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DIABETES IN CONTROL.com NEWSLETTER
The Newsletter for Professionals in Diabetes Care

November 2, 2002 Issue 124

From the Editors Desk:

I had a chance to speak with **Dr. Steve Witherly** at the Weight Management Food and Dietary Supplements conference in Phoenix last week and he had some fascinating things to share with me.

Evan David Rosen, M.D., Ph.D., brings us his feature An ACE in the hole-From HOPE to DREAM

If you notice some older people at the gym these days then check out **Item #8**. It seems that high-intensity weight training coupled with a moderate weight-loss program can help older men and women with type 2 diabetes.

We have picked winners from those of you who filled out the survey. [Click here to see if you won, more winners next week.](#) **If you faxed in your winning entries from AADE, your prizes will be mailed this week.**

We have a feedback survey coming up for professionals who stand on their feet. If you spend time on your feet each day please [click here to get more info.](#)

Dave Joffe
Editor-in-Chief

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News Flash - News Flash

UPDATE:

New refined insulin seen as key to saving millions of diabetics!

Nanomized Insulin made of smaller particles and reduces number of daily injections.

Melbourne (dpa) - A new kind of insulin containing drug particles as fine as smoke could result in far fewer injections for diabetics and save millions of lives. **See Item #3**

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New Product



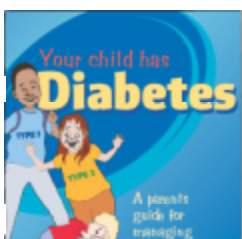
Just 4 U Temporary Tattoos are a fun way to get kids to wear diabetes identification.

These were developed by diabetes educators. Each package also includes three tattoos suitable for adults.

These tattoos are safe, washable, and fun to wear. Intended as an adjunct to wearing medical diabetes alert jewelry, temporary tattoos make medical identification more appealing..

: They come in Feminine or Sport themes and cost \$2.59 for a package of 12 tattoos. For more information visit www.dibonsystems.com

Tools for your Practice: "Your Child has Diabetes"



Getting Back to the Basics: A new book which serves as a guide for parents of Children with Diabetes.

Helping parents learn about diabetes and how to manage it can be a difficult task. This book was designed with the parents in mind. It covers the basics of diabetes management including injecting insulin, meal planning, exercise, high and low blood glucose emergencies and taking diabetes to school. This helpful guide also provides

parents with some helpful tips for helping their child deal with the emotional aspect of diabetes. Published by Pritchett and Hull, the 40-page book can be ordered for \$3.25. To order call 800-241-4925 or on line at www.p-h.com

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Product Update: A1cNow is Less Than 9 Dollars!

Now less than 9 dollars for the first and only NGSP A1c test that is instant and disposable. For more info on how you can now use it in your office practice [click HERE!](#) 75% of patients with diabetes are not getting the recommended A1c testing.

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This newsletter is the condensed version. If you would like to see the full newsletter go to <http://www.diabetesincontrol.com/Issue124index.htm>

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OPEN STUDIES: For Your Participation *(Educators have said that just by participating in a study, they can get better outcomes)*

1. [The FIBER Study \(Click Here\)](#)
2. RELAXATION – WarmFeet® study Version II [Click Here](#)

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This Weeks Items:

1. **Experts Reach Consensus on Causes of Type 2 Diabetes***
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[Click Here](#)
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ITEMS For The Week:

Item #1

Experts Reach Consensus on Causes of Type 2 Diabetes

Genetics, fetal origins, lifestyle and stress may all be risk factors of Type 2 diabetes

Genetics, fetal history, lifestyle and stress may all favor the occurrence of Type 2 diabetes, according to experts at a recent meeting in Colombo, Sri Lanka. 350 international experts including representatives of the International Diabetes Federation (IDF) and the World Health Organization (WHO) met on 6-7 July under the banner of Diabetes in Asia 2002 to discuss the causes that could be at the origin of Type 2 diabetes. The subsequent consensus could help develop a primary prevention strategy to defuse the escalating incidence of this form of diabetes worldwide.

Type 2 diabetes is rising dramatically, with at least 170 million people with diabetes worldwide and a predicted increase to 300 million by 2025. More and more children and adolescents are developing Type 2 diabetes, a form of diabetes that used to be found mostly in adults. Up until now, scientists mainly focused on obesity due to lifestyle changes as being a cause of Type 2 diabetes, however, new studies reveal that genetics, fetal history and, possibly, stress may also play a role in the development of the condition.

Genetics was identified as a significant factor that causes diabetes. There is firm evidence from genetic studies that the association of some genes is at the root of causing Type 2 diabetes.

Low birth weight was recognized as another risk factor for Type 2 diabetes. Epidemiological studies have reported a higher incidence of Type 2 diabetes in people who had a low birth weight. Animal studies confirm that poor nourishment of the fetus increases the risk of metabolic syndrome and Type 2 diabetes. Furthermore, postnatal over-nutrition may aggravate the syndrome.

Obesity has long been associated with diabetes, Impaired Glucose Tolerance (IGT) and Cardiovascular Disease (CVD). Lifestyle changes, including bad eating habits and physical inactivity all contribute to obesity.

Finally, compelling animal evidence and mechanistic studies suggest a relationship between stress and insulin resistance leading to Type 2 diabetes.

"This consensus is likely to highlight the urgent need for the primary prevention of Type 2 diabetes." Said Professor Sir George Alberti, President of the IDF. "We hope that the consensus will facilitate the introduction of programs to increase awareness and promote education at all levels. There is urgent need for government action to promote healthy lifestyles now." [Read the Consensus Document](#).

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(Public Service)

If your patients are having a problem paying for their medications go to www.diabetesmeds.org and download the application that will allow them to get all of their medications for 10 dollars or less for a 90 day supply.

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Item #2

High Cholesterol Can Predict Childhood Obesity

Although conventional wisdom is that obesity causes high cholesterol, results of a study in the September issue of the American Journal of Clinical Nutrition suggest that, at least for girls, high cholesterol can be a marker of obesity developing later in childhood.

"It is not clear how hypercholesterolemia is linked to high adiposity," write Andrew M. Tershakovec, from the Children's Hospital of Philadelphia, Pennsylvania, and colleagues. "It seems more likely that hypercholesterolemia acts as a marker of altered metabolism, which results in excessive adiposity."

This spin-off from the Bogalusa Heart study compared 58 hypercholesterolemic children (low-density lipoprotein [LDL] levels greater than 75th percentile) with 215 children who had normal cholesterol levels (LDL less than 60th percentile). Subjects were age 5 to 6 years at study enrollment, and none were obese. There were equal numbers of girls and boys, and 41% of the children were black. Although the nonhypercholesterolemic children were taller than the hypercholesterolemic children, there were no other significant differences between the two groups.

At three- and six-year follow-up, body mass index (BMI) in the hypercholesterolemic girls increased at a greater rate than in the normocholesterolemic girls. By age 11 to 12 years, 45.2% of the hypercholesterolemic girls were overweight or obese, as were 21.6% of the girls with normal cholesterol. This effect was not observed in boys, and it was independent of race in girls.

Associations between BMI and cardiovascular risk factors including blood pressure, insulin, and blood lipids were stronger with increasing age, and in some cases were stronger in hypercholesterolemic children and girls.

"Hypercholesterolemia is associated with increased relative weight in girls," the authors write. "The increased relative weight, even at an early age, is associated with a deleterious effect on blood lipids and other cardiovascular disease risk factors in hypercholesterolemic children, although the strength of these associations is sex dependent." *Am J Clin Nutr.* 2002;76: 730-735

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FACT

Americans are eating an average of 400 calories more than they did decades ago -- at that rate an average person can expect to gain 41.7 pounds a year.
NIH

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Item #3

New Insulin Seen as Key to Saving Millions of Patients with Diabetics!

Nanomized Insulin made of smaller particles and reduces number of daily injections.

People with diabetes may only need a third of their usual dose when taking the new form of insulin, a team of Australian scientists has shown. It is made up of tiny particles under 100 nanometres (100 millionths of a millimeter) across.

In tests on rats conducted at Deakin University, near Melbourne, 0.15 units per kilogram of body weight produced the same response as 0.5 units of normal insulin.

The study did not set out to establish a minimum dose, and experts believe the new insulin may be more than three times as potent as the traditional form. The new drug also produced a more sustained effect, *New Scientist* magazine reported.

Normal insulin starts to lose its effect after 30 minutes, but the nanomised insulin continued to act strongly for at least an hour. That means diabetics might be able to cut back from five injections a day to only two or three, said *New Scientist*.

The new insulin was produced by Eiffel Technologies of Melbourne using a "supercritical fluid" process also being developed by other companies. To nanomize insulin, a gas is first put under such high pressure that it becomes "supercritical" and starts to behave like a liquid.

Normal insulin is dissolved in the supercritical fluid, which is suddenly decompressed, making the insulin precipitate out in particles. If it lives up to its promise nanomised insulin could relieve a worldwide shortage of insulin that is causing the deaths of millions of diabetics in developing countries.

It is not clear why nanomized insulin is more efficient or why it lasts longer. An expert who reviewed the Deakin study said insulin molecules normally "cluster together in a six-pack" configuration which the body has to convert back to a single form. With nanomized insulin, this process may not be necessary.

The scientists believe the technique could also improve the effectiveness of other drugs and allow them to be delivered in easier ways, such as through skin patches.

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Item #4

Isosorbide Spray On the Feet Reduces Neuropathic Pain in Diabetics

Spraying the feet with an aerosolized form of isosorbide dinitrate (ISDN) appears to provide temporary relief of diabetic neuropathy pain.

That, according to the results of a small pilot study conducted in the UK.

Although questions remain about the exact cause of diabetic neuropathy, experts believe that the condition is related to impaired nitric oxide (NO) generation. ISDN is a well known NO donor with potent vasodilating properties.

Previously, Dr. Kevin C. J. Yuen, from Addenbrooke's Hospital in Cambridge, and colleagues found that topical application of ISDN appeared to reduce the severity of symptoms associated with diabetic neuropathy.

In the current study, the researchers evaluated the effectiveness of an aerosolized form of ISDN in 22 people with diabetic neuropathy. The patients were instructed to use the spray on both feet each night before bedtime.

Half of the group used ISDN spray for 1 month while the other half used an inactive placebo spray. At the end of the month, the groups went 2 weeks with no treatment and then switched to the other treatment regimen for another month. The findings are published in the October issue of Diabetes Care.

Overall, pain and burning sensations were reduced more when patients used the ISDN spray than when they used the placebo, the report indicates. Two patients developed mild headaches when using the ISDN spray, but the headaches resolved and the patients continued therapy.

"At study completion, 11 patients (50%) reported benefit and wished to continue using the ISDN spray, 4 (18%) preferred the placebo spray, 4 (32%) were undecided," the authors write.

Dr. Yuen's team also found that patients reported improvements in sleep, mobility and mood when using the ISDN spray.

"Some patients reported an increased exercise threshold, and one patient reported uninterrupted sleep at night, something she had not experienced for several years because of her painful neuropathy," according to the report.

Still, the investigators are calling for larger studies to confirm their findings. The drug's effect may only be short-lived or it may not work for all diabetic patients with the condition. *Diabetes Care* 2002; 25: 1699-1703.

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Item #5

HRT Tied to Better Glycemic Control in Diabetic Women

Diabetic women who receive hormone replacement therapy (HRT) have lower glucose levels and better cholesterol profiles than their counterparts who do not receive HRT

That, according to a report published in the October issue of *Diabetes Care*.

In addition, in non-diabetic women, HRT use is associated with a reduction in non-HDL and a rise in HDL cholesterol levels, the report notes.

The current findings follow recent negative news about HRT. In July, a major US trial was stopped because HRT use appeared to increase the risk of breast cancer and cardiovascular disease. Earlier this month, one drug maker, Wyeth, changed the labels on its HRT products to reflect the safety concerns.

In the current study, Dr. Carlos J. Crespo, from the State University of New York at Buffalo, and colleagues analyzed data from 2,786 postmenopausal women who participated in the Third National Health and Nutrition Examination Survey, conducted between 1988 and 1994. All of the women underwent oral glucose tolerance testing, had blood drawn for lipid profiling, and responded to a questionnaire about HRT use.

As a group, diabetic women had worse lipid profiles than their non-diabetic peers, the authors note.

In diabetic women, current HRT use was associated with lower levels of total cholesterol, non-HDL cholesterol, fibrinogen, glucose, insulin, and glycosylated hemoglobin compared with never use. In addition, HRT use was tied to increased apoA levels in diabetic women.

In non-diabetic women, current HRT users had significantly lower non-HDL cholesterol levels and significantly higher HDL cholesterol levels than non-users or previous users.

The study, published in the current issue of *Diabetes Care*, adds yet another twist to the murky risks-benefits scenario surrounding HRT.

The federal government suspended a nationwide clinical trial of HRT in July, citing, among other concerns, that the combination of estrogen and progesterone used in the trial did not protect against cardiovascular disease as expected.

Yet, the UB researchers found that HRT had a positive effect on two important risk factors for heart disease -- blood levels of fats and glucose -- in a population-based study of 2,786 diabetic and non-diabetic postmenopausal women between the ages of 40 and 74. Carlos Crespo, Ph.D., associate professor of social and preventive medicine in the UB School of Medicine and Biomedical Sciences and lead author on the study, noted that the national HRT clinical trial did not include women with diabetes and that scientists haven't researched the benefits or risks of hormone replacement in this group.

"Although there may be some risk in using certain types of HRT among certain women, there might be a segment of women who would be better off using HRT," Dr. Crespo said in a statement. "These findings indicate that diabetic women may be one such segment," he added. *Diabetes Care* 2002;25:00-00.

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Item #6

Diabetes-Associated Amputations Deemed Avoidable With Antibiotic Therapy

A significant percentage of amputations stemming from complications of diabetes could be avoided by early and proper treatment with antibiotics, according to a German researcher.

Bacterial infections play a role in about 40% of all diabetic foot syndrome-related amputations according to Dr. Bernd Drewelow, director of the Institute for Clinical Pharmacology at the University of Rostock.

"Using antibiotics to treat diabetic foot syndrome could save a lot of feet," he said. He estimates that 20% to 50% of amputations due bacterial infections could be avoided with early and proper treatment with antibiotics.

But many physicians treating diabetic foot syndrome are not knowledgeable about the possibility of infection, Dr. Drewelow said. "I think this is a problem all over the world," he said.

Dr. Drewelow and his team have been focusing on two newer antibiotics, linezolid and moxifloxacin.

Because of poor circulation in the feet, many antibiotics are not able to reach the infected areas at effective levels, he said. Emphasizing that further research is necessary, he said that early evidence suggests linezolid and moxifloxacin in some cases can reach the infected areas at concentrations high enough to be effective.

Furthermore, the two agents appear to be effective against some of the most common bacteria associated with diabetic foot syndrome.

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DID YOU KNOW: Children could be eligible for Free or Low-Cost Health Insurance:

If you don't have insurance, your children could be eligible for free or low-cost health insurance, which is available in each state through the Department of Health and Human Services. The program, which insures children through age 18, is available even if you have a job— although there are income limitations for eligibility.

Among other things, the insurance pays for doctor visits, prescriptions and hospitalizations. For more info call 877-543-7669 or log on to www.insurekidsnow.gov/states.htm and click on your state.

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Coming Soon: A1cNow Monitors will be available without a prescription very shortly, Stay tuned. www.a1cnow.net

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Item 7

Moderate Drinking May Help Control Blood Glucose

Drinking moderate amounts of wine, beer or hard alcohol is associated with better blood glucose control among healthy adults, particularly women, study findings indicate.

Women who drank any kind of alcohol had lower hemoglobin A1c (HbA1c) levels than non-drinkers, regardless of their body mass index (BMI).

In men, however, only wine was associated with lower blood glucose levels, the researchers report in the September issue of the European Journal of Clinical Nutrition. Lifestyle and personality traits associated with wine drinking may account for the finding, they note, as previous studies have linked beer drinking among men to smoking, hostility and a less healthy diet.

Drinking wine, on the other hand, is associated with healthy lifestyle behaviors, such as not smoking and avoiding obesity, as well as a higher level of education. Wine also tends to be consumed with meals, which would blunt the effects of alcohol on the body.

Whatever the reason, the results support those of previous studies and "provide further evidence that moderate alcohol consumption may be one component of a healthy lifestyle," Dr. N. J. Wareham, from the University of Cambridge in the UK, and colleagues conclude.

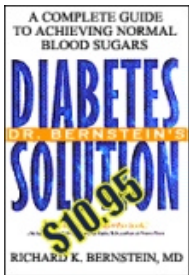
The results are based on interviews with more than 6400 white adults, 40 to 78 years of age, who were participating in a study on diet and chronic disease.

Overall, adults who consumed the most alcohol tended to be younger and to have lower blood glucose levels. Those who consumed alcohol also tended to be more educated, to smoke, and to report exercising.

BMI declined as alcohol intake rose among women. Among men, however, BMI rose in tandem to the amount of alcohol consumed.

Men and women also differed in the type of alcohol they drank. Men drank more beer, while women tended to drink more wine. Fruit and vegetable consumption was associated with wine but not beer intake. *Eur J Clin Nutr* 2002; 56: 882-890.

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Item 8

Seniors Pumping Iron To Control Diabetes

High-intensity weight training coupled with a moderate weight-loss program can help older men and women with type 2 diabetes to improve their blood sugar control and also boost their muscle strength and lean body mass, researchers report.

The added muscle is particularly beneficial to people with diabetes, according to Dr. David Dunstan, the study's lead author, because muscles are "major clearance sites" for circulating blood sugar, or glucose. In type 2 diabetes, the body loses its ability to respond to the blood sugar-regulating hormone insulin, so high levels of glucose can build up in the blood.

Dunstan is director of physical activity programs and research at the International Diabetes Institute in Victoria, Australia.

The magnitude of the response, noted study co-author and institute director Dr. Paul Zimmet, was surprising. "The effects of the resistance training program were as great as those typically seen with drugs for diabetes," he explained.

The researchers assigned 36 people aged 60 to 80 to one of two exercise groups: high-intensity resistance training and moderate weight loss; or moderate weight loss plus a control program, for 6 months. Study participants in the control group did stretching exercises instead of lifting weights.

The goal of the high-intensity lifting program is to train with weights that are around 80% of the maximum poundage a person can lift for one repetition. The weight-lifting patients did nine different exercises three times a week that worked muscles in their legs, arms and abdomen, and were closely monitored by staff.

A test of long-term blood sugar control showed significant improvements in the weight-lifting group after 3 months of exercise, and improved further by 6 months. People in both groups lost weight and fat, but the weight-lifters showed gains in lean body mass while those who didn't lift weights showed losses.

Encouraging high-intensity weight lifting for people with diabetes could reduce the risk of diabetes complications--which can include eye and nerve damage, as well as kidney problems--in the long term, Dunstan said. The more tightly blood sugar is controlled, the less likely complications are to develop.

These results, said Dunstan, "support the recent recommendations of the American College of Sports Medicine that resistance training should be included as part of a well-rounded exercise program for all people with type 2 diabetes." Patients should consult their doctor first before beginning training, he added.

Dunstan encourages gym owners to make gyms more accommodating to older people so it will be less intimidating for them to work out. "Who knows--for many gymnasiums this could be a totally untapped market," he said. *Diabetes Care* 2002;25:1729-1736.

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FACT

Women who snore are more likely to develop type 2 diabetes, according to the results of a study conducted by doctors at Harvard. The study showed that snoring was a risk factor for type 2 diabetes independent of other risk factors such as weight and age. *American Journal of Epidemiology* 3/01/02

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Item 9

'Surprising' Mechanism For Thiazolidinedione-Related Weight Gain Uncovered

If obesity is the leading cause of type II diabetes, then why do thiazolidinediones (TZDs), the only available drugs that treats this form of diabetes, actually cause more weight gain?

Thiazolidinediones stimulate the uptake of fatty acids by adipocytes and the production of triglycerides, leading to weight gain.

That, according to a multicenter team of researchers reports in an advance online publication of Nature Medicine for September 23rd. Researchers at the University of Pennsylvania School of Medicine address the fundamental workings of TZDs (also known as glitazones or under brand names such as Actos® and Avandia®), and provide a potential new target for further study.

Their research describes how TZDs trigger the creation of glycerol kinase, an enzyme that causes fat cells to store fatty acids faster than it produces them.

"It is what researchers call a 'futile' cycle. Just as fat cells release their larder of fatty acids, glycerol kinase causes the fat cells to put them back in storage," said Mitchell A. Lazar, MD, PhD, Chief of the Division of Endocrinology, Diabetes, and Metabolism and Director of the Penn Diabetes Center. "The glycerol kinase is packing the pantry faster than fat cells can pull the cans off of the shelves. The net influx of fatty acids into fat tissue contributes to reduced fatty acids in the bloodstream that, in turn, leads to increased sensitivity to insulin."

Type II, or adult-onset diabetes, occurs as cells lose the ability to respond to insulin, a hormone which allows cells to absorb sugar for fuel. The disease affects millions, and has become an epidemic in the industrialized world. According to Lazar, two big mysteries remain concerning type II diabetes: how cells become insulin resistant and how TZDs cause them to lose resistance to insulin. By studying how the drug works, the researchers have uncovered a fundamental clue that may allow the development of better therapies "Right now, our findings suggest that weight gain is an inherent part of how TZDs function and diabetics should bear in mind the role of a healthy diet in combination with drug therapy," said Lazar. "TZDs actually lower insulin requirements in diabetics, and this is likely to be beneficial in terms of the risk of hypertension and heart disease associated with diabetes."

Despite their beneficial qualities, it seems that TZDs have little respect for medical textbooks. "According to conventional medical knowledge, fat cells do not produce glycerol kinase for precisely the reason that helps TZDs to be effective," said Lazar.

Fatty acids are stored in fat cells as triglycerides (TGs). When the body senses that it needs fuel, such as what happens when diabetic cells cannot absorb blood sugar, fat cells breakdown TGs to produce glycerol, which travels to the liver to make the sugar glucose, and fatty acids, which muscles use an emergency fuel source.

TZDs, however, reverse this process as it happens. When the drug binds to a receptor in fat cells called PPARgamma, TZD causes the cells to uncharacteristically produce glycerol kinases. These enzymes then recombine glycerol and fatty acids into TGs. They also open the cell's door to trap passing fatty acids, which lowers the amount of fatty acids in the bloodstream.

In addition, researchers have found that TZDs may also alter the chemical signals produced by fat cells, which may prove beneficial in producing the next generation of anti-diabetes drugs.

"We have come to understand that fat cells are more than just storage bins for excess fats," said Lazar. "They produce hormones and actively regulate how our bodies process and use fats. Future drug discovery may depend on the role of fat itself." *Nature Med 2002* **University Of Pennsylvania Medical Center**

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Special News Bulletin

Pyridoxamine Protects Against Diabetic Retinopathy

Study shows efficacy of pyridoxamine in preventing aspects of diabetic retinopathy

See item 15

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Item 10

Framingham Model Underestimates Cardiovascular Risk in Diabetes

The risk of cardiovascular disease in patients with type II diabetes may be some 30% higher than that indicated by the Framingham model, according to preliminary new research.

Researchers at the Poole Diabetes Centre in Poole, Dorset, and the University of Southampton, who presented their findings at the 46th annual scientific meeting of the Society for Social Medicine in Liverpool last week, said their findings suggest some high-risk patients may not be receiving adequate intervention to reduce cardiovascular disease.

The study was designed to see if assessment based on the Framingham risk model was identifying all those at risk. The researchers followed all patients newly diagnosed with type II diabetes in the Poole area between 1996 and 1998. At the same time, a control group of non-diabetes sufferers matched for age and sex was also monitored.

The results revealed the Framingham model was failing to identify an average of one in three cardiovascular events.

"The Framingham model has been promoted for routine clinical use in the UK as the best available protection tool for assessing the risk of developing cardiovascular diseases," said Mark Mullee, a statistician from the University of Southampton, who took part in the research.

"We have to be cautious in interpreting these findings, because of the relatively short follow-up period of our study," he said, "but our research shows that using this model may underestimate the risk."

Dr. Wendy Gatling, who led the study, told Reuters Health that the problems may be due to the fact that the Framingham study included very few diabetics. "Maybe that's the reason it's underestimating the risk. We saw these results across the board--in men and women and in different age groups."

Early findings from the Poole study also suggest type II diabetes is associated with a two-fold risk of death compared to healthy controls, even in the early years following diagnosis. Most of this is accounted for by the increased risk seen in diabetic women, who are three times as likely to die as their non-diabetic counterparts.

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Item 11

Study Confirms Relation Of Heredity, Behaviour To Diabetes Risk

A study of female college graduates confirmed the strong association between heredity, modifiable behavior, and the risk of non-insulin-dependent diabetes.

Grace Wyshak, PhD, at Harvard Medical School and the Harvard School of Public Health, in Boston, Massachusetts, United States, conducted a follow-up study of 3,940 college alumnae, who took part in a 1981-1982 study comparing the health of college athletes with non-athletes.

The subjects included 1,945 former college athletes and 1,995 non-athletes. The follow-up study, which involved a self-administered questionnaire on medical history, health, family history, and behavioral practices, was conducted in 1996 to 1997, Professor Wyshak reported.

About 1.3 percent of the women reported physician-diagnosed diabetes. One point seven percent were non-athletes and 0.9 percent were former athletes. Former athletes had a significantly lower risk of non-insulin-dependent diabetes, with an age-adjusted odds ratio of 0.41, she reported.

Insulin-dependent diabetes was associated with a history of paternal diabetes (odds ratio of 4.7) and also with a history of diabetes in siblings (odds ratio of 6.7). Dependent-dependent diabetes was associated with a history of maternal diabetes (odds ratio of 8.0).

No association was found between behavioral factors and insulin-dependent diabetes. However, certain behavioral factors were inversely related to dependent-dependent diabetes. The odds ratio for being an athlete was 0.4. For women who reported current regular exercise, the odds ratio was 0.4, and the odds ratio for low body mass index compared with high body mass index was 0.2, Professor Wyshak reported.

"The findings that insulin-dependent diabetes is associated with paternal diabetes and that dependent-dependent diabetes may be maternally transmitted are not widely known, although the mode of transmission of diabetes is receiving increasing attention in the medical and genetic literature," the researcher noted. "This study confirms that modifiable behavioral practices, such as physical activity and weight control (i.e., optimal body mass index), reduce the risk of dependent-dependent diabetes." *J Womens Health Gend Based Med 2002; 11: 549-554*

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DID YOU KNOW

People with diabetes are more likely to use alternative medicine. *In the US, people with diabetes are 1.6 times more likely to use complementary and alternative medicine (CAM) than people without diabetes, according to researchers from the Medical University of South Carolina. In addition, greater age and higher education are associated with the use of CAM, say the researchers. Further analysis showed that people with a college education, women, individuals ages 35 to 49 and those with a household income of more than \$50,000 per year were the most likely to use alternative medicine.*

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Item 12

Different Risk Factors Differentially Affect Vascular Complications of Diabetes

Elevated blood pressure and increased glucose levels are risk factors for the microvascular complications of type 2 diabetes. In contrast, blood pressure, but not glucose levels, appears to influence the risk of macrovascular complications.

That from the Findings from a longitudinal study conducted in Poland indicate that Previous studies have yielded conflicting results regarding the impact of glucose levels on the risk of macrovascular complications, according to the report published in the July/August issue of the Journal of Diabetes and Its Complications.

To clarify the risk factors for vascular complications, Dr. Wladyslaw Grzeszczak and colleagues, from Diabetes and Nephrology in Zabrze, Poland, analyzed the medical records of all patients with newly diagnosed type 2 diabetes who presented to a diabetes clinic between 1980 and 1994. A total of 2175 patients were identified.

The researchers found that the risk of developing nephropathy and proliferative retinopathy increased as fasting plasma glucose and mean blood pressure increased. In addition, blood pressure, but not

glucose level, was directly related to the risk of stroke and cardiovascular disease. High cholesterol levels were found to increase the risk of coronary artery disease and proliferative retinopathy.

Similar findings have been reported previously, the authors note. "The main advantage of our study was its longitudinal design," they point out. "Contrary to previously reported cross-sectional studies, the outcome occurred after the measurement of independent variables and not at the same time." *J Diabetes Complications 2002; 16:271-276.*

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Item 13

Pyridoxamine Protects Against Diabetic Retinopathy

Pyridoxamine, an inhibitor of advanced glycation end products (AGEs), appears to protect against pathological changes in the retinas of diabetic rats and may be a new treatment for diabetic retinopathy.

"This preclinical study is a demonstration of efficacy of pyridoxamine in preventing aspects of diabetic retinopathy in an experimental animal model," Dr. Alan Stitt from Royal Victoria Hospital, Belfast, Northern Ireland, told Reuters Health.

Dr. Stitt and colleagues compared the effects of pyridoxamine with the antioxidants vitamin E and R-alpha-lipoic acid in streptozotocin-induced diabetic rats, according to their report, published in the September issue of Diabetes.

The researchers gave the rats pyridoxamine 1g/L drinking water or 2,000 IU of vitamin E per kilogram diet or 0.05% per kilogram diet of R-alpha-lipoic acid.

"The approach we used looked at physical death of retinal capillaries during diabetes and some pathophysiological measures," Dr. Stitt said. The investigators examined the retinas of the animals after 29 days, looking for pathogenic changes and alterations in extracellular matrix gene expression and accumulation of immunoreactive carboxymethyl lysine from AGE and lipoxidation end products.

Compared with untreated rats, the pyridoxamine-treated animals were protected from capillary death, limited laminin protein up-regulation, extra-cellular matrix mRNA expression and an increase in carboxymethyl lysine in the retinal vessels.

"Interestingly, co-study of antioxidants did not have anywhere near the same effect in these animals," Dr. Stitt said. Rats treated with vitamin E or R-alpha-lipoic acid show no protection against retinal capillary closure and showed inconsistent effects on diabetes-related up-regulation of extracellular matrix mRNAs, the researchers found.

"This study shows that AGEs probably play an important role in diabetic retinopathy, although to be definitive about this there would need to be more studies conducted," Dr. Stitt said.

"This finding is important because diabetic retinopathy is a major cause of blindness in developed countries and there are no real therapeutic options for diabetic patients, beyond pan-retinal laser photocoagulation, which is very destructive of healthy retina and is only effective in the late stages," he added. "Further development of this therapeutic approach, or closely related strategies, have potential for preventing retinopathy in diabetic patients."

BioStratum, Inc., in Durham, North Carolina, is developing pyridoxamine as a drug called Pyridorin, Dr. Stitt noted. *Diabetes* 2002;51:2826-2832.

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FACT

Type 2 diabetes can be predicted by increases in microalbuminuria (a measure of protein in the urine). In addition, the association between increased protein in the urine and rising blood-glucose levels was present even when blood-glucose levels were below those used to diagnose diabetes. *Diabetes Care*, June 2002

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Item # 14

Atorvastatin More Effective Than Pravastatin for Atherosclerosis

Atorvastatin 80 mg/day lowered low-density lipoprotein (LDL) cholesterol levels further than did pravastatin 40 mg/day, and it also reversed atherosclerosis as reflected by reduced carotid intima-media thickness (CIMT).

That, according to results of a head-to-head trial published online Sept. 23 in *Circulation*.

"This is the first comparison of two statin drugs in a general population that looked at more than their cholesterol-lowering abilities," lead author Allen J. Taylor, MD, director of cardiovascular research at Walter Reed Army Medical Center in Washington, D.C., says in a news release. "Previous studies found that patients in whom plaque stabilized – or stopped progressing – had the lowest risk of heart attacks and other cardiovascular disease problems. In general, past studies have shown that regression [of plaque] is uncommon."

This single-center, randomized clinical trial followed 161 patients who met National Cholesterol Education Program (NCEP) II criteria for lipid-lowering therapy. Mean age was 60 years, 71.4% were male, and 46% had known cardiovascular disease. Baseline CIMT and other clinical characteristics were similar in both groups.

After 12 months of treatment, LDL cholesterol levels were 76 +/- 23 mg/dL in the atorvastatin group (-48.5%) and 110 +/- 30 mg/dL in the pravastatin group (-27.2%; *P*<.001). Blinded, serial ultrasound of the far wall of the distal common carotid artery revealed progressive CIMT regression in the atorvastatin group (change in CIMT, -0.038 +/- 0.021 mm) and stable CIMT in the pravastatin group (change, 0.026 +/- 0.017 mm; *P*=.03). CIMT decreased in 54% of atorvastatin-treated patients and in 39% of pravastatin-treated patients.

"We need to carefully define at what point lower LDL values have the greatest benefit in lowering the risk of heart disease," Taylor says. "This study would suggest that LDL values much lower than 100 mg/dL appears better than a value of around 100."

In an accompanying editorial, Prediman K. Shah, MD, from Cedars Sinai Medical Center in Los Angeles, California, notes that several large-scale trials are underway to compare the effect of moderate versus aggressive cholesterol lowering on coronary plaque and cardiac events.

"The data provided by Taylor are of potential interest and could have significant implications for clinical practice," he writes. "However, before we conclude that more LDL-lowering means less atherosclerosis progression or clinical events, more in depth research is necessary." *Circulation*. Published online Sept. 23, 2002.



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Item #15

Diabetes Contributes to Cholesterol Metabolism Regardless of Obesity

Study shows that diabetes modulates cholesterol metabolism more than obesity alone.

The purpose of the study was to investigate cholesterol metabolism in obesity with and without diabetes.

They performed cross-sectional metabolic studies in obese individuals with and without type 2 diabetes. The study population consisted of 16 obese (BMI >30 kg/m²) diabetic subjects with a mean age of 52 ± 2 years (SE) and 16 nondiabetic control subjects of similar age and weight. Cholesterol absorption efficiency was measured with peroral dual isotopes and cholesterol synthesis with sterol balance.

The Results showed that serum total cholesterol did not differ between the groups, but LDL and HDL cholesterol were significantly lower and VLDL cholesterol and serum total and VLDL triglycerides were higher in the diabetic group than in the control group. Cholesterol absorption efficiency was 29 ± 1% in diabetic subjects vs. 42 ± 2% in the control subjects ($P < 0.01$). Cholesterol synthesis was higher (17 ± 1 vs. 14 ± 1 mg · kg⁻¹ · day⁻¹; $P < 0.05$) and neutral sterol and bile acid excretion and cholesterol turnover tended to be higher in the diabetic group than in the control group. Blood glucose was positively related to cholesterol synthesis in the diabetic group ($r = +0.663$, $P < 0.01$) and in the control group ($r = +0.590$, $P < 0.05$), suggesting that the higher blood glucose level, the higher the cholesterol synthesis. In addition, blood glucose was significantly positively related to fecal neutral sterol excretion in both groups.

From the results it was concluded that cholesterol absorption efficiency was lower and cholesterol synthesis was higher in obese subjects with diabetes than in those without diabetes, suggesting that diabetes modulates cholesterol metabolism more than obesity alone.

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Quote of the Week-----

Here I am, 58, and I still don't know

what I'm going to be when I grow up."

-----Peter Drucker

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