

DIABETES IN CONTROL.com Newsletter

The Newsletter for Professionals in Diabetes Care

May 9 2007 - Issue #363

Top Diabetes Stories:

1. Tight Control in Type 1 Diabetes No Cognitive Threat*

<http://www.diabetesincontrol.com/results.php?storyarticle=4789>

3. Diabetes Damaging Men's Sperm*

<http://www.diabetesincontrol.com/results.php?storyarticle=4787>

4. Eating Pistachios Reduces Impact of Carbohydrates*

<http://www.diabetesincontrol.com/results.php?storyarticle=4786>

5. Are NovoLog and Humalog Interchangeable?*

<http://www.diabetesincontrol.com/results.php?storyarticle=4785>

6. Noninvasive Type 2 Diabetes Screening More Sensitive Than Standard Tests*

<http://www.diabetesincontrol.com/results.php?storyarticle=4784>

9. Hyperglycemia linked to Cancer Risk*

<http://www.diabetesincontrol.com/results.php?storyarticle=4781>

11. Aspirin Less Effective Heart Treatment for Women than Men*

<http://www.diabetesincontrol.com/results.php?storyarticle=4779>

12. Diabetics With Cancer Have Less Aggressive Treatment, Worse Survival*

<http://www.diabetesincontrol.com/results.php?storyarticle=4778>

From the editor's desk

When you read Diabetes in Control you have to know that we are first and foremost diabetes professionals and secondly journalists. Often I share my heart on my shirtsleeve with you. This week our **Publisher, Stephen Freed, BSPHarm**, has prepared a compelling feature [The Expanding Evidence for Diabetes Prevention](#) that will let you know why we are your best partners for diabetes care.

<http://www.diabetesincontrol.com/results.php?storyarticle=4790>

Richard K. Bernstein, M.D., F.A.C.E., F.A.C.N., C.W.S. shares his insight on fiber from his new book. Click here to read [WHAT ABOUT DIETARY FIBER?](#)

<http://www.diabetesincontrol.com/results.php?storyarticle=4791>

Sherri Shafer, R.D., CDE returns to Diabetes in Control after an extended hiatus. In keeping with our publisher's focus on prevention she has contributed a feature on [Preventing and Treating Type 2 Diabetes with Weight Control and Exercise](#)

<http://www.diabetesincontrol.com/results.php?storyarticle=4792>

dLife May 13PM ET on CNBC

How to start a successful diabetes support group; mastering diabetes through martial arts; and the inspirational story of Jeanette Jordan, a diabetes educator who uses the power of faith to improve diabetes care in her community. Tune in to this encore 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 #2: Lap Band Gastric Bypass Surgery Improves Insulin Resistance
- Item #7: A Cherry on Top: Tart Cherries May Alter Heart/Diabetes Factors
- Item #8: Lung Cancer Risk Lower in Diabetics Taking Thiazolidinediones
- Item #10: Obesity May be Linked to Middle Ear Effusions in Children
- Item #13: Sibutramine of Little Benefit in Obese Adolescents
- Item #14: Honey as a Treatment for Diabetic Ulcers
- Item #15: Common Genetic Variation Increases Heart Disease Risk

Check out this weeks **“Test Your Knowledge”** question.
<http://www.diabetesincontrol.com/results.php?storyarticle=4793>

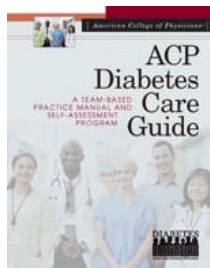
Dave Joffe, *Editor-in-Chief*

NEWS FLASH:

Amylin building \$400M facility in West Chester to manufacturer the long-acting release (once a week) formulation of exenatide (Byetta®)

Tools for your Practice:

Free ACP Diabetes Care Guide and Companion CD-ROM: A Team-Based Practice Manual and Self-Assessment Program. Are You Ready to Improve Diabetes Care?



Especially for physicians, physician assistants, nurse practitioners, nurses, and diabetes educators/dietitians and produced by the editors of the Medical Knowledge Self-Assessment Program® (MKSAP®), the *Diabetes Care Guide* will help you provide better care across multidisciplinary lines. The book includes special tools for the health-care team as well as for patients. Tools designated *For Better Practice* facilitate effective team collaboration and education. Tools designated *For Better Health* are for handing out to patients to improve patient education and self-care, with advice on how to manage medications, exercise, diet, lifestyle changes, and other issues of importance. The companion CD-ROM allows you to test your knowledge by answering 81 multiple-choice questions modeled after the questions used for internal medicine's certifying examination. By completing the test and submitting it online, you can qualify for any of the following:

- ?? 15 *AMA PRA Category 1 Credits™* if you are a physician
- ?? 15 non-physician Continuing Medical Education credits if you are a physician assistant, as authorized under AMA guidelines
- ?? 15 Continuing Education credits if you are a nurse practitioner or nurse
- ?? 15 Continuing Professional Education credits if you are a dietitian

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New Product:



Artificial 'snot' improves sensor smell With all the problems we have had with tainted food lately, manufacturers are looking for ways to keep our food safe. Smell sensors have been used for years, and now artificial mucus can help.

This Week's Items:

1. **Tight Control in Type 1 Diabetes No Cognitive Threat***
<http://www.diabetesincontrol.com/results.php?storyarticle=4789>
2. **Lap Band Gastric Bypass Surgery Improves Insulin Resistance**
<http://www.diabetesincontrol.com/results.php?storyarticle=4788>
3. **Diabetes Damaging Men's Sperm***

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<http://www.diabetesincontrol.com/results.php?storyarticle=4783>

8. Lung Cancer Risk Lower in Diabetics Taking Thiazolidinediones

<http://www.diabetesincontrol.com/results.php?storyarticle=4782>

9. Hyperglycemia linked to Cancer Risk*

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10. Obesity May be Linked to Middle Ear Effusions in Children

<http://www.diabetesincontrol.com/results.php?storyarticle=4780>

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14. Honey as a Treatment for Diabetic Ulcers

<http://www.diabetesincontrol.com/results.php?storyarticle=4776>

15. Common Genetic Variation Increases Heart Disease Risk

<http://www.diabetesincontrol.com/results.php?storyarticle=4775>

ITEMS For The Week:

Item 1

Tight Control in Type 1 Diabetes No Cognitive Threat

Even if glucose levels plunge periodically in patients with type 1 diabetes, cognitive function stays on an even keel, researchers found.

<http://www.diabetesincontrol.com/results.php?storyarticle=4789>

Over 18 years, no evidence of a substantial long decline in mental ability was found in a large group of patients with type 1 diabetes, despite relatively high rates of severe hypoglycemia stemming from tight control.

Forty percent of the cohort of more than 1,000 patients reported having had at least one hypoglycemic coma or seizure, said Alan M. Jacobson, M.D., of the Joslin Diabetes Center, Harvard Medical School here, and colleagues. Yet whether the patients belonged to a tight-control group in the study or a conventional-therapy group was not associated with a decline in cognitive function.

Long-standing concern about the effects of type 1 diabetes on cognitive ability has increased with the use of therapies designed to bring glucose levels close to the non-diabetic range and the attendant increased risk of severe hypoglycemia, Dr. Jacobson said.

To address this concern the researchers analyzed results from two interlocked studies over 18 years. From 1983 to 1989 1,441 patients (mean age 27) with type 1 diabetes were enrolled in the Diabetes Control and Complications Trial (DCCT) and were followed for six years with a comprehensive battery of cognitive tests.

Of these patients, 711 were randomly assigned to intensive therapy, including three or more insulin injections daily or subcutaneous infusion of insulin, guided by frequent self-monitoring of blood glucose, and a goal of preventing severe hypoglycemia.

The remaining 730 patients were assigned to conventional therapy with one or two insulin injections daily, no target glucose levels, and a goal of preventing hyperglycemia symptoms or frequent or severe hypoglycemia.

In 1993, at the end of 6.5 years, 1,375 of 1,428 surviving members volunteered to participate in an observational follow-up, known as the Epidemiology of Diabetes Interventions and Complications (EDIC) study and were

followed for 12 years with the same battery of cognitive tests. Thus the two phases of the study amounted to 18 years of follow-up for these patients.

The cognitive tests, which required four to five hours to complete, included, for example, five subtests from the Wechsler Adult Intelligence Scale, four subtests from the Halstead-Reitan Neuropsychological Test Battery, subtests from the Wechsler Memory Scale, the Digit Vigilance Test, and the Verbal Fluency Test, among many others. Capillary blood glucose levels were routinely monitored immediately before testing and at the midpoint to rule out hypoglycemia during testing.

Severe hypoglycemia was defined as any event, including seizure or coma that required the assistance of another person and in which the blood glucose level was less than 50 mg/dL or the symptoms were reversed by oral carbohydrate, injected glucagon, or IV glucose.

Cognitive ability was adjusted for age at baseline, sex, years of education, length of follow-up, visual acuity, self-reported sensory loss due to peripheral neuropathy, and to control for practice effects, the number of cognitive tests taken since the start of DCCT.

During the entire 18-year follow-up, a total of 1,355 episodes of coma or seizure were reported (896 in 262 patients in the intensive treatment group and 459 in 191 patients in the conventional treatment group). However, neither the original treatment assignment nor the cumulative number of hypoglycemic events influenced performance in any cognitive domain, the researchers reported.

Higher values of glycated hemoglobin were associated with moderate declines in psychomotor efficiency ($P < 0.001$) and motor speed ($P = 0.001$), but no other cognitive domain was affected, the researcher emphasized.

Referring to their earlier examination of the DCCT cohort, the researchers said that after an average follow-up of 6.5 years, they found that cognitive function was not affected by recurrent hypoglycemia.

In the EDIC study, after 18 years of follow-up of 85% of the available DCCT participants, no deleterious effects of previous intensive therapy or recurrent hypoglycemia were evident, despite the substantially longer exposure to diabetes and its glycemic changes, and the fact that the patients were now in a later phase of their lives.

These findings should be reassuring to patients for whom intensive therapy is strongly recommended, Dr. Jacobson said.

Despite the substantial strengths of this study, the researchers said, limitations included a lack of data for young children diagnosed with type 1 diabetes before they entered the study. Information was also lacking on the effect of intensive therapy on the elderly or those living for more than 30 years with diabetes.

The findings of this study, the researchers wrote, provide an important message about the cognitive safety of intensive diabetes therapy for those diagnosed with the disorder as adolescents or young adults.

Within the limits mentioned, they said, one can be confident that although acute hypoglycemic events can be dangerous at the time they occur, recurrent severe episodes associated with intensive diabetes therapy do not appear to have long-term adverse cognitive effects.

"This conclusion," the researchers said, "lends further support to the use of intensive diabetes therapy to reduce the long-term risks of retinopathic, nephropathic, neuropathic, and cardiovascular complications in type 1 diabetes."

Practice Pearls:

Explain to interested patients that this study found no evidence of a mental decline for patients with type 1 diabetes treated with tight control of glucose levels.

Explain that tight control may protect patients from the serious long-term medical complications of diabetes.

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Item 2

Lap Band Gastric Bypass Surgery Improves Insulin Resistance

A new study examining the overall and gender-related effects of laparoscopic gastric banding surgery (LGBS) on insulin resistance, body composition, and metabolic risk markers six months post-surgery has found significant improvements in insulin resistance. The improvements occurred despite continuing obesity.

<http://www.diabetesincontrol.com/results.php?storyarticle=4788>

Overweight and obesity have reached epidemic proportions in the United States. In fact, 65 percent of Americans are currently considered overweight or obese. Using body mass index (BMI) standards, overweight is defined as BMI between 25-30 kg/m²; obesity is defined as BMI >30 kg/m².

Excess body fat is not simply a cosmetic problem; it constitutes a health risk as well. As the amount of adipose tissue (body fat) increases, the concentrations of substances produced in adipose tissue can become grossly abnormal. In addition, fat becomes deposited in the pancreas, liver and muscle, leading to metabolic derangements such as insulin resistance and/or diabetes. Obesity causes hypertension and abnormal levels of fat in the blood.

Because of the low success rate of calorie restriction (i.e., diets) in reducing morbid obesity, surgical intervention is increasingly common. Individuals are considered candidates for surgery if BMI >40 kg/m², or if BMI is 35-40 kg/m² with significant co-morbidities.

Gastric Bypass (RYGB) is the most commonly performed bariatric operation in the US, and often considered the "gold standard" by which other surgical procedures are judged. This procedure involves a rearrangement of the gastrointestinal (GI) architecture so that food bypasses about 95 percent of the stomach and large parts of the small intestine. In contrast, LGBS involves only a restriction on the stomach, so that less food can be ingested. In this procedure, an inflatable silicone band is placed around the top of the stomach in order to create a small stomach pouch. The band can be filled with varying volumes of saline so that the outlet from the small stomach pouch can vary in size. Thus, the speed of emptying food from the stomach can vary. With LGBS, there is no rearrangement of the gastrointestinal architecture and food that is ingested does not bypass any of the GI tract.

Many studies have shown that RYGB is very successful in controlling diabetes, even before substantial weight loss has occurred. Fewer studies investigating reductions in cardiovascular and metabolic risk factors after LGBS have been published. This study was undertaken to determine the overall and gender-related effects of LGBS on body composition, insulin resistance, and metabolic risk markers six months after LGBS.

Volunteers were recruited from a physician practice performing LGBS surgery. The intent was to follow patients for one year post-surgery. As of March 2007, 12 men and 17 women have been followed for six months post-surgery.

Before surgery, the team evaluated body composition using a variety of methods. Fasting blood samples were taken to evaluate metabolic risk biomarkers, including blood lipids, insulin, glucose, cardiac C-reactive protein (CRP), fatty acids, homocysteine, hemoglobin A1c (HbA1c), ApoA1, and ApoB. Resting blood pressure was also measured. Insulin resistance was estimated using a simple index (HOMA) that is based on fasting plasma insulin and glucose concentrations.

The researchers found the following: prior to surgery, there were expected gender differences in body composition measures. Men were heavier, had greater waist circumferences, L4L5 VAT, total VAT, and HbA1c. Women had higher a percentage of body fat.

Six months after surgery the overall group had a 15 percent reduction in body weight (275 vs. 233 pounds), a 14 percent reduction in BMI (43.4 vs. 37.3), a 13 percent reduction in body fat percentage (49 vs. 43 percent), a 13 percent reduction in waist circumference (53 vs. 46 inches) and a 10 percent reduction in hip circumference (57 vs. 51 inches). Total VAT was reduced by 20 percent (6.5 vs. 5.2 kg).

The insulin resistance was reduced 60 percent, according to a HOMA score. This was due primarily to a 50 percent reduction in fasting insulin concentrations with no change in fasting glucose concentrations.

There were a few gender differences in surgery-related changes. In women only, the waist-to-hip ratio tended to decrease (0.92 vs. 0.86), and the HbA1c tended to decrease (5.8 vs. 5.6 percent). In men only, total VAT was significantly reduced (8.7 vs. 6.6 kg). Diastolic blood pressured tended to decrease (81 vs. 75 mmHg) and CRP tended to decrease (8.3 vs. 4.7 mg/L).

Many studies have shown the benefit of RYGB surgery for improvement in insulin resistance in morbidly obese patients. This study demonstrates that there are also significant improvements in insulin resistance six months after LGBS. After six months, the largest and most significant changes in the group were variables suggestive of insulin resistance. These improvements occurred despite the fact that patients were still clinically obese. Rapid improvements in insulin resistance after surgery will have a positive impact on long-term patient health and may delay or prevent progression to diabetes.

Dr. Carroll presented the findings at the 120th annual meeting of the American Physiological Society (APS; <http://www.The-APS.org>)

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DID YOU KNOW:

Physical Activity Improves Erectile Dysfunction: 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 -- all it took was about 30 minutes of walking a day. 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

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Item 3

Diabetes Damaging Men's Sperm

Diabetes may be damaging to sperm, which could affect men's fertility
<http://www.diabetesincontrol.com/results.php?storyarticle=4787>

In one of the first studies to compare DNA in sperm from diabetic and non-diabetic men, the researchers found more DNA damage in sperm cells of men with diabetes -- a possible sign of reduced fertility.

Researchers at Queen's University in Belfast, Northern Ireland, studied sperm from 27 men with type 1 diabetes, with an average age of 34, and 29 non-diabetic men of similar age.

They found that while semen volume was lower in diabetic men, all other measures including sperm concentration, output, form, structure and ability to move appeared normal.

However, when they looked at the DNA, they found much more damage in the sperm of diabetic men.

Sperm damage can impair male fertility and has been associated in couples with a history of miscarriages, the team notes in the journal Human Reproduction.

They recruited their volunteers from a center for endocrinology in Belfast and among men who had sought to have their fertility tested. Because the volunteers who were not diabetic were men seeking fertility treatment, the researchers said they may also have more damaged sperm than the average man.

"Any significant differences demonstrated between diabetic men and this control group would be of even greater significance if compared with a fertile population," they write.

The study concluded that: "Diabetes is associated with increased sperm nuclear and mtDNA damage that may impair the reproductive capability of these men." Deletions and fragmentation of DNA results in loss of genetic material which, in the case of nuclear DNA, causes infertility as the sperm is not able to deliver its full complement of genetic codes in fusion with the egg to create a viable embryo.

Mitochondrial DNA (MtDNA) is found in mitochondria -- tiny "power-stations" inside cells that make energy to fuel cell activity. In humans and many other organisms, sperm cell mitochondria are destroyed when the sperm's

nuclear DNA combines with the egg's nuclear DNA and only the egg's mitochondria go on to survive in the new individual.

A number of studies have suggested that high levels of mtDNA deletions in sperm cells is linked to lower fertility in men.

Dr Agbaje said: "As far as we know, this is the first report of the quality of DNA in the nucleus and mitochondria of sperm in diabetes. Our study identifies important evidence of increased DNA fragmentation of nuclear DNA and mitochondrial DNA deletions in sperm from diabetic men." "These findings cause concern, as they may have implications for fertility," he added.

Dr Agbaje suggested that: "If the increasing trend in the incidence of type I diabetes continues, this will result in a 50% increase over the next ten years. As a consequence, diabetes will affect many more men prior to and during their reproductive years."

"Infertility is already a major health problem in both the developed and developing world, with up to one in six couples requiring specialist investigation or treatment in order to conceive," he added.

The researchers point out that semen quality has been declining over the last 50 years and poor sperm is thought to cause infertility in 40 to 50 per cent of infertile couples.

"The increasing incidence of systemic diseases such as diabetes may further exacerbate this decline in male fertility. However, it is not clear to what extent clinics consider information about the diabetic status of their patients when investigating fertility problems," said Dr Agbaje.

The researchers said the study was small and more research was needed to understand just how diabetes damages sperm and what it might mean. Given the rise in diabetes globally, the issue may be of increasing concern, they said.

journal Human Reproduction May 2007; "Insulin dependant diabetes mellitus: implications for male reproductive function." I.M. Agbaje, D.A. Rogers, C.M. McVicar, N. McClure, A.B. Atkinson, C. Mallidis, and S.E.M. Lewis. Hum. Reprod. Advance Access published on May 3, 2007. [Click here for Abstract.](#)

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Item 4

Eating Pistachios Reduces Impact of Carbohydrates

Pistachios, when eaten with some common high-carbohydrate foods, may actually slow the absorption of carbohydrates into the body, resulting in a lower than expected blood sugar level according to a study.

<http://www.diabetesincontrol.com/results.php?storyarticle=4786>

Pistachios have been shown to decrease risk factors for heart disease, however little has been known about the specific effects of pistachios on blood glucose until now. Our preliminary findings demonstrate that suppressing the glycemic (blood sugar) response of high carbohydrate foods may be part of the mechanism by which pistachios contribute to cardiovascular health and to the prevention and control of diabetes. More research is definitely warranted."

"Glycemic Response of Pistachios – A Dose Response Study and Effect of Pistachios Consumed with Different Common Carbohydrate Foods on Postprandial Glycemia was presented to more than 10,000 scientists at the Experimental Biology Conference in Washington, DC. The study is the first of its kind to examine the effects of pistachios and glucose levels in combination with carbohydrates. The research was led by University of Toronto's

Dr. Cyril Kendall and Dr. David Jenkins - researchers well known for their studies of the glycemic index which measures how rapidly sugars from foods are absorbed into the blood stream. Certain carbohydrates elevate blood sugar levels more quickly than other foods – like pistachios – that contain higher levels of protein, fiber and monounsaturated fat. In general, foods that do not quickly raise blood sugar are often considered healthier than their more processed counterparts.

Drs. Jenkins and Kendall and their research colleagues studied 10 healthy individuals who participated in a number of acute dietary studies over the course of two months. After an overnight fast, participants were given a one-, two- or three-ounce serving of pistachios alone or served with a slice of white bread and blood sugar levels were measured over a two-hour period. The findings suggest that consumption of pistachios with a carbohydrate-rich meal significantly lowered the blood glucose response. As consumption of pistachios increased, the blood sugar lowering response was enhanced. In addition, when pistachios were consumed alone, the rise in blood glucose was minimal.

The researchers also monitored the effect of pistachios consumed with different common carbohydrate foods on postprandial glycemia, or blood sugar levels after eating. The addition of pistachios to a number of other commonly consumed carbohydrate-rich foods – such as mashed potatoes, pasta and rice – also resulted in significant reductions in the blood sugar response, compared to when these foods were eaten alone.

In July 2003, the U.S. Food and Drug Administration (FDA) approved a much-awaited qualified health claim for nuts and heart disease prevention. The claim states, "Scientific evidence suggests but does not prove that eating 1.5 ounces per day of most nuts, such as pistachios, as part of a diet low in saturated fat and cholesterol may reduce the risk of heart disease." According to the California Pistachio Commission, the University of Toronto's research findings are important for individuals who are living a heart-healthy lifestyle and those that monitor their blood sugar levels.

"Most people with diabetes have other risk factors – such as high blood pressure and cholesterol that increase one's risk for heart disease and stroke. When combined with diabetes, these risk factors can add up to serious health problems," explains Constance Geiger, PhD, RD, and consultant to the California Pistachio Commission. "Recent research has suggested that pistachios are a heart-healthy, high-protein snack. Now people have yet another reason to grab a handful – they may blunt the blood sugar response of meals and may be beneficial for assisting with long-term blood glucose control."

Study conducted by the University of Toronto and funded by a grant from the California Pistachio Commission.

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DID YOU KNOW:

There are approximately 1.5 million dialysis patients worldwide, and this number is growing at a rate of approximately 7% every year. More than 300,000 patients in the United States are receiving hemodialysis for end-stage renal disease with predicted increases to 650,000 by 2010 and **2 million by 2030**; more than 26,000 are receiving peritoneal dialysis.

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Item 5

Are NovoLog and Humalog Interchangeable?

What is the relationship between NovoLog and Humalog? Molecular structure aside, can they be directly substituted for each other?

<http://www.diabetesincontrol.com/results.php?storyarticle=4785>

Insulin aspart (NovoLog, made by Novo Nordisk) and insulin lispro (Humalog, made by Eli Lilly) are rapid-acting insulin analogs indicated for treatment of type 1 and type 2 diabetes. Some institutions do substitute these agents for one another. Their pharmacokinetic parameters as reported in the product information are very similar.^[1,2] A number of small clinical trials have been performed comparing their pharmacokinetic and pharmacodynamic profiles, which suggest that few meaningful differences exist between the 2 products.

A randomized, double-blind, cross-over trial of patients with type 1 diabetes was performed to determine differences in the pharmacokinetic and pharmacodynamic profiles of insulin aspart and insulin lispro. Twenty-four subjects were given a single prandial dose of each agent tailored to individual dosing needs. Blood samples drawn before and after insulin administration demonstrated no statistical differences in relative blood glucose concentrations between the 2 agents over a 6-hour period. Similarly, there were no statistical differences in pharmacokinetic parameters, including peak insulin concentrations, insulin area-under-the-curve (AUC) at 4 and 6 hours, and time to peak insulin concentrations. The authors concluded that the 2 agents were equally effective.^[3]

However, an earlier study also performed in subjects with type 1 diabetes found some differences in pharmacokinetic parameters between the 2 agents. Fourteen subjects were randomized to a single dose of each agent before a standardized breakfast, with the alternate agent given to each subject after a 5- to 21-day washout period. While there were no statistically significant differences in glucose levels or insulin AUC between the agents over a 4-hour period, insulin lispro demonstrated more rapid absorption and elimination.^[4] These differences were statistically significant, but the clinical importance remains questionable, given the similar effects seen on glucose values.

A third study done in healthy volunteers had contrasting results, with insulin aspart demonstrating more rapid absorption and higher peak insulin concentrations. Again, absolute differences in pharmacokinetic parameters were statistically significant but small, and likely insignificant from a clinical standpoint.^[5]

Any differences in pharmacokinetic parameters are unlikely to be clinically relevant, and as such, these 2 agents may be interchanged. However, it is important to keep in mind that the pharmacokinetics and clinical response to all insulin products can vary between individuals due to a variety of factors. Individual patients switched from 1 agent to the other should be especially cautious about monitoring their blood glucose initially after the change.

1. *A third rapid-acting insulin analogue, insulin glulisine (Apidra, made by Aventis), recently came to market. This agent appears to be more rapidly absorbed than the other 2 drugs. Head-to-head studies comparing these agents are not available, so substituting insulin glulisine for aspart or lispro should be avoided at this point.*
2. *Novo Nordisk Inc. Novolog (insulin aspart [rDNA origin] injection) package insert. Princeton, NJ: Novo Nordisk; 2002.*
3. *Eli Lilly and Company. Humalog (insulin lispro injection [rDNA origin]) package insert. Indianapolis, Ind: Eli Lilly; 1996.*
4. *Plank J, Wutte A, Brunner G, et al. A direct comparison of insulin aspart and insulin lispro in patients with type 1 diabetes. Diabetes Care. 2002;25:2053-2057. [Abstract](#)*
5. *Hedman CA, Lindstrom T, Arnqvist HJ. Direct comparison of insulin lispro and aspart shows small differences in plasma insulin profiles after subcutaneous injection in type 1 diabetes. Diabetes Care. 2001;24:1120-1121. [Abstract](#) von Mach MA, Brinkmann C, Hansen T, Weilemann LS, Beyer J. Differences in pharmacokinetics and pharmacodynamics of insulin lispro and aspart in healthy volunteers. Exp Clin Endocrinol Diabetes. 2002;110:416-419. [Abstract](#)*

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http://www.diabetesincontrol.com/annodyne/anodyne10_31_01.php

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Item 6

Noninvasive Type 2 Diabetes Screening More Sensitive Than Standard Tests

Spectroscopic measurement of dermal advanced glycation end products (AGEs) is a more effective and noninvasive technology for prediabetes and diabetes screening compared with fasting plasma glucose and glycated hemoglobin (A_{1c}) tests, according to the results of a study published in the May issue of Diabetes Care.
<http://www.diabetesincontrol.com/results.php?storyarticle=4784>

"This study compared the performance of a novel noninvasive technology to fasting plasma glucose (FPG) and A_{1c} tests for detecting undiagnosed diabetes and impaired glucose tolerance," write John D. Maynard, MS, from VeraLight in Albuquerque, New Mexico, and colleagues. "Current screening methods for type 2 diabetes and prediabetes are inadequate due to their inconvenience and inaccuracy.... A more accurate and convenient screening method could dramatically improve early detection of type 2 diabetes and its precursors, facilitating interventions

that can prevent or at least delay the development of type 2 diabetes and its related micro- and macrovascular complications."

Elevated skin AGEs are biomarkers of diabetes, are highly correlated with the complications of diabetes, and predict future diabetic retinopathy and nephropathy. Individuals with diabetes accumulate skin AGEs faster than do individuals with normal glucose regulation. Until the recent development of novel noninvasive technology to measure AGEs, a punch biopsy was needed to quantify skin AGE levels. Spectroscopic measurement of dermal AGEs (SAGE) measures skin fluorescence caused by AGEs and provides a quantitative diabetes risk score. It does not require fasting, creates no biohazards, automatically compensates for subject-specific skin differences, and provides an immediate result.

This head-to-head evaluation in a naive population of 351 subjects compared results from FPG and A_{1c} tests with results from testing with a noninvasive device that detects the fluorescence of skin AGEs.

The positive screening class was defined as subjects with 2-hour oral glucose tolerance test (OGTT) values of 140 mg/dL or greater (n = 84; prevalence, 23.9%). The performances of the noninvasive device, FPG, and A_{1c} were evaluated for sensitivity and specificity using the OGTT results as the gold standard.

At the impaired fasting glucose threshold of FPG of 100 mg/dL, sensitivity of FPG was 58% and specificity was 77.4%. At that same specificity, the sensitivity for A_{1c} testing was 63.8%, whereas the noninvasive testing sensitivity was 74.7%. The increase in sensitivity of the noninvasive device compared with both blood tests for detecting diabetes and prediabetes was statistically significant ($P < .05$).

"The noninvasive technology showed clinical performance advantages over both FPG and A_{1c} testing," the authors write. "The sensitivity differential indicated that the noninvasive device is capable of identifying 28.8% more individuals in the OGTT-defined positive screening class than FPG testing and 17.1% more than A_{1c} testing. The combination of higher sensitivity and greater convenience — rapid results with no fasting or blood draws — makes the device well suited for opportunistic screening."

Practice Pearls

- ?? The SAGE technique is a noninvasive measure of skin fluorescence to detect glycation end products associated with diabetes risk.
- ?? The sensitivity of the SAGE technique is higher than that of FPG and A_{1c} for detection of type 2 diabetes and impaired glucose tolerance.

Diabetes Care. 2007;30:1120-1124.

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

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Item 7

A Cherry on Top: Tart Cherries May Alter Heart/Diabetes Factors

Tart cherries may be good for more than just making pie. Researchers report that rats that received powdered tart cherries in their diet had lower total cholesterol, lower blood sugar, less fat storage in the liver and lower oxidative stress, compared with rats that didn't receive cherries.

<http://www.diabetesincontrol.com/results.php?storyarticle=4783>

Tart cherries may be good for more than just making pie, according to new data from an animal study conducted by University of Michigan Health System researchers and presented at a major scientific meeting.

In a study involving rats, the researchers report that animals that received powdered tart cherries in their diet had lower total cholesterol, lower blood sugar, less fat storage in the liver, lower oxidative stress and increased

production of a molecule that helps the body handle fat and sugar, compared with rats that didn't receive cherries as part of an otherwise similar diet. All of the rats had a predisposition toward high cholesterol and pre-diabetes, but not obesity.

The researchers say the correlation between cherry intake and significant changes in metabolic measurements suggest a positive effect from the high concentrations of antioxidant compounds called anthocyanins that are found in tart cherries.

A U-M team will soon launch a small clinical trial to start to find out. Meanwhile, additional research is being carried out in animals prone to both obesity and diabetes.

"Rats fed tart cherries as 1 percent of their total diet had reduced markers of metabolic syndrome," says Seymour. "Previous research by other groups studied pure anthocyanin compounds rather than anthocyanin-containing whole foods, and they used concentrations of anthocyanins that would be very difficult if not impossible to obtain in the diet."

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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

Lung Cancer Risk Lower in Diabetics Taking Thiazolidinediones

Use of thiazolidinediones (glitazones) is associated with a reduced risk of lung cancer in diabetic patients, according to a new report.

<http://www.diabetesincontrol.com/results.php?storyarticle=4782>

Dr. Ranganwamy Govindarajan from the University of Arkansas for Medical Sciences, Little Rock, stated that, "This is preliminary observational work which is retrospective in nature." "Physicians should be cautioned not to start using these agents for cancer prevention."

Dr. Govindarajan and colleagues investigated the effect of thiazolidinediones on the risk of lung, prostate, and colorectal cancer in male veterans diabetics aged 40 years and older with diabetes, using a database covering 10 Veterans Affairs medical centers.

Among 87,678 individuals identified, there were 1137 cases of colorectal cancer, 3246 cases of prostate cancer and 1371 cases of lung cancer.

After adjusting for all other risk factors, patients who were prescribed thiazolidinediones had a 33% lower risk of lung cancer than patients who were not prescribed thiazolidinediones, the researchers report.

There were statistically nonsignificant trends toward reduced risk of prostate and colorectal cancer with thiazolidinedione use, the report indicates.

The lung cancer risk reduction associated with thiazolidinedione use was much greater among African American men (a 62% reduction) than among white men (26%), the researchers note. Similar subgroup analyses yielded inconsistent results for prostate and colorectal cancer.

"We are still in the process of designing further studies," Dr. Govindarajan said.

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FACT:

Medicare Fund Will Be Exhausted in 2019: The U.S. Medicare Hospital Insurance trust fund will exhaust its assets in 2019 instead of the 2018 date forecast last year due to bigger payroll tax collections, a report from the fund's trustees. The Social Security trust fund also extended its exhaustion date by a year to 2041. Despite the slight improvement reported by the trustees, the Bush administration said the two popular programs for the elderly needed urgent reform. "Without change, rising costs will drive government spending to unprecedented levels, consume nearly all projected federal revenues and threaten America's future prosperity," Treasury Secretary Henry Paulson said in a statement. The Medicare report raised a "funding warning" that is meant to trigger congressional debate over trimming costs of the health care program, which faces huge strains from rapidly rising costs and the aging baby boom generation. The trustees projected Social Security outlays to outstrip tax income in 2017, the same date as forecast last year. Paulson said time was of the essence for lawmakers to address the projected funding shortfall for the two programs. "The longer we delay, the larger the required adjustments will be -- and the burden of making those adjustments will fall more heavily on future generations," he said.

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Item 9

Hyperglycemia linked to Cancer Risk

High fasting glucose was associated with risk for pancreatic, endometrium and urinary tract cancers.

<http://www.diabetesincontrol.com/results.php?storyarticle=4781>

A recent study has linked abnormal glucose metabolism to an increased risk of cancer in women.

Pär Stattin, MD, PhD, and colleagues from Umea University Hospital in Sweden found a significant association of hyperglycemia with overall cancer risk in women and an increase in risk for cancer at many sites in both men and women.

"We found a modest increase in the risk of all cancers combined in women with abnormal glucose tolerance. For women with still higher glucose levels, the risk was even higher."

Researchers from Umea University Hospital identified 2,478 incident cases of cancer in 33,293 women and 31,304 men in the Vasterbotten Intervention Project. Fasting and plasma glucose concentrations were available for these cases.

The researchers calculated relative risk of cancer for levels of fasting and post-load glucose using Poisson models, with adjustment for age, year of recruitment, fasting time and smoking status.

"Total cancer risk increased in women with rising plasma levels of fasting and post-load glucose, up to a RR for the top vs. bottom quartile of 1.26 (95% CI, 1.09-1.47) and 1.31 (95% CI, 1.12-1.52)," the researchers wrote in *Diabetes Care*.

When they corrected for random error in glucose measurements, the risk increased to 1.75 (95% CI, 1.32-2.36) and 1.63 (95% CI, 1.26-2.18). For men, the corresponding uncorrected RR was 1.08 (95% CI, 0.92-1.27) and 0.98 (95% CI, 0.83-1.16).

High fasting glucose was significantly associated with the risks of pancreatic (RR 2.49; 95% CI, 1.23-5.45), endometrium (RR 1.86; 95% CI 1.09-3.31) and urinary tract cancers (RR 1.69; 95% CI, 0.95-3.16), as well as malignant melanoma (RR 2.16; 95% CI, 1.14-4.35).

When the researchers adjusted for BMI, it did not affect any risk estimates. Hyperglycemia proportions were highest among obese patients. According to the researchers, the absolute number of people with hyperglycemia was larger in women and men who were overweight or normal weight.

"We speculate that the lack of association among men is explained by the inverse association between prostate cancer incidence and high blood glucose. Excluding prostate cancer, we saw a mild increase (17%) in risk for men," Stattin said.

The association of hyperglycemia and total cancer risk provides further evidence for an association between abnormal glucose metabolism and cancer, the researchers wrote in *Diabetes Care*.

"Not only obese patients, but also overweight and normal weight people, should eat more fibers, less saturated fat and refined carbohydrates and engage in more physical activity, in order to decrease their risk of diabetes, cardiovascular disease and cancer," Stattin said.

The researchers also recommended a lifestyle that decreases plasma glucose levels, in hopes that it might reduce overall cancer risk and prevent diabetes and cardiovascular disease among overweight, obese and normal weight patients.

Stattin P, Bjor O, Ferrari P, et al. Prospective study of hyperglycemia and cancer risk. Diabetes Care. 2007;30:561-567.

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Item 10

Obesity May be Linked to Middle Ear Effusions in Children

Childhood obesity may be associated with a condition known as otitis media with effusion, which consists of fluid build-up in the middle ear space without symptoms of acute ear infection.

<http://www.diabetesincontrol.com/results.php?storyarticle=4780>

Otitis media with effusion, a condition in which fluid is retained in the middle ear space, but without earache, fever or other symptoms, has become increasingly frequent in children, according to background information in the article. Obesity has also become more prevalent in children, but the relationship between these two conditions has not been explored.

Jong Bin Kim, M.D., Kyung Hee University, Seoul, Korea, and colleagues studied 155 children age 2 to 7 (85 boys and 70 girls) who were treated with ear ventilation tubes for otitis media with effusion between 2004 and 2006. The children's body mass index (BMI), total cholesterol and triglyceride (a type of fat in the blood) levels were compared with those of 118 children (76 boys and 42 girls) who underwent operations for conditions unrelated to ear diseases and had never had this type of ear condition.

The average BMI in the group of children with otitis media with effusion was higher than in the control group (22 vs. 16.3), as was the average total cholesterol level (195 milligrams per deciliter vs. 159.3 milligrams per deciliter). Triglyceride levels did not differ significantly between the two groups.

The researchers also divided the group of children with otitis media with effusion into two groups, one obese and one non-obese, and compared their treatment paths. The analysis was performed defining obesity by BMI and by triglyceride and total cholesterol levels, although standards for obesity using blood cholesterol levels have not been definitively established. "For both triglycerides and total cholesterol, we defined obesity as values not within the normal range for age and sex," the authors write. "Using serum triglyceride concentration as the standard, we found that 34.7 percent of children who underwent ventilating tube insertion were obese, whereas with serum total cholesterol concentration as the standard, only 19.2 percent were obese."

"The frequency of ventilating tube insertion in the experimental group was not related to obesity, whether measured by BMI or triglyceride or total cholesterol concentration," the authors write.

"In comparing children with and without otitis media with effusion, we found that childhood obesity was significantly higher in children with otitis media with effusion," the authors conclude. "Childhood obesity may be associated with the occurrence of otitis media with effusion."

Archives of OtolaryngologyHead & Neck Surgery, May, 2007 one of the JAMA/Archives journals.

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Item 11

Aspirin Less Effective Heart Treatment for Women than Men

A new study shows that aspirin therapy for coronary artery disease is four times more likely to be ineffective in women compared to men with the same medical history.

<http://www.diabetesincontrol.com/results.php?storyarticle=4779>

Historically, studies have shown that aspirin therapy is less effective in women than in men, but it has remained unclear how much less effective and whether this affects patient outcomes, said Michael Dorsch, PharmD, BCPS, clinical pharmacist and adjunct clinical instructor at the University of Michigan College of Pharmacy.

Originally, Dorsch and his team set out to determine if patients with a history of heart attacks were more apt to be aspirin resistant than those with coronary artery disease but no history of heart attack. They found that gender and not medical history was a predictor for aspirin resistance, Dorsch said. The results surprised him.

"I was surprised by how big of a difference it was for females," said Dorsch, who has appointments at the U-M Health System and the U-M College of Pharmacy, and started the study as a resident at the University of North Carolina. "This is another piece of information that affirms we need more studies in women."

Aspirin therapy is a cornerstone in managing heart disease because it inhibits blood clotting. Aspirin therapy can reduce the risk of a nonfatal heart attack or stroke by about 23%, and an estimated 20 million men and women take a low dose of aspirin (81-325 mg daily) to control heart disease. But despite its effectiveness, there is evidence that aspirin is less effective in some patients, and researchers don't really know why. This can be frightening because most doctors do not check for aspirin resistance before prescribing aspirin therapy and therefore presume it's working in the patient when it may not be, he said.

There isn't enough evidence to show if people who are aspirin resistant can simply take larger doses, but Dorsch warns that people taking aspirin on the advice of a doctor shouldn't stop therapy on account of these results.

Not only did the study quantify how much more effective aspirin therapy is for men than for women, it is also the first study that Dorsch knows of to measure aspirin resistance in men and women with stable coronary artery disease. Previous studies have looked at the impact of aspirin therapy on people who have had a heart attack.

For the study, researchers randomly selected 100 patients who were visiting their cardiologist for a regularly scheduled appointment. All had coronary artery disease but only half had a history of heart attack. Researchers used a device called VerifyNow Aspirin Assay to test the percentage of platelet reactivity after blood samples were exposed to a chemical that causes clotting.

Aspirin works by causing platelet inhibition in the blood, which means that platelets cannot stick together and this slows the formation of blood clots that cause a heart attack or stroke.

"This does happen in women, but it doesn't happen in as many women and it's not as effective," Dorsch said. The testing device uses an optical sensor to "see" what percentage of the platelets in the blood sample clump together. Anything less than 40% platelet inhibition is considered aspirin resistant.

"We really don't know the mechanism," Dorsch said. "It could be that women have a more active platelet system in the body so it's less likely that platelet action would be inhibited."

In the future, researchers hope to look at aspirin therapy outcomes in women only and see if those outcomes can be changed. The majority of testing for aspirin therapy has been on men, so not much is known about how women respond.

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DID YOU KNOW:

Diabetes is Damaging Men's Sperm: Diabetes may be damaging to sperm, which could affect men's fertility. In one of the first studies to compare DNA in sperm from diabetic and non-diabetic men, the researchers found more DNA damage in sperm cells of men with diabetes -- a possible sign of reduced fertility. Researchers at Queen's University in Belfast, Northern Ireland, studied sperm from 27 men with type 1 diabetes, with an average age of 34, and 29 non-diabetic men of similar age. They found that while semen volume was lower in diabetic men, all other measures including sperm concentration, output, form, structure and ability to move appeared normal. However, when they looked at the DNA, they found much more damage in the sperm of diabetic men. Sperm damage can impair male fertility and has been associated in couples with a history of miscarriages, the team notes in the journal Human Reproduction. See this week's Item #3

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Item 12

Diabetics With Cancer Have Less Aggressive Treatment, Worse Survival

Diabetic patients with cancer are often treated less aggressively and have a worse overall prognosis than those without diabetes.

<http://www.diabetesincontrol.com/results.php?storyarticle=4778>

Dr. Lonneke V. van de Poll-Franse, of the Comprehensive Cancer Center, Eindhoven, and colleagues examined the prevalence of diabetes in subjects recently diagnosed with cancer, along with the influence of diabetes on cancer stage at diagnosis, treatment and overall survival. The subjects included 58,498 patients diagnosed between 1995 and 2002 and entered in the Eindhoven Cancer Registry. Patients were followed until January 1, 2005.

Nine percent of all cancer patients had diabetes at diagnosis. The prevalence of diabetes was highest among patients with pancreatic or uterine cancer, 19% and 14%, respectively. The lowest prevalence was in older men with prostate cancer or non-Hodgkin's lymphoma.

Patients with diabetes were more often diagnosed with a higher tumor stage than non-diabetics. In addition, diabetics were treated less aggressively for cancer, including less chemotherapy and radiation therapy than those without diabetes.

Overall, 3902 of 5555 cancer patients with diabetes and 29,909 of 52,943 cancer patients without diabetes died during follow-up. "After adjusting for the confounding effects of different stage at diagnosis, age, gender, treatment and even cardiovascular disease, we found that patients with diabetes experienced a significant increase in overall mortality, ranging from 0 to 40% for different types of cancer, compared to those without diabetes," the investigators conclude.

"With the ageing of the population, the number of persons who suffer from more than one chronic disease is increasing," the researchers added.

"As a consequence, more and more patients require a multidisciplinary approach for their multiple diseases. One disease with its specific treatment can influence the treatment and prognoses of other comorbid conditions."

Int J Cancer May 2007;120:1986-1992.

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Item 13

Sibutramine of Little Benefit in Obese Adolescents

When given in combination with an energy-restricted diet and exercise prescription, sibutramine does not lead to an additional decrease in body mass index in obese adolescents.

<http://www.diabetesincontrol.com/results.php?storyarticle=4777>

Sibutramine has been shown to result in a dose-dependent weight loss and to enhance the effects of a low-calorie diet for up to 2 years in obese adults, note Dr. Edgar G. A. H. Van Mil, of the VU University Medical Center, Amsterdam, and colleagues in the April issue of the Journal of Clinical Endocrinology and Metabolism.

They explain that sibutramine reduces energy intake by increasing satiety and by increasing energy expenditure by stimulating thermogenesis, but it is unclear whether the medication has the same effects on energy metabolism in obese adolescents.

The researchers examined the effect of sibutramine (10 mg daily) on body composition and energy expenditure in 24 obese adolescents, in a randomized, double-blind, placebo-controlled study.

The subjects were randomly assigned to sibutramine or placebo in combination with an energy-restricted diet and exercise plan for 12 weeks. This was followed by an identical treatment period (follow-up) without medication.

The primary measure of efficacy was the change in body mass index (BMI) SD score. It was comparable in both groups after the intervention, the researchers report. Further decreases in BMI were observed during follow-up in placebo patients. BMI stabilized in the sibutramine patients.

The team also measured body composition and total energy expenditure by stable isotopes and calculated according to a four-component model, using underwater weighing and dual x-ray absorptiometry. The changes in the percentage of fat mass were not different between the sibutramine and placebo groups, and there were no significant changes in total energy expenditure, the investigators found.

They measured basal metabolic rate (BMR) by ventilated hood adjusted for sex and body composition. The adjusted BMR decreased in the placebo group and remained constant in the sibutramine group. During follow-up, it decreased in the sibutramine group, and increased in the placebo group.

It's possible, the team says, that the potential effect of sibutramine may have been masked by the strict lifestyle management undertaken in the study.

J Clin Endocrinol Metab 2007;92:1409-1414.

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FACT:

Increasing Proportion of Cardiovascular Disease Due to Diabetes Over the Last 50 Years: A new study shows that as rates of diabetes have risen in the U.S., the proportion of cardiovascular disease (CVD) linked to diabetes has also increased. These findings emphasize the need for increased efforts to prevent diabetes and to aggressively treat and control CVD risk factors among those with diabetes, according to the results from the Framingham Heart Study. The researchers compared risk factors for cardiovascular disease and cardiovascular "events" such as heart attacks in Framingham study participants from two different time periods. The first group was examined between 1952 and 1974 and the more recent group was examined between 1975 and 1998. A total of 9,540 individuals age 45 to 64 were evaluated. The risk attributable to diabetes was 5.2 percent in the earlier time period, compared to 7.8 percent in the later period. Most of the increased risk was observed among men. The scientists also reported that the prevalence of diabetes among those with CVD almost doubled between the earlier and later time periods and there was also an increase in the prevalence of obesity. *"Increasing Cardiovascular Burden Due to Diabetes: the Framingham Heart Study" is published in the March 27th issue of Circulation and is also currently available online (March 12 Rapid Access issue).*

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Item 14

Honey as a Treatment for Diabetic Ulcers

Experts believe that treating wounds with honey has tremendous potential for the approximately 200 million people in the world with diabetes, 15 percent of whom will develop an ulcer, usually because of impaired sensation in their feet.

<http://www.diabetesincontrol.com/results.php?storyarticle=4776>

The sore on Catrina Hurlburt's leg simply wouldn't heal. Complications from a 2002 car accident left Hurlburt, a borderline diabetic, with recurring cellulitis and staph infections. One of those infections developed into a troublesome open sore that, despite the use of oral antibiotics, continued to fester for nearly eight months. The sore on Catrina Hurlburt's leg simply wouldn't heal.

Complications from a 2002 car accident left Hurlburt, a borderline diabetic, with recurring cellulitis and staph infections. One of those infections developed into a troublesome open sore that, despite the use of oral antibiotics, continued to fester for nearly eight months.

Then Hurlburt's physician, Jennifer Eddy of UW Health's Eau Claire Family Medicine Clinic, suggested she try using topical honey.

Within a matter of months, the sore had healed completely.

"I remember thinking, holy mackerel-what a difference," says Hurlburt, who can't use topical antibiotics because of allergies. "It's a lot better than having to put oral antibiotics into your system."

With funding provided by the Wisconsin Partnership Fund for Health and the American Academy of Family Physicians Foundation, Eddy is currently conducting the first randomized, double-blind controlled trial of honey for diabetic ulcers. Eddy first successfully used honey therapy a few years ago with a patient who was facing amputation after all medical options had been exhausted.

Currently, every 30 seconds someone somewhere in the world undergoes amputation for a diabetic foot ulcer. In 2001, treating diabetic ulcers and amputations in U.S. patients cost \$10.9 billion.

"Patients like Catrina Hurlburt are a great example of the potential health care savings," explains Eddy, who is also assistant professor of family medicine at University of Wisconsin School of Medicine and Public Health. "Unsuccessful conventional care for ulcers can cost thousands of dollars. Therapy with honey may only cost a few hundred."

Diabetics typically have poor circulation and decreased ability to fight infection. Diabetic ulcers treated with long courses of systemic antibiotics can become colonized with drug-resistant organisms--so-called "superbugs" such as Methicillin-resistant Staphylococcus aureus (MRSA). Since honey fights bacteria in numerous ways, it is essentially immune to resistance. Honey's acidic pH, low water content (which effectively dehydrates bacteria), and the hydrogen peroxide secreted by its naturally-occurring enzymes make it ideal for combating organisms that have developed resistance to standard antibiotics.

Patients in the clinical trial will receive ulcer care and treatment by an expert podiatrist. Half will be randomly assigned to receive honey, while the other half will receive a wound-care gel that has been compounded with inert components to give it the flavor and color of honey. The ulcers will be measured to see how quickly they heal, to evaluate whether honey or the standard wound gel is better for healing.

If honey proves the more effective method, Eddy cautions patients against using it at home without a physician's involvement. "Unfortunately, diabetic ulcers are very complicated, and honey would only be part of the solution," she says. Successful care also requires off-loading-avoiding walking and putting weight on the sore-and the sterile removal of dead skin and bacteria from the wound.

"If we can prove that honey promotes healing in diabetic ulcers, we can offer new hope for many patients," says Eddy. "Not to mention the cost benefit, and the issue of bacterial resistance. The possibilities are tremendous."

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Item 15

Common Genetic Variation Increases Heart Disease Risk

The risk of heart disease increases in the presence of a common genetic variation carried by a large percentage of Caucasians, according to two reports.

<http://www.diabetesincontrol.com/results.php?storyarticle=4775>

The findings are the latest in a flurry of reports of new genetic findings that have emerged from a technique known as genome-wide association scanning. Last week, three groups reported using the method to find several genetic variations linked to type II diabetes. One of the variations identified in those diabetes studies lies in a region that contains no known genes -- and is the same locus where today's research puts a heart disease risk variation.

"This is a stunner," said Francis Collins, M.D., Ph.D., director of the National Human Genome Research Institute. "It seems like this one place carries all of that weight for two very common and very dangerous diseases."

Dr. Collins, one of the senior researchers involved with the diabetes studies, commented, "Not only did they find a variation that is associated with heart disease, but in the very same place, where a week before, three different groups found the same association with a different disease," Dr. Collins said.

The region in question lies near two genes known as *CDKN2A* and *CDKN2B* genes on chromosome nine, according to Ruth McPherson, M.D., Ph.D., of the University of Ottawa (Ontario) Heart Institute.

But, she and colleagues said, the genetic variation they found is not associated with established coronary heart disease risk factors such as plasma lipoproteins, hypertension, or diabetes.

The finding -- like all genome-wide association scanning -- is based on comparing the genes of people with and without the disease of interest, in a case-control fashion using microarray technology.

In this case, Dr. McPherson and colleagues analyzed the genomes of 322 people with severe early coronary heart disease taking part in the Ottawa Heart Study, and compared them with those of 312 healthy controls.

Variations identified in that analysis were then studied in an independent sample of 311 cases and 326 controls from Ottawa and the 11,478-participant Atherosclerosis Risk in Communities study in the U.S. The research narrowed candidate variations down to two single nucleotide polymorphisms (SNPs) within 20 kilobases of each other on chromosome nine.

Finally, the researchers studied the variations in three more independent groups -- one from Copenhagen, one from Dallas, and a thirds set from the Ottawa Heart Study.

The analysis showed that roughly 25% of Caucasians have two copies of the so-called risk allele, which was associated with between a 30% and 40% increased risk of early coronary heart disease.

About half of all Caucasians have one copy of the allele, and they have between a 15% and 30% increase in risk, Dr. McPherson and colleagues said.

The Icelandic study, led by Kari Stefansson, M.D., of deCODE genetics, paralleled the Canada-U.S. probe, except that the researchers chose myocardial infarction as their target. Starting with 1,097 Icelanders who had early-onset MI and 6,728 controls who had no history of coronary disease, Dr. Stefansson and colleagues found several suspect SNPs.

They repeated the analysis using an independent set of Icelanders, as well as Caucasian case-control cohorts in Philadelphia, Atlanta, and Durham, N.C., and narrowed the suspects down to three SNPs on chromosome nine.

Again, the Icelandic researchers found that 21% of Caucasians carry two copies of the risk allele (homozygous), which confers about a 64% increase in risk of MI, while those with one copy (heterozygous) face about a 26% increase in risk.

Neither group was able to say exactly how the suspect regions increase risk, especially because no known genes reside in the area. One possibility, Dr. McPherson and colleagues said, is that the region contains a regulatory element that governs genes some distance away.

Interestingly, neither group found that their heart disease signal was associated with diabetes. In the Canada-U.S. study, for example, those with diabetes were explicitly excluded.

Scienceexpress: McPherson R et al. ["A Common Allele on Chromosome 9 Associated with Coronary Heart Disease."](#) Science 2007; 10.1126/science.1142447.

Scienceexpress: Helgadóttir A et al. ["A Common Variant on Chromosome 9p21 Affects the Risk of Myocardial Infarction."](#) Science 2007; 10.1126/science.1142842.

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Quote of the Week!

“We Must Become the Change We Want to See”

.....Mahatma Gandhi

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