which was designed to investigate the etiology and natural history of atherosclerosis and its sequelae.

All study participants underwent a lifetime headache history using International Headache Society diagnostic criteria, as well as retinal photography. The mean age of the study participants was 60 years. Most (56%) were women, and 21% were African Americans. Of the total group, 40% had hypertension, 15% had diabetes, and 19% had less than a high school education. Almost 78% of the study cohort reported no history of headaches lasting 4 or more hours.

In terms of retinal outcomes, the study showed migraine was more strongly associated with retinopathy than the study's 2 other retinal microvascular signs: focal arteriolar narrowing and arteriovenous nicking.

While individuals in all 3 headache groups were more likely to have retinopathy than those without a history of headache, the association was "modestly stronger" for individuals without hypertension or diabetes who had migraine/other headache with aura and migraines without aura.

The authors note that while retinal microvascular signs are more prevalent in the elderly and those with high blood pressure and diabetes, the study suggests they can also occur in middle-aged adults who do not have these conditions.

"The association of retinopathy with migraine in younger people independent of these factors suggests that other pathophysiologic processes not directly examined here (e.g., inflammatory factors, endothelial dysfunction) may explain these observations," they write.

The current study demonstrates that retinopathy is more common among patients with headaches vs patients without headaches. This main result was true of both patients with migraine and patients with other headaches.

Neurology. 2007;68:1694-1700.

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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

Enzymes and Exercise Curb Insulin Resistance

*An oversupply of fatty acids plays a key role in the development of **insulin resistance** in the skeletal muscle of obese individuals.*

<http://www.diabetesincontrol.com/results.php?storyarticle=4820>

Two related studies show that exercise and expression of the enzyme diacylglycerol acyltransferase 1 (DGAT1) have important effects on the development of insulin resistance.

In the first of these two studies, Simon Schenk and Jeffrey Horowitz from the University of Michigan have shown that a single session of endurance exercise on a treadmill was sufficient to prevent insulin resistance in healthy, non-obese women. The authors showed that exercise triggered a corresponding increase in triglyceride synthesis within skeletal muscle as well as a parallel increase in the expression of the enzymes DGAT1 and mitochondrial glycerol-3-phosphate acyltransferase (mGPAT). By directing more fatty acids towards triglyceride synthesis within muscle, toxic fatty acid metabolite accumulation was reduced, which protected against fatty acid-induced insulin resistance. The study suggests that regularly performed endurance exercise may help improve insulin resistance in people with excess levels of available fatty acid, such as those with obesity.

In a related study, Yi-Hao Yu and colleagues from Columbia University also observed an increase in DGAT1 activity in skeletal muscle and that fatty acids were channeled into triglycerides following exercise. In addition, the author studied mice that over expressed DGAT1 in skeletal muscle and found that they were protected against high-fat diet-induced insulin resistance. The data illustrate how exercise can enhance muscle insulin sensitivity and the authors suggest that increasing muscle DGAT activity may offer a potential new approach to prevent and treat insulin resistance in type 2 diabetes.

Journal of Clinical Investigation appearing online on May 17 in advance of publication in the June print issue

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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

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Item 8

Diabetes Drug Costs Soar 70%

The introduction of new treatment options and a growing number of diabetes patients will drive costs upward
<http://www.diabetesincontrol.com/results.php?storyarticle=4819>

According to a report released last Thursday by Medco Health Solutions Inc, a growing diabetes epidemic and more aggressive treatment with combination drug therapies could result in a rise of nearly 70% in drug spending on the disease through 2009,

Medco's 2007 Drug Trend Report found diabetes treatments trailing only cholesterol medications in total prescription drug spending growth in 2006.

The director of medical policy for Medco stated that, "There are going to be a lot more drugs coming out and more and more people with type 2 diabetes will catapult diabetes to the number one class in driving year over year spending growth." The analysis projects that, by 2009, spending on medicines to treat diabetes could soar by 60% to 68% from 2006 levels.

Spending on diabetes treatments increased 14.5% from 2005 to 2006 and the use of diabetes drugs increased 5.1%. The U.S. sales of diabetes drugs reached \$9.88 billion in 2005, according to data from IMS Health Inc..

An aging population and the alarming rise in obesity -- a leading cause of diabetes -- are expected to push spending growth rates on diabetes drugs up 16% to 20% annually.

Use is expected to increase by 8% to 10% each year, with patients more frequently using new drug combinations to reach target blood sugar levels, the Medco analysis of likely future prescription drug spending and utilization found.

A wave of new diabetes treatments, such as Merck & Co.'s, Januvia, and Byetta from Eli Lilly and Co. and Amylin Pharmaceuticals Inc., and others expected to hit the market from the likes of Novartis AG and Novo Nordisk A/S, will help push up treatment costs, the report said.

Some newer drugs that act on new targets are increasingly being prescribed as first-line therapy and are frequently being used in combination with other drugs, driving up costs this year and going forward, the report said.

Use of lower cost generic drugs could mitigate pricing pressures, said Medco, a pharmacy benefits manager that negotiates prescription drug costs for companies and other large clients.

But while new medicines and combination therapies can be expensive, the cost of treating complications from untreated diabetes would create a much larger burden on government and private health plans and patient pocketbooks.

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FACT:

Dose-Response Relation Between Physical Activity and Fitness The observation of improved fitness with as little as 72 minutes a week of physical activity dovetails well with data from the Women's Health Study investigating a clinical end point (vs fitness, a risk factor); women who walked as little as 1 to 1.5 hours a week, also approximately equivalent to 50% of the surgeon general's recommendation, had half the risk of developing coronary heart disease than did sedentary women. These data should be encouraging to sedentary individuals because they indicate that an achievable dose of physical activity may be sufficient to begin reaping health benefits. *JAMA*. 2007;297:2137-2139.

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Item 9

Initial Serum Glucose Level Points to Outcome After MI

The first serum glucose level measured in the emergency department is an independent prognostic factor in patients who have sustained a first acute myocardial infarction, researchers report.
<http://www.diabetesincontrol.com/results.php?storyarticle=4818>

Dr. Kuo-Liong Chien of the National Taiwan University, Taipei and colleagues note that the initial glucose level in the emergency department shows the early glucose response to acute myocardial infarction and is not influenced by glucose-containing solutions or treatment by the referring institution.

To gain further information on the prognostic value of this parameter, the researchers retrospectively studied 198 MI patients. Of this group, 94 had a normal glucose level (less than 140 mg/dL), 53 had an intermediate level (140 to 200 mg/dL) and the remaining 51 had a level of 200 mg/dL or more.

In total, 18% of patients in the normal group had at least one adverse event in the first month post-MI. The corresponding proportion in the other two groups was 40%.

The adjusted odds ratio for adverse events in the first month was 3.87 in the intermediate group and 5.16 in the high level group, compared to the normal level group.

Mortality at 1 year was 3% in the normal group, 15% in the intermediate group and 18% in the high glucose level group.

Dr. Chien stated that, "after a first myocardial infarction, it appears that the initial glucose level measured in the emergency department may be an important prognostic factor in determining cardiovascular outcome."

Ann Emerg Med 2007;49:618-626.

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Item 10

New Finding Discovers How Embryos Create Beta-Cells

Scientists have discovered a key aspect of how embryos create the cells that secrete insulin.

<http://www.diabetesincontrol.com/results.php?storyarticle=4817>

Researchers hope that their findings will enable the development of new therapies for diabetes, a condition caused by insufficient levels of insulin.

The study reveals that glucose plays a major role in enabling healthy beta cells, which secrete insulin, to develop in the pancreas of an embryo. Glucose prompts a gene called Neurogenin3 to switch on another gene, known as NeuroD, which is crucial for the normal development of beta cells. If glucose levels are low this gene is not switched on.

Insulin is the principal hormone that regulates the uptake of glucose and if the beta cells are unable to produce sufficient insulin, this can cause diabetes.

The scientists, from Imperial College London and an INSERM Unit at Necker Hospital, Paris, hope that understanding how to switch on the gene that produces beta cells could eventually enable researchers to create the latter from stem cells. They could then transplant beta cells into patients with type 1 diabetes, which causes the immune system to attack patients' beta cells.

The researchers hope that scientists will be able to develop drug therapies that enhance the action of glucose and hence encourage the growth of healthy beta cells.

Professor Guy Rutter, from the Division of Medicine at Imperial College and one of the authors of the paper, said: "We hope that by demonstrating that 'extrinsic' factors like glucose can regulate the way in which insulin secreting cells develop, we may eventually be able to reverse defects in the growth of these cells in patients with diabetes.

"Research like ours is opening up whole new sets of targets for drug treatments."

The scientists reached their conclusions after conducting research on tissues cultured from the primordial pancreas of very young rat embryos.

Using an in vitro system, rather than looking at cells in vivo, enables researchers to gain a greater understanding of when and how different genes are being switched on.

Journal of Biological Chemistry. May 17, 2007

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Item 11

Diabetes Drug Use Triples for Girls

The number of adolescent girls taking drugs for Type 2 diabetes nearly tripled in just five years.

<http://www.diabetesincontrol.com/results.php?storyarticle=4816>

The study, an analysis of prescription drug use from 2001 to 2006 among 370,000 insured children aged 10 to 19, was conducted by Medco Health Inc. of Franklin Lakes, N.J., the country's biggest prescription benefit manager, and released exclusively to The Associated Press.

Experts say the findings raise questions about physical health problems in youth, the appropriateness of putting them on strong, long-term medicines mostly designed for adults, and whether it might be better to focus on other strategies, such as counseling, exercise and changes in diet, caffeine intake and bedtime routine.

"There's increasing use of medication in children the last 20 years, but does that mean we're treating them successfully or that we're overmedicating?" said Dr. Thomas Insel, director of the National Institute of Mental Health. Probably both, he said, but some children aren't getting needed help.

Dr. Wayne Snodgrass, chairman of the American Academy of Pediatrics' committee on drugs, said the levels of medication usage found in the study might be appropriate, but it's hard to know without details on why each prescription was written.

The most striking trend was a 167 percent spike in girls 10 to 19 taking pills for type 2 diabetes, formerly called adult-onset diabetes. Medco found it jumped from 0.1 percent in 2001 to 0.27 percent in 2006; among boys, prevalence up 33 percent, to 0.08 percent.

Dr. John Buse, president-elect of the American Diabetes Association, said those figures are a bit higher than prior data but track U.S. increases in diabetes and obesity the past 15 years. "It's really scary to think about people in their teens developing a disease that in the past only developed in the 40s, 50s and 60s," Buse said.

The big gap between the sexes, he said, likely is partly due to girls taking a generic diabetes drug, metformin, linked to weight loss and also prescribed for a hormonal condition that involves abnormal insulin function, causes male sex traits and increases cancer risk. Also, hormone changes in puberty can trigger insulin resistance, or prediabetes. Puberty starts a couple years earlier in girls, so many more girls than boys in the study were in puberty.

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DID YOU KNOW:

Insulin and Low-Glycemic Load vs Low-Fat Diets: Differing physiological characteristics may be an explanation for inconsistent outcomes of dietary interventions for weight loss. Ebbeling and colleagues investigated whether insulin secretion affects weight loss in obese young adults who were randomly assigned to

either a low-glycemic load or a low-fat diet. At the 18-month follow-up, the authors found that among participants whose insulin secretion at baseline was above the median, loss of weight and body fat were greater in persons assigned to the low-glycemic load vs the low-fat diet. The low-glycemic load diet was associated with greater improvements in high-density lipoprotein cholesterol and triglyceride levels and the low-fat diet with more improvement in low-density lipoprotein cholesterol levels. See this week's item # 1 JAMA. 2007;297:2053

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Item 12

Study Links Premature Birth to Blood Sugar Problems in Young Adults

Preterm babies born at very low birth weight may be more prone blood sugar problems as young adults.

<http://www.diabetesincontrol.com/results.php?storyarticle=4815>

They studied 332 young adults who were 18-27 years old. The group included 163 people who had been born prematurely at very low birth weight (ranging from 1.3-3.3 pounds). The remaining 169 participants had been born from full-term pregnancies.

Participants provided blood samples and completed questionnaires about their medical history, exercise habits, and family history of diabetes.

The researchers tested participants' blood samples and found that while none of the participants had diabetes, blood sugar problems and high systolic blood pressure were more common in the preterm group. Those blood sugar problems included prediabetes and insulin resistance, which are early warning signs of diabetes risk.

The study doesn't pinpoint the causes of participants' blood sugar problems or high blood pressure.

The differences between the preterm and full-term groups didn't appear to be due to weight or body fat levels, note the researchers. The findings were statistically significant, meaning it wasn't likely due to chance. But the gap between the two groups wasn't large.

Preterm babies face many challenges as a result of not being able to complete a healthy pregnancy. Those challenges may have long-term health consequences, note the researchers.

It's not clear exactly how preterm birth affects adult health, but it's an important topic, notes Ingelfinger. "Now that many more extremely premature babies are surviving to adulthood, ensuring their health is crucial," writes Ingelfinger.

Hovi, P. The New England Journal of Medicine, May 17, 2007; vol 356: pp 2053-2063. Ingelfinger, J. The New England Journal of Medicine, May 17, 2007; vol 356: pp 2094-2095.

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Item 13

Urine Test Predicts Diabetic Kidney Disease

Looking at various proteins in urine may help doctors predict the development of diabetic nephropathy in type 2 diabetes patients well before they develop the condition.

<http://www.diabetesincontrol.com/results.php?storyarticle=4814>

Dr. Ravi Thadhani, from Massachusetts General Hospital and Harvard Medical School in Boston, states that, "We have identified a set of urine proteins almost 10 years before the onset of diabetic nephropathy that identify those who will go on to get diabetic nephropathy, the most common cause of renal failure in the U.S. and the world." Diabetic nephropathy is a serious complication of diabetes in which the kidneys lose their ability to function over time.

Thadhani and colleagues compared urinary protein profiles among 62 Pima Indians with type 2 diabetes and normal kidney function who were followed for 10 years for the development of diabetic kidney disease.

The authors identified a protein "signature" that proved highly predictive of the development of diabetic nephropathy.

"While these findings require a significant amount of work to identify and test the robustness of these markers, they offer the potential for clinicians one day to be able to tell whether a diabetic patient will get renal failure well before the development of this devastating condition, and, hence, offer hope for early intervention to prevent its onset," Thadhani said.

"First we need to confirm the identification of the proteins we uncovered, then we need to test this profile in other populations with type 2 diabetes to determine if the same predictive potential remains," Thadhani explained. "Then we will carry out prospective studies in larger populations."

Diabetes Care March 2007.

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FACT:

Association between metabolic syndrome and CVD can not be explained entirely by hyperglycemia. A Chinese study of the cardiovascular incidence relating to diabetes, pre-diabetes, and the metabolic syndrome showed that the Both hypertension and dyslipidemia, which are common in people with metabolic syndrome, are likely to play an equal or greater role in the causation of CVD. Thus, the increased CVD risk in individuals with impaired fasting glucose or diabetes was largely driven by the coexistence of multiple metabolic disorders, rather than hyperglycemia alone. *American Heart Journal, 153 (552-558): Liu J, Grundy S, Wang W, Smith S Jr, Vega G, Wu Z, Zeng Z, Wang W, Zhao D Ten-year risk of cardiovascular incidence related to diabetes, prediabetes, and the metabolic syndrome*

Item 14

Comparison of Insulin Detemir and Insulin Glargine in Type 1 Diabetes

Treatment with twice-daily insulin detemir or once-daily insulin glargine, each in combination with insulin aspart, resulted in similar glycemic control.

<http://www.diabetesincontrol.com/results.php?storyarticle=4813>

To compare glycemic control and risk of hypoglycemia of twice-daily insulin detemir with once-daily insulin glargine in subjects with Type 1 diabetes. Methods In this 26-week, multicenter, open-label, parallel-group trial, 320 subjects with Type 1 diabetes received either insulin detemir twice daily or insulin glargine once daily. each in combination with premeal insulin aspart.

The results showed that after 26 weeks, HbA(1c) had decreased from 8.8 to 8.2% in the insulin detemir group and from 8.7 to 8.2% in the insulin glargine group. Home-measured fasting plasma glucose (PG) was lower with insulin glargine than with insulin detemir (7.0 vs. 7.7 mmol/l, P < 0.001). The overall shape of the home-measured nine-point PG profiles was comparable between treatments (P = 0.125). Overall, there was no significant difference in within-subject variation in PG (P = 0.437). Within-subject variation in predinner PG was lower with insulin detemir than with insulin glargine (P < 0.05).

The overall risk of hypoglycemia was similar with no differences in confirmed hypoglycemia. However, the risk of severe and nocturnal hypoglycemia was 72% and 32%, respectively, lower with insulin detemir than with insulin glargine (P < 0.05). Body weight gain was not significantly different comparing insulin detemir and insulin glargine (0.52 kg vs. 0.96 kg, P = 0.193).

From the results it was concluded that, treatment with twice-daily insulin detemir or once-daily insulin glargine, each in combination with insulin aspart, resulted in similar glycemic control. The overall risk of hypoglycemia was comparable, whereas the risks of both severe and nocturnal hypoglycemia were significantly lower with insulin detemir.

Diabet Med. 2007 Mar 22

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Item 15

Study Links Obesity to Protein in Infant Formula

The results of the EU Childhood Obesity Program indicate that low-protein content in infant formula may have metabolic, endocrinal and developmental benefits for babies - which may also have an impact on obesity at a later age.

<http://www.diabetesincontrol.com/results.php?storyarticle=4812>

Subject to further follow-up, the findings add weight to the idea that a tendency towards obesity is set in earliest childhood. They come shortly after another study indicated that tendency towards obesity could be genetic.

Professor Berthold Koletzko, project co-coordinator from the University of Munich, Germany, said the results *"emphasize the importance of promotion of and support for breastfeeding, together with the development of the right composition of infant formula, and support for the choice of appropriate complementary food."*

The study involved 990 infants and ran from October 2002 to July 2006, when the youngest participants reached the age of two.

The researchers hypothesized the primary hypothesis that one possible causal factor for the difference in long-term obesity risk between breast and formula-fed infants is the much lower protein content of breast milk compared to infant formula.

The infants were randomized to receive either a low-protein formula (1.8g/100kcal, then 2.25g/100kg in follow on formulas) or a high protein formula (3g/100kcal, then 4.5g/100kcal).

The intervention lasted for 12 months from birth, and the infants were followed until they reached the age of two. A group of breast-fed children was also followed.

In addition to a body growth rate similar to that of breast-fed babies, those in the low protein group were seen to have metabolic and endocrinal benefits too.

It is emphasized that the low protein content in the formula is considered safe and is in accordance with the formula composition authorized by the EU. No untoward effects were seen during the study.

The program is part of the Early Nutrition Programming Project (EARNEST), an EU-funded project to investigate the link between nutrition in earliest childhood and health outcomes later in life.

The results were presented at the pre-congress EARNEST satellite conference of the 15th European Congress on Obesity in Budapest by Prof Koletzko.

A spokesperson told NutraIngredients.com it is expected that the study will be published, but it is not yet known when and in which journal. However these results are not the end of the story.

"These first results of the EU Childhood Obesity Program contribute to the growing body of scientific evidence that early nutrition can exert important long term 'programming' effects on early development and later health," said Prof Koletzko.

Further follow up of the children is planned under the aegis of EARNEST, to investigate whether the observed effects at age two are associated with a lower risk of obesity at a later age.

The study will be published, but it is not yet known when and in which journal.

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Quote of the Week!

"Well done is better than well said."

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