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DIABETES IN CONTROL.com NEWSLETTER

The Newsletter for Professionals in Diabetes Care

July 3 2002, Issue 111

From the Editors Desk:

I have been using the new FreeStyle Tracker with my PDA for the past 2 weeks and will have a follow-up in next weeks issue.

Due to the amount of information from ADA and ENDO 2002 we will have 20 news items in the newsletter for a few weeks to catch up with all that is happening in Diabetes.

Eric S. Freedland, MD, brings us part 10 Manipulating Macronutrient Ratios, learn how the ratios have changed over the years and how the changes have overlooked obvious shortfalls.

We had some exclusive interviews at the ADA and ENDO conferences and will have those for you starting next week.

Make sure you read this weeks' feature from **Sheri Shafer RD, CDE**; Antioxidants- What we know, What we need to know

The Pritchett and Hull Patient Handout Program is full thanks to all participants, however there are a few more spots available for the SnoreQuell Study.

Watch for information for the upcoming AADE convention in Philadelphia. We will have a booth with some exciting information. Make sure you put it in your calendar to stop by our booth #919 and check it out.

Dave Joffe
Editor-in-Chief

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Sheri Shafer RD CDE: Feature "ANTIOXIDANTS"

Antioxidants have received a lot of attention in recent years, in relation to wellness and disease prevention. More studies are needed to better understand how antioxidants may affect diabetes management and treatment. [Click Here](#)

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Dr. Rosen's Feature

"Looking For Lipid In All The Wrong Places" *Learn what new drugs might suppress enzymes that promote lipid deposition where they are not supposed to be.*

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News Flash - News Flash

Diabetes Breakthrough- Scientists Get Stem Cells to Release Insulin

Diabetes sufferers may someday be able to throw away their needles

PORTLAND - Diabetes sufferers may someday be able to throw away their needles thanks to a recent breakthrough at Oregon Health Sciences University.

Researchers there have developed embryonic stem cells from monkeys that produce and release insulin. The hope is that this discovery will lead to a method of transplanting the stem cells into an insulin patient, ending the "Diabetes lifestyle" as patients now know it.

Further research will be necessary - the researchers want to perform the entire process on a diabetic monkey before trying to develop a procedure for human patients. If successful, this breakthrough could mean the successful end of an entire century of efforts to develop insulin-producing cells to replace non-functioning ones in a diabetic's body. OHSU can be reached at (503) 494-8231.

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New Product Information: Cholesterol 1,2,3

Non-invasive cholesterol test for risk assessment of heart disease.



WASHINGTON (The FDA) - FDA today cleared a new laboratory test to measure skin cholesterol in adults with severe coronary artery disease. The test can help determine the amount of cholesterol in skin using the palm of the hand. Other cholesterol tests currently used by laboratories measure cholesterol from blood samples.

Click her for more information:

Product Update: [A1cNow is Less Than 9 Dollars!](#)

Metrika receives NGSP Certification for their A1cNow instant A1c test.

Now less than 10 dollars for the first and only A1c test that is instant and disposable. For more info on how you can now use it in your office practice and quantity discounts, [click HERE!](#)

Dr. Richard Bernstein's Corner:

Check out Dr. Bernsteins Corner for Insights for Controlling Blood Sugars

<http://www.diabetesincontrol.com/bernsteinarchive.htm>

Dr. Bernsteins Feature: Foot Care

The following guidelines are essential for all diabetics, to prevent foot injury and the potentially grave consequences that may ensue. Print the 19 steps to prevent amputations. [Click HERE!](#)

This newsletter is the condensed version. If you would like to see the full newsletter go to

<http://www.diabetesincontrol.com/Issue11index.htm>

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

1. The Pritchett & Hull **CLOSED** Medical Professional Experience Survey—receive high quality patient handouts at no charge, and [any your feedback. Click Here](#)

2. SnoreQuell Patient Experience Survey: will evaluate the effectiveness of this product in decreasing or eliminating snoring. This will be determined by comparing before and after questionnaires to be completed by each participant. This survey is open to educators, diabetes patients and their partners. [Click Here](#)

3. Gym Study II: Gymnemosupium II, a combination of the extracts of Gymnema sylvestre, Pterocarpus marsupium, Diachrome and Vanadium. [Click Here](#)

4. RELAXATION – WarmFeet® study Version II Open For Registration (less labor intensive version) Learn More: [Click here](#)

SOON TO OPEN STUDIES for your participation

1. [The Fiber Study: Adding a natural soluble fiber supplement with each meal to lower postprandial BG and A1c's](#)
2. [The S.T.E.P. study, 10,000 Steps To Enhanced Prevention](#)

This Weeks Items:

1. [ADA: Prevent Diabetes by Walking Just 30 Minutes a Day](#)

[Click Here](#)

2. **ADA: Good Glycemic Control Is Not Enough in Managing Diabetes**

[Click Here](#)

3. **ADA: Noninvasive Blood Glucose Monitor Tested in Diabetics***

[Click Here](#)

4. **ADA: Insulin Patch May Help Dodge the Needle**

[Click Here](#)

5. **66% of Heart Attack Patients have Undiagnosed Diabetes or PreDiabetes***

[Click Here](#)

6. **Ghrelin, A Hunger Hormone' Linked to Long-Term Body Weight Regulation**

[Click Here](#)

7. **Stem Cell Research Considered A Source of New Therapies to Treat Diabetes**

[Click Here](#)

8. **GLP-1 Analog Has An "Anti-Diabetic" Effect When Glucose Levels are Elevated**

[Click Here](#)

9. **Efficacy of an Oral Insulin Spray (Oralin) Delivered Through The Buccal Mucosa**

[Click Here](#)

10. **Effects of a Ketogenic, or High-Fat, Diet as a Treatment for Obesity**

[Click Here](#)

11. **Growth Hormone and Metformin Reduces Fat Mass and CVD Factors**

[Click Here](#)

12. **Postmenopausal Women Taking Folic Acid Reduce Risk of Heart Disease**

[Click Here](#)

13. **ADA: Artificial Pancreas Safe and Effective***

[Click Here](#)

14. **ACC, AHA, NHLBI Clinical Advisory Confirms Safety, Effectiveness of Statins**

[Click Here](#)

15. **"Globesity" 22 Million Children Worldwide are Overweight or Obese**

[Click Here](#)

16. **Increased Concentration of Nitric Oxide in Type 2 Diabetes with Insulin Resistance**

[Click Here](#)

17. **Importance of Family History of Diabetes in Patients with Type 2 Diabetes**

[Click Here](#)

18. **Cozaar (Losartan) Lowered Risk Of Total Mortality In Patients With Diabetes By 39% Versus**

Atenolol

[Click Here](#)

19. **INGAP Peptide - An Initiator of Beta Cell Growth***

[Click Here](#)

20. **INGAP Peptide Induces Islet Cell Neogenesis from Human Duct-like Islet Progenitor Cells**

[Click Here](#)

ITEMS For The Week:

Item #1

ADA: Prevent Diabetes by Walking Just 30 Minutes a Day

Overweight, middle-aged people who don't exercise are at high risk of Type II diabetes, but modest exercise alone can improve their odds.

That's the word from Florida researchers who followed 18 previously sedentary, overweight subjects for six months. They presented their findings recently at the American Diabetes Association's Scientific Sessions in San Francisco.

Glen E. Duncan, a postdoctoral research fellow at the University of Florida who led the study, says risk factors declined just by adding the exercise and not improving the diet.

"Even though they did not lose weight, their insulin sensitivity improved nearly twofold from when they started," Duncan says.

The better a person's insulin sensitivity, the lower the risk of getting Type II diabetes, which now affects about 8 percent of U.S. adults. The more insulin-resistant a person is, the higher the risk.

The Florida research follows a much larger study released last year in the New England Journal of Medicine, in which more than 3,000 subjects in the Diabetes Prevention Program reduced their risk of Type 2 diabetes by 58 percent if they adopted intensive lifestyle changes, including a low-fat diet and daily exercise.

The more recent study suggests, however, that exercise alone may be a good start.

The subjects in the Florida study were, on average, 52 years old and had body mass indexes (BMIs) of nearly 29. A person who is 5-foot-10 and weighs 200 pounds has a BMI of 29, as does someone who is 5-foot-2 and weighs 160 pounds.

Duncan and his colleagues assigned the men and women to different exercise groups. Everyone walked for 30 minutes a session, but some walked at higher frequencies -- almost five to seven days a week compared to three to four -- and higher intensities -- 65 percent to 75 percent of their aerobic capacity versus 45 percent to 55 percent.

The researchers told the subjects not to try to lose weight, just to focus on the exercise. After six months, the researchers took tests such as glucose tolerance tests and noted BMIs. While the BMIs did not change, the subjects' insulin sensitivity improved greatly. Levels of an enzyme that helps in fat metabolism improved, too, Duncan says.

While those at risk for Type 2 diabetes should also eventually try to lose weight, Duncan says exercise may be the best and easiest place to start. "People have a hard time doing two things, diet and exercise. And even modest amounts of exercise in the absence of weight loss reduces the risk factors for Type 2 diabetes," he says.

The study makes sense to another expert who often cares for those with Type 2 diabetes and counsels others on how to avoid it.

"It's an important study because any time you can document something [of benefit] we can relay that into clinical practice," says Dr. Katja Van Herle, chief of endocrinology at Santa Monica-UCLA Medical Center.

"When you use skeletal muscle [during workouts] it allows insulin to be more effective at opening the cell door to get the sugar in [from the bloodstream]," she says. "As we gain more fat cells and don't exercise our skeletal muscles, the doors to the cells get 'stuck.' The pancreas makes more insulin. Sugar levels rise. This study underscores the importance of exercise at reversing this insulin resistance."

Another expert, Cathy Mullooly, a certified diabetes educator at the Joslin Clinic in Boston, praises the length of the study. "This study reinforces the preventive aspects of exercise," she says.

Watch for the Diabetes In Control S.T.E.P. study, starting soon!

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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

ADA: Good Glycemic Control Is Not Enough in Managing Diabetes

Priorities are misplaced because coronary artery disease is the major cause of death in patients with type 2 diabetes mellitus

When it comes to managing diabetes, doctors may achieve good glycemic control but have a lower priority for controlling or treating other cardiovascular risk factors, according to two presentations at the annual American Diabetic Association meeting.

"An opportunity exists to improve treatment rates and goal attainment for glycemic, lipid, and blood pressure control among patients with diabetes," write Richard Bergenstal, from the International Diabetes Center in Minneapolis, Minnesota, and colleagues. "Only by understanding how physicians prioritize and address these risk factors will we be able to develop more effective strategies to reach goals and reduce the burden of cardiovascular disease in diabetes."

This 12-month, multicenter, observational study was one of the first and largest prospective studies to investigate how clinicians approach major cardiovascular risk factors and how this approach ultimately affects HbA_{1c}, blood pressure, and low-density lipoprotein (LDL) cholesterol.

About 2,300 newly referred or newly diagnosed diabetes patients, aged 40 years and older, were enrolled from 144 sites. Mean age was 61 years, and 87% of patients had type 2 diabetes. Baseline medications included glycemic therapy in 70%, antihypertensives in 67%, and lipid-lowering therapy in 44%. The percentage of patients meeting goal at baseline was 33.5% for HbA_{1c}, 30.4% for LDL cholesterol, and 17.6% for blood pressure.

"Physicians indicated a primary focus on glycemic control," the authors write. "Controlling blood pressure or lipid levels were lower priorities and commonly listed as secondary or tertiary goals."

In a separate presentation, Silvio E. Inzucchi, from Yale University School of Medicine in New Haven, Connecticut, and colleagues noted that these priorities are misplaced because coronary artery disease is the major cause of death in patients with type 2 diabetes mellitus. Although glycemic control is not definitely known to reduce the incidence of coronary artery disease, other features of the metabolic syndrome, including hypertension, dyslipidemia, body weight, and hypercoagulability, appear to be more important.

The Detection of Ischemia in Asymptomatic Diabetics (DIAD) Study is a multicenter study of the prevalence of silent myocardial ischemia in patients with type 2 diabetes, using Adenosine-Sestamibi perfusion imaging.

Of 402 subjects screened since September 2000, 55% are achieving the ADA HbA_{1c} target of less than 7.0%. Even in these well-controlled subjects, control of other cardiovascular risk factors was quite variable.

"In our study population, large proportions of patients under seemingly excellent diabetic control are not achieving an optimal overall coronary artery disease risk profile," the authors write. "To impact substantively upon the risk of coronary artery disease in type 2 diabetes, emphasis on managing these other cardiovascular risk factors, in addition to glucose control, is necessary." *ADA Annual Meeting: Abstracts 624-P, 32-OR. June 15, 2002.*

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FACT

On average, each 1% reduction in HbA_{1c} is associated with a 37% decrease in the risk of microvascular endpoints and a 21% decrease in the risk of any diabetes-related endpoint or death. **REFERENCE**¹. Stratton IM, Adler AI, Neil HAW, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ.* 2000;321:405-412.

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Item #3

ADA: Noninvasive Blood Glucose Monitor Tested in Diabetics ***Coming soon or just another pipe dream?***

ADA: Unlike currently available blood glucose monitors, which require finger prick or other invasive testing for calibration one or more times daily, a new blood glucose monitor presented at the American Diabetes Association 62nd Scientific Sessions in San Francisco, California, is completely noninvasive.

"The tool is based on occlusion technology where the cessation of blood flow in the finger triggers a change over time of the optical characteristics of blood," write Ohad Cohen, from Chaim Sheba Medical Center in Tel Hashomer, Israel, and colleagues. "Increase of glucose concentration reduces the refractive index mismatch, which in turn reduces the scattering coefficient. This phenomenon is utilized in a clinically applicable apparatus to measure blood glucose levels."

During hyperinsulinemic hypoglycemic clamp studies in 5 men with type 1 diabetes, insulin was infused at a constant rate, and stepped hypoglycemia was achieved by varying glucose infusion. The Roche Reflectron glucometer measured arterial blood glucose in parallel with 140 noninvasive readings, with values ranging from 40 to 270 mg/dL. Blood glucose levels obtained by the two methods showed a high degree of correlation (r=0.91) and mean error less than 10%.

"The excellent match [with arterial blood glucose measurements] prove the reliability of this novel non-invasive glucose measuring technology that is currently ready for large scale evaluation," the authors write. Orsense Ltd., in Rehovot, Israel, developed this blood glucose monitor. ADA Annual Meeting: Abstract 485-P. June 15, 2002.

See our archived feature on all the current noninvasive monitors at <http://www.diabetesincontrol.com/features/feature72.shtml>

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Item #4

ADA: Insulin Patch May Help Dodge the Needle

A 24-hour insulin patch to provide painless, needle-free, basal insulin delivery for people with diabetes coming closer.

Avoiding insulin injections would greatly improve quality of life for many diabetics, and new products presented at the American Diabetic Association annual meeting promise to do exactly that. These include insulin in transdermal, oral pills, oral spray, and pulmonary inhaled forms.

"Studies are underway to develop a convenient 24-hour insulin patch to provide painless, needle-free, basal insulin delivery for people with diabetes," write Alan M. Smith and colleagues. "Basal insulin infusion has been achieved using a transdermal patch containing an unmodified approved insulin formulation without the use of chemical enhancers, iontophoresis or ultrasound."

In this pharmacokinetic study, 5 nondiabetic volunteers tested an insulin patch delivery system containing a commercially available insulin lispro formulation in a liquid reservoir patch, creating shallow microscopic pores through the stratum corneum of the volar forearm. Serum lispro levels showed a steady infusion throughout the 12-hour patch application, with decline to baseline in approximately 2 hours. On average, serum insulin lispro levels were maintained above 5 mcU/mL between 1 and 12 hours.

To complement the basal insulin patch, diabetics could take orally absorbed insulin in a pill with maximal effect at 30-50 minutes.

"Oral administration of capsules containing the insulin/[Emisphere] delivery agent combination provides insulin absorption at clinically significant levels," write Richat Abbas and colleagues from Emisphere Technologies Inc. in Tarrytown, N.Y.

In this pharmacokinetic and pharmacodynamic study of human insulin after oral administration in 29 healthy subjects, insulin was rapidly absorbed into the systemic circulation, and plasma concentrations peaked within 25 minutes. Corresponding maximum reductions in both plasma glucose and C-peptide concentrations occurred within 1 hour. Insulin alone or the Emisphere delivery agent alone given orally did not affect plasma insulin or glucose levels. The most common adverse event was hypoglycemia, but there were no serious adverse events, and all doses were well tolerated.

A similar study by Miriam Kidron and colleagues from Hadassah-Hebrew University Medical Center in Jerusalem also showed that oral dosing of insulin using the Emisphere oral delivery agent appears to be practical.

"Much effort and research have been invested in finding alternative routes of insulin administration, namely, nasal, dermal, pulmonary, and oral," they write. "The combination of insulin and an Emisphere delivery agent enables the absorption of insulin from the gastrointestinal tract."

In 12 nondiabetic volunteers, nadir of plasma glucose occurred 30-50 minutes after the oral dose, suggesting that the absorption site is in the upper part of the gastro-intestinal tract, most likely the duodenum. Plasma C-peptide levels decreased with increased amounts of exogenous insulin absorbed, suggesting suppression of secretion of endogenous hormone. With higher oral insulin doses, blood glucose and C-peptide levels decreased by 50%. There were no adverse effects detected during the study or up to 12 weeks later. *ADA Annual Meeting: Abstracts 197-OR, 526-P, 191-OR. June 15-16, 2002.*

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FACT: Childhood type 2 yields dialysis, miscarriage and death in 20 year olds.

ADA Abstract #99, showed that as the prevalence of type 2 diabetes in children increase, we are also seeing the first crop grow into adulthood – and the results are alarming. In this group of 51 people diagnosed before age 18 and now age 18 to 33, a high rate of deaths (9%), dialysis (6.3%), and miscarriage (38%) was seen – plus one toe amputation and one case of blindness – and generally poor blood sugar control. What tragedies lay ahead?

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Item #5

66% of Heart Attack Patients have Undiagnosed Diabetes or PreDiabetes

Testing patients who have had heart attacks for signs of diabetes before they leave the hospital may identify those with the highest risk of future heart attacks, researchers report.

Researchers found that many people hospitalized for a heart attack have undiagnosed diabetes or prediabetes, a term coined to describe the millions of overweight and obese people who have blood sugar levels suggesting an elevated risk of full-blown diabetes.

Because diabetes increases the risk of death from heart disease, the study "opens up new possibilities for preventing relapses of (heart attack) and untimely death," said lead author Dr. Lars Ryden, of Karolinska Hospital in Stockholm, Sweden.

Medications, exercise and diet changes, all of which can restore normal glucose levels, may reduce the risk of heart attacks in patients who have already had a heart attack, he said.

Patients with prediabetes have been shown to be at higher risk of heart disease, and among people who have a heart attack, those who have diabetes are more likely to die, the report indicates.

Conditions that can lead to diabetes often go undetected, however, so the investigators, under the leadership of Dr. Anna Norhammar, set out to see how many heart attack patients have blood sugar irregularities even though they had not been diagnosed with diabetes.

The testing revealed that a substantial percentage of 181 heart attack patients in the study had blood sugar abnormalities, the researchers report in the June 22nd issue of the medical journal *The Lancet*. At hospital discharge, 31% of patients were diagnosed with diabetes and 35% with signs of prediabetes. The abnormalities were not temporary: 3 months later, 25% of patients had diabetes and 40% had signs of prediabetes.

Based on the results of the study, the authors recommend that heart attack patients be tested for signs of diabetes before being discharged from the hospital.

The percentage of heart attack patients with previously undiagnosed diabetes or impaired glucose intolerance is higher than expected, writes Dr. Steven M. Haffner, of the University of Texas Health Science Center at San Antonio, in an accompanying editorial. *The Lancet* 2002;359:2127-2128, 2140-2144.

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Advertorial

Snoring increases diabetes risk. A recent study in the *American Journal of Epidemiology* Vol. 155, No. 5 : 387-393 indicated that snoring was an independent risk factor in the eventual diagnosis of diabetes. In addition irregular sleep patterns have been associated with hormonal imbalance, possibly affecting fasting glucose values. If you have diabetes and live with a snorer, your interrupted sleep patterns can affect your glucose as well.

Traditional products often have side effects and are not highly successful in reducing or eliminating snoring. The ingredients in GlucoFree SnoreQuell are proven to decrease or eliminate snoring without raising blood glucose levels. [Learn More here.](#)

Item #6-12

ENDO 2002: New Diabetes, Obesity and Metabolic Syndrome Research Highlighted at Endocrine Society Annual Meeting *Items 6-12*

San Francisco, CA, June 20, 2002 – New research presented in a press conference at ENDO 2002, the 84th Annual Meeting of The Endocrine Society, may provide new treatments for diabetes, obesity and metabolic syndrome. Researchers presented their findings on novel treatments for diabetes, such as oral insulin spray and a synthetic hormone; the effects of high-fat diet for obese patients; and hormone therapy for metabolic syndrome. Additionally, new research was presented on the role of ghrelin-a 'hunger hormone'-in regulating body weight.

Item #6

Ghrelin, A Hunger Hormone' Linked to Long-Term Body Weight Regulation

Hyperghrelinemia may contribute to the severe obesity

Obesity, a disease that has been linked to several other serious health complications such as heart disease and diabetes, is one of the fastest growing epidemics in the world. Dr. David Cummings, a researcher at the University of Washington and Veterans Affairs Puget Sound Health Care System, presented his findings on ghrelin, a recently discovered 'hunger hormone' that has been linked to long-term body weight regulation, during the press conference. Ghrelin has been shown to stimulate hunger and short-term food intake in humans. Dr. Cummings and his colleagues demonstrated that ghrelin levels rise shortly before a meal and fall shortly after a meal. Additionally, conditions of negative energy balance, such as low-calorie diets, chronic exercise, cancer anorexia, cardiac cachexia and anorexia nervosa, cause ghrelin levels to increase. Most recently, Dr. Cummings and his colleagues showed that gastric bypass surgery suppresses ghrelin levels in patients.

"Research has shown that ghrelin probably plays a compensatory, rather than causal role in common obesity," explained Dr. Cummings during the press conference. "However, we find that people with Prader-Willi syndrome, which is the most common form of syndromic obesity, experience significantly increased ghrelin levels. As a result, hyperghrelinemia may contribute to the severe obesity that is associated with Prader-Willi syndrome. Our findings suggest a physiologic role for ghrelin in both the short- and long-term regulation of human appetite and body weight."
ENDO 2002

Item 7

Stem Cell Research Considered A Source of New Therapies to Treat Diabetes

Stem cells are a potential source of tissue for treating diabetes.

Embryonic stem cell research is considered to be a possible source of new therapies to treat some of the most devastating diseases, including diabetes. Now, researchers at Oregon & Health Sciences University (OHSU) have developed the first step in a monkey model of stem cell transplantation-monkey cells that can produce and release insulin.

"Our research confirms that stem cells are a potential source of tissue for treating diabetes," said Dr. Linda Lester, a researcher at OHSU who presented the findings. "To our knowledge, we are the first group to establish this with monkey cells."

The next step for Dr. Lester and her colleagues is to transplant similar cells into diabetic animals and develop a pre-clinical model for stem cell transplantation. They hope this work will facilitate clinical trials using stem cells and eventually result in cell-based therapies for diabetes. *ENDO 2002*

Item 8

GLP-1 Analog Has An "Anti-Diabetic" Effect When Glucose Levels are Elevated

Blood glucose levels were lowered to near normal levels in the fasting state and after meals.

Another new diabetes treatment that is being developed by researchers at Eli Lilly and Company was also reviewed during the press conference. Dr. Michael Trautmann presented the results of an early-phase clinical trial, which studied the effects of an analog of glucagon-like peptide 1 (GLP-1), a naturally occurring hormone that exerts an "anti-diabetic" effect when blood glucose levels are elevated. Unlike the GLP-1 that is produced by the body, which experiences rapid degradation, the GLP-1 analog created by the researchers at Lilly is protected against the rapid destruction. In the study, 24 overweight, type-2 diabetes patients were divided into three groups-each receiving one of three dosage injections of the GLP-1 analog for either six or 21 days.

"In all three groups, blood glucose levels were lowered to near normal levels in the fasting state and after meals," explained Dr. Trautmann, the primary investigator on the study. "Additionally, the treatments caused patients to lose weight. Patients lost just over two pounds after six days and about four and one half pounds after 21 days."

Dr. Trautmann stressed that although the results are encouraging, future research is needed to evaluate the longer-term effects of this compound on a larger group. *ENDO 2002*

Item 9

Efficacy of an Oral Insulin Spray (Oralin) Delivered Through The Buccal Mucosa

A combination of OralinTM and oral agents significantly increased the insulin levels

For years, diabetes researchers have searched for an alternative to injected insulin. A study presented at the ENDO 2002 press conference shows the efficacy of an oral insulin spray, called OralinTM, which is delivered inside of the mouth through the buccal mucosa, that has been developed by Genex Biotechnology Corporation. Researchers

studied the effects of Oralin™ on 13 subjects with type-2 diabetes in combination with oral agents as well as oral agents alone, and followed both by a 360-calorie meal.

“Our data shows that a combination of Oralin™ and oral agents significantly increased the insulin levels,” said Dr. Jaime Guevara-Aguirre, an Ecuadorian researcher who worked with researchers from Generex on the study. “Oralin™ also helped keep the glucose and c-peptide levels lower when compared with oral agents alone.”

Dr. Guevara-Aguirre noted the need for larger and longer studies to further test the effectiveness of oral insulin spray. *Endo 2002*

Item 10

Effects of a Ketogenic, or High-Fat, Diet as a Treatment for Obesity

All chronic disease markers-improved with the high fat diet.

Another part of the press conference focused on new obesity research. Dr. Hussein Dashti presented a study on the effects of a ketogenic, or high-fat, diet as a treatment for obesity. This type of diet Researchers in Kuwait treated 63 obese patients with high glucose and cholesterol levels (both males and females) who were on a ketogenic diet for 12 weeks. The Kuwaiti researchers set out to find an alternative to common dietary treatments for obesity. Their research shows that contrary to popular belief, a high-fat diet might actually help treat obesity.

“Cholesterol, fatty acids and higher-than-normal blood glucose levels-,” explained Dr. Dashti. “Additionally, the high fat diet has minimal side effects. Dr. Dashti noted that although this diet has been used to treat epileptic disorder for some time, this new research may revive the ketogenic diet as a possible treatment for obesity. *ENDO 2002*

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73% of graduating students have some type of guaranteed student loan. You can refinance those loans at a much lower rate. [Click here to get more info](#)

Item 11

Growth Hormone and Metformin Reduces Fat Mass and CVD Factors

Growth hormone and metformin may be effective treatments for metabolic syndrome.

Metabolic syndrome, a disorder that includes a cluster of health problems including obesity, high blood pressure, poor lipid levels and high blood sugar, is one of the fastest growing health concerns among both doctors and patients. Growth hormone has previously been shown to reduce abdominal fat, which is a symptom of metabolic syndrome. German researchers conducted an 18 month double-blind, placebo controlled study to determine whether a combination of growth hormone and metformin reduce fat mass and improve cardiovascular risk factors without the negative effects on glucose metabolism in male patients with metabolic syndrome. The study's 24 subjects were non-smoking men with an average age of 50 who did not suffer from heart disease or hyperlipidemia. The men received daily injections of growth hormone or placebo as well as twice daily metformin tablets.

“Patients who were treated with metformin and growth hormone experienced a slight decrease in their body fat,” said Dr. Burkhard Hermann, a researcher at the University of Essen and the lead investigator on the study. “However, the glucose metabolism was similar in the metformin and metformin plus growth hormone groups. This demonstrates that growth hormone and metformin may be effective treatments for metabolic syndrome.” *Endo 2002*

Item 12

Postmenopausal Women Taking Folic Acid Reduce Risk of Heart Disease

HDL, or 'good' cholesterol, increased with the folic acid, while LDL, or 'bad' cholesterol, decreased with the folic acid.

Dr. Giancarlo Paradisi, a researcher at Catholic University of Rome, Italy, presented the second study on the health of aging women. The Italian study found that postmenopausal women who take folic acid may reduce their risk of developing heart disease. Researchers studied 10 healthy postmenopausal women who were not taking hormone replacement therapy and found that one month of folic acid did not affect glucose, insulin, total cholesterol, triglycerides, non-esterified fatty acids and blood pressure.

“HDL, or 'good' cholesterol, increased with the folic acid, while LDL, or 'bad' cholesterol, decreased with the folic acid,” noted Dr. Paradisi. “In addition, the endothelial function was markedly improved with the folic acid. These results show that folic acid may a safe and effective treatment for postmenopausal women. Larger and longer studies are now needed to confirm these results.” *ENDO 2002*

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Did you know?

Poor outcomes are due to provider behavior. In Poster study #87 at ADA Lower socioeconomic groups and many minority groups suffer substantially higher rates of diabetes complication. The study showed that African Americans and Hispanics had poorer blood glucose control but received less intense therapy – fewer insulin units prescribed – compared to non-Hispanic whites.

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Advertisement

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Learn how to purchase the A1cNow for less than 10 dollars for your office or clinic. go to www.A1cNow.net

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Item #13

ADA: Artificial Pancreas Safe and Effective

An artificial pancreas without the need for injections found safe and effective.

An "artificial pancreas" designed to deliver the key blood sugar-regulating hormone insulin to diabetic patients without the need for injections has been found safe and effective in a preliminary study with 10 patients, an international research team reports.

The device delivers insulin into the bloodstream when a sensor detects rising blood sugar levels. Normally, the pancreas produces insulin, but in people with type 1 diabetes the organ can't produce the hormone. These patients must give themselves frequent insulin injections to keep their blood sugar levels under control.

Dr. Eric Renard and colleagues at Lapeyronie Hospital in Montpellier, France, working with investigators at Medtronic MiniMed of Northridge, California, tested the long-term sensor system in type 1 diabetes patients with relatively stable disease. The first patient received the device in April 2001, and the study lasted 6 months.

Renard presented the findings at the American Diabetes Association's annual meeting last week.

He described the device as an insulin reservoir, implanted in the tissue lining the abdominal cavity and connected to a sensor implanted in the jugular vein. The reservoir requires insulin refills every month or so, he said. When the sensor detects an increase in blood glucose, the reservoir delivers the required amount of insulin.

Renard reported that blood glucose levels were controlled more than 60% of the time in the study group, compared with 25% of the time for the average patient using injectable insulin. This was a result of the accuracy of the sensor, he said.

The most difficult time for type 1 diabetes patients to keep their blood sugar levels stable with insulin injections is after a meal.

The sensor is able to keep a read on glucose levels by taking measurements as many as 288 times during a 24-hour period. The so-called artificial pancreas is "working very well" over time, Renard said.

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Item #14

ACC, AHA, NHLBI Clinical Advisory Confirms Safety, Effectiveness of Statins

Joint Advisory Reassures Physicians, Patients About Drugs' Importance in Lowering Cholesterol

June 2002 (Newstream) -- -- The cholesterol-lowering drugs known as statins are both safe and effective and physicians should continue to use them, according to a six-page joint clinical physician advisory released today by the American College of Cardiology (ACC), American Heart Association (AHA), and the National Heart, Lung, and Blood Institute (NHLBI). The clinical advisory reinforces previously published clinical guidelines (ACC/AHA) and is a follow-

up to the media advisory issued by the ACC and AHA last August in the wake of the voluntary withdrawal of the statin Baycol (cerivastatin) because of reported deaths and serious muscle damage among a very small portion of patients taking the drug.

Following the Baycol withdrawal, some patients taking a statin voiced concern about the drugs' safety and some even stopped taking the medication. In this joint clinical advisory, the ACC, AHA, and NHLBI stress that the five statins still on the market are safe and effective for the majority of patients, and that, along with lifestyle changes such as a heart healthy diet and regular exercise, serve as critically important weapons in the arsenal for fighting heart disease.

"The bottom line is that when statins are given properly and monitored appropriately, they can do a tremendous amount to reduce cardiac risk in our patients," said Richard C. Pasternak, MD, of the ACC, who chaired the committee that developed the advisory. This conclusion, Dr. Pasternak added, is buttressed by many clinical studies including the soon-to-be published 20,000-patient Heart Protection Study that have confirmed statins' safety and efficacy in lowering cholesterol levels and reducing the risk of heart disease.

While physicians can never let down their guard about the side effects of any drug, Dr. Pasternak emphasized, "There is an enormous difference between the Baycol experience and other statins," he said. Although approximately 1 out of 1,000 patients experience some degree of muscle discomfort, the rate of fatal muscle damage, known as rhabdomyolysis, has been extremely rare with the other statins, less than 1 in a million. This side effect with Baycol, while still rare, was 16 - 80 times more frequent than with the other statins.

"We have many years of clinical experience with the other statins in practice, including tens of thousands of patients who have been entered into carefully run and monitored trials," said Dr. Pasternak. "The degree of problems seen with Baycol has not been seen with the other statins."

The advisory outlines specific characteristics that may predispose some patients taking a statin to muscle pain and weakness, or myopathy, and stresses that these patients should be monitored more carefully. The advisory also advises physicians to strongly encourage their patients to report unintended side effects such as muscle soreness or weakness or brown urine.

The advisory will be most helpful, said AHA Chief Science Officer and writing committee member Sidney Smith, MD, in helping physicians identify and effectively monitor patients most likely to be at risk for muscle problems, particularly rhabdomyolysis. Patients with predisposing risk factors for statin myopathy, the advisory notes, include those who:

- ?? Are of extreme old age especially more than 80 years;
- ?? Have a small body frame and frailty;
- ?? Have multisystem disease, such as chronic renal insufficiency; or
- ?? Are taking other drugs with which statins might interact.

"Statins and other cholesterol-lowering drugs are meant to be an adjunct to lifestyle changes such as diet and exercise, both of which are important components in efforts to reduce cholesterol and heart disease risk," said Dr. Smith. "Patients on any statin who have experienced side effects such as muscle aches should alert their physician. If they develop dark urine they should stop taking the drug and immediately consult their physician."

The complete clinical advisory is available on the ACC Web site at www.acc.org/clinical/alerts/statinsjune02.htm, the NHLBI Web site at www.nhlbi.nih.gov/guidelines/cholesterol

The advisory will be published in the August 7, 2002 issue of the Journal of the American College of Cardiology and August 20, 2002 issue of Circulation: Journal of the American Heart Association.

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FACT ADA: New Buzz word "Inflammation"

New studies from ADA find that type 2 diabetes is an inflammatory disease. Poster #441 shows an extra benefit for thiazolidinediones, in that they have a potent anti-inflammatory effect in obese adults without diabetes. So it can offer a double benefit for people with diabetes, who are at such high risk for CVD, also now believed to involve inflammation. ADA Posters #573 and 633 showed increased vasodilation in the heart and periphery, improving blood flow.

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Item #15

"Globesity" 22 Million Children Worldwide are Overweight or Obese

Weaknesses in the science behind the BMI, because it does not distinguish between fat mass and lean mass.

WASHINGTON, June 27 -- "Globesity" is the public health issue of the moment. Southwest Airlines has said it will now charge two fares for obese passengers. Ted Kennedy has held Senate hearings on the issue. The World Health Organization is so worried by the fact that, according to its calculations, 22 million children worldwide are overweight or obese that it has advocated taxes and marketing restrictions on sugary food and drink. There is a widespread perception that Americans are too fat, and this is backed up by the official statistics.

But there's a problem. Under federal body mass standards adopted in 1998, Tom Cruise is now probably obese. So is Russell Crowe. Even Michael Jordan is overweight. The guidelines, from the National Heart, Lung and Blood Institute, moved 29 million Americans who had previously been defined as healthy into a category that doctors should regard as being at risk because of their weight. Even more alarmingly, 61 percent of Americans are now categorized as overweight and 26 percent as obese. The trouble is that the scientific debate on this issue is far from settled.

The standards rely on something called the Body Mass Index, BMI, which is derived by dividing weight in kilograms by the square of the height in meters, thus getting a good indicator of weight adjusted for height. Researchers generally agree that a BMI up to 24 is an indicator of little or no risk to health. A BMI of 27 or above is linked to higher risk of heart disease, diabetes, stroke and other weight-related problems. The risks increase especially when the BMI is greater than 30. The problem is what to do with the band whose BMI is 24 to 27. The National Center for Health Statistics has only ever classified those with a BMI of 27 or above as "overweight," but the new standards start that category at a BMI of 25, well below the level clearly associated with health risks.

This categorization is controversial. "I'd rather see a caution zone from 25 to 26.9, where you tell people, 'Don't gain more weight, become physically active,'" says Judith Stern, professor of Nutrition at the University of California. She went on, "There's no evidence that BMIs lower than 27 are associated with significant increases in mortality."

Moreover, there are weaknesses in the science behind the BMI. It does not distinguish between fat mass and lean mass. That's how Michael Jordan can be classified as overweight. Most body-builders, without an ounce of fat on their bodies, will also count as overweight. This is because BMI derives its authority from the traditional method of assessing risk associated with weight, which has been to look at how mortality corresponds with weight. This is problematic, as many causes of death also cause people to lose weight. Smoking is a prime example, as smokers tend to weigh less but die earlier than non-smokers. On the other hand, alcoholism often leads to weight gain, which might be incidental to the death of the alcoholic.

But it is those athletic film stars and glamorous athletes who sum up the greatest problem with the BMI. It is perfectly possible to be healthy, attractive and "overweight." Waist circumference is perhaps the best way to tell whether someone is overweight and unhealthy (fat is stored primarily at the waist). Some physicians do correct for waist circumference. Michael Jordan's BMI under this system falls to 21. Shaquille O'Neill, however, who has only 5 percent body fat, despite his much-publicized consumption of burgers, still comes out as overweight.

The simple lesson is that BMI is a useful tool, but it doesn't tell you everything about an individual. As for whether America is worryingly overweight, we do not know how many of the 35 percent of adult Americans who the government now classes as overweight are actually in Stern's "caution zone," but we do know that 26 percent -- well over 50 million people -- have a BMI of 30 or greater. That is well into the "danger zone."

It is interesting, however, that Americans don't view this as a public health problem. In a recent survey by Harvard and Princeton researchers, 65 percent blamed individuals for lacking the willpower to diet and exercise. They may have a point. Studies carried out at Dallas' Cooper Institute seem to indicate that even moderately active overweight people have far lower death rates than sedentary people of the same weight. Even one half-hour walk per day takes overweight people out of the risk categories. The will to exercise, it seems, may be a more important factor in determining health than a simple measure of weight.

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Item #16

Increased Concentration of Nitric Oxide in Type 2 Diabetes with Insulin Resistance

It is still controversial that a decrease in the ability of insulin to increase endothelial NO release results in impaired insulin-mediated vasodilatory response.

Insulin resistance (IR) is a key element in the pathogenesis of NIDDM. The recent experiments on insulin-mediated vasodilatation have suggested that vascular insensitivity is a component of IR. However, it is still controversial that a decrease in the ability of insulin to increase endothelial NO release results in impaired insulin-mediated vasodilatory response.

Plasma concentrations of NO were examined in 26 patients with NIDDM, and 78 nondiabetic volunteers during a 180 min iv infusion of insulin (25 mU/m²/min), sandostatin (60 ug/h following a bolus of 25 ug) and glucose (240 mg/m²/min).

The test measured the efficacy of insulin in promoting disposal of the infused glucose load, in which the steady state plasma glucose (SSPG) during the 150-180min of the test was used as an index of IR. All subjects had 12h of overnight fast and no food intake during the examination. Plasma NO levels were assayed by measurement of the stable end products of their metabolism (NO₂/NO₃-). Comparison of the plasma NO levels between groups were performed by Wilcoxon-Mann-Whitney test, between serial observations over time by Friedman statistics. Relationships between different variables were analyzed by Pearson correlations. Statistical significance was accepted at the p=0.05 level.

Our results showed that there were no significant increase of NO during the insulin infusion in both the diabetic and nondiabetic groups. However, the plasma NO levels at basal and 30, 60, 120, 150 min after insulin infusion were significant higher in the diabetic group. When the nondiabetic subjects were analyzed according to their SSPG levels, there was no difference of plasma NO levels between those with SSPG > 160 mg/dl and those with SSPG < 160 mg/dl. There were no statistical difference of NO levels between those with a family history of NIDDM and those without. In the nondiabetic group, SSPG correlated with BMI, fasting insulin, triglyceride, and HDL-chol, but not with plasma NO levels.

Conclusion: 1) Impaired insulin-mediated vasodilatation in NIDDM is not caused by the impaired ability of insulin to increase endothelial NO release. The pathogenesis probably involves impaired biological effect of NO rather than its production. 2) Altered NO pathway is not an early event in IR individuals. These changes will not be apparent until NIDDM develops. *Poster at Endo 2002 [P1-81]*

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Did You Know: Stress-buster

A brisk 15-minute walk is equivalent in relaxation power to taking 5 milligrams of Valium. "It has biochemical effects, washing away of stress chemicals. It's very soothing. You release endorphins when you exercise. It has a calming and mood-elevating effect."

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Item #17

Importance of Family History of Diabetes in Patients with Type 2 Diabetes

The patients with type 2 DM with both diabetic parents are 9.9 years younger than those without family history of diabetes.

Genetic factors are important determinants of type 2 diabetes mellitus but the role of heredity has been difficult to establish because to the interplay environmental factors. Therefore, the influence of inheritance varies among populations.

We carried out a cross-sectional study in a group of 300 patients (80 men and 220 women) with type 2 diabetes mellitus (DM). The patients answered a questionnaire by verbal questioning, we collected the clinical characteristic of diabetes and family history in the preceding generation, and first and second degree relatives.

We divided the groups according to family history of type 2 DM as follow: group 1, without family history of DM; group 2, father with DM; group 3, mother with DM; and group 4, both parents with DM. We evaluated the metabolic control with blood glucose and HbA1c, insulin, albuminuria, plasma creatinine, total cholesterol, triglyceride, Homa-IR, and Homa.

The results showed that the group of patients with both diabetic parents had significantly younger (F= 9.47, p=0.000006), and earliest initiation of diabetes 9.8 years in comparison to patients without DM relatives (F=12.0, p<0.000001). Male and female patients with both diabetic parents were younger as compared with the group without history of diabetes, (F=4.24, p=.009) and (F=6.23, p=.0005) respectively; Among females the parity was lower: 4.1 children for the group with both parents with diabetes as compared with 7.7 children (p=.002) for the group without family history of diabetes. In regards to complications of diabetes we did not find significant differences between the groups according to family history of diabetes, neither blood glucose, HbA1c, insulin, albuminuria, plasma creatinine, total cholesterol, triglyceride levels, Homa-IR, or Homa.

From the study they concluded:

- 1.- The patients with type 2 DM with both diabetic parents are 9.9 years younger than those without family history of diabetes, and initiated diabetes at an earliest age.
- 2.- Among women parity was lower for the group with both parents with diabetes.

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Item #18

Cozaar (Losartan) Lowered Risk Of Total Mortality In Patients With Diabetes By 39% Versus Atenolol

Treatment with losartan resulted in a 24 per cent reduction in the primary composite endpoint of cardiovascular death, stroke and heart attack.

In a pre-specified subgroup of hypertensive patients with diabetes, Cozaar® (losartan) was significantly more effective in reducing the combined risk of cardiovascular death, heart attack and stroke, according to an analysis of the landmark LIFE trial.

These results were presented Thursday at the joint International Society of Hypertension/ European Society of Hypertension meeting in Prague, Czech Republic. This finding is consistent with the beneficial effects of losartan in reducing the combined cardiovascular morbidity and mortality demonstrated in the overall LIFE study population.

"Patients with diabetes are an important patient group, as they have double the risk of cardiovascular disease, and this risk is further increased by hypertension," said Lars H. Lindholm, M.D., principal investigator of the diabetes subgroup analysis, and professor, Umeå University Hospital, Umeå, Sweden. "Losartan has now been shown to be superior in reducing the combined risk of cardiovascular disease and death in diabetic patients in the LIFE trial."

"The observation that losartan has much greater impact on reducing stroke and the death rate overall obliges us to rethink the way we treat patients with diabetes who have high blood pressure in Canada," said Dr. John Floras, President of the Canadian Hypertension Society, staff cardiologist and Director of Research, Toronto's University Health Network and Mount Sinai Hospital Division of cardiology.

Findings from the LIFE (Losartan Intervention For Endpoint reduction in hypertension) substudy in 1195 hypertensive patients with diabetes showed that treatment with losartan resulted in a 24 per cent reduction in the primary composite endpoint of cardiovascular death, stroke and heart attack compared to the beta-blocker atenolol ($p=0.03$). Blood pressure and pulse pressure reductions were similar with both therapies. In addition, losartan significantly reduced the risk of cardiovascular death by 37 per cent ($p=0.03$) and total mortality by 39 per cent ($p=.002$).

"A 39 per cent reduction in total mortality with losartan is an important observation given that the observed reduction is versus an established antihypertensive, atenolol. The LIFE study showed that it matters how we lower blood pressure," Dr. Lindholm said.

In comparison, in the 9,193-patient LIFE study as a whole, losartan significantly reduced the combined risk of cardiovascular death, heart attack and stroke -- the primary endpoint of the study -- in patients with hypertension and left ventricular hypertrophy (LVH) by 13 per cent compared to atenolol ($p=0.021$). In addition, losartan reduced the risk of stroke by 25 per cent ($p=0.001$). These results occurred even though blood pressure was reduced to a similar level in both the losartan and atenolol treatment groups.

"In another pre-specified subgroup of patients with isolated systolic hypertension, the findings on stroke with losartan versus atenolol were consistent with those seen in the overall study population," said Sverre Kjeldsen, M.D., Ph.D., a LIFE Steering Committee member, and adjunct professor of medicine, University of Michigan, and chief physician of Cardiology, Ullevaal University Hospital, Oslo, Norway. "The data on this important group of patients are scheduled for presentation later this year. It is widely accepted that elevated systolic blood pressure is an even stronger risk factor for cardiovascular events than diastolic blood pressure."

Diabetic study patients were 55-80 years old with previously treated or untreated hypertension and signs of LVH as measured by electrocardiogram (ECG). Patients were randomized to losartan or atenolol after one to two weeks of placebo if trough sitting blood pressures were 160 to 200 mmHg systolic and 95 to 115 mmHg diastolic. Mean follow-up time was 4.7 years with patients having regular visits and upward titration of medication to reach a blood pressure goal of less than 140/90 mmHg.

In the overall LIFE trial, the results of the primary endpoint were consistent across 23 of the 24 study subgroups examined. However, additional analyses of the treatment effect by ethnicity suggested that black patients treated with atenolol were at lower risk of experiencing cardiovascular death and disease compared to patients treated with losartan.

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Did You Know?

That the statins that are prescribed for high LDL levels may also have an anti-inflammatory effect and there's evidence that type 2 may also be an inflammatory disease. ADA Poster # 982 showed that over 5 years, the concurrent use of a statin was associated with an average 1.2 year delay in progression from oral drugs to insulin therapy.

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Item #19

INGAP Peptide - An Initiator of Beta Cell Growth

You will be hearing more about INGAP in upcoming newsletters

Recent studies have shown that induction of islet neogenesis from adult pancreatic stem cells has the potential for restoring beta cell mass in diabetes.

We have previously hypothesized that these stem cells can develop along either a neural or a neuroendocrine path. The factors regulating this development are unknown. We examined the role of INGAP peptide in islet neuroendocrine cell development *in vivo*. Forty dogs (20 males, 20 females) were randomly divided into 4 groups. Group 1 received daily IM injections of vehicle alone, while the other 3 groups received 0.5, 1.5 or 10 mg/kg injections of INGAP peptide. After 30 days of treatment the animals were sacrificed and pancreatic tissues collected. Analysis was performed with ImagePro software on confocal microscopy images of tissues stained for insulin, the essential islet transdifferentiation transcription factor PDX-1 and the pan-neuroendocrine marker PGP9.5.

The results showed a significant ($p < 0.001$) increase in the percentage of insulin positive cells in animals treated with INGAP peptide ($p < 0.001$, ANOVA, Table 1), with 1.5 mg/kg being the most effective dose, more than doubling controls (Dunnett's Test, $p < 0.05$). PGP 9.5 was increased, based on stain intensity, in large ducts of treated animals, suggesting development of neuroendocrine cells from ductal elements in response to INGAP. PDX-1 was increased in 1.5mg/kg-treated pancreas especially in isolated cells and duct epithelium.

These results indicate that adult islet stem cells in pancreas of normal dogs are induced to develop along a neuroendocrine pathway in response to INGAP peptide. The expression of PDX-1 and PGP 9.5 in duct cells suggests that INGAP is an initiator of neuroendocrine cell and PDX-1 expression in the path to islet neogenesis. ENDO 2002 [P1-27]

% Insulin Positive Area

Control	0.5mg/kg INGAP	1.5mg/kg INGAP	10mg/kg INGAP
1.2±0.1	1.8±0.2*	2.9±0.2*†	1.5±0.2

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Item #20

INGAP Peptide Induces Islet Cell Neogenesis from Human Duct-like Islet Progenitor Cells

The results support the notion that INGAP peptide is a potent inducer of islet cell neogenesis.

We have previously described the *in vitro* induction of human adult islet-to-duct cell transdifferentiation in which the cells of the resulting duct-like cystic structures exhibit a primitive epithelial morphology.

We hypothesize that some or all these cells may exhibit developmental plasticity and could thus be used as an expandable pool of islet cell progenitors.

Islet neogenesis associated protein (INGAP) is a mediator of *in vivo* islet cell neogenesis from pancreatic duct epithelial cells in several species.

The aim of the present study was to induce islet cell neogenesis *in vitro* by treating these putative progenitor cells with INGAP peptide, a pentadecapeptide of the native protein.

Freshly isolated adult human pancreatic islet cells (>95% pure) were induced to differentiate into duct-like epithelial cells in a collagen gel supplemented with a defined basal medium containing cholera toxin (100ng/ml) (CT). As shown by immunohistochemistry (IHC), islet-to-duct transformation was characterized by the loss of expression of PDX-1 and islet cell hormones, and the appearance, in all cells, of the duct-epithelial cell marker CK-19. After 10 days, cultures were either supplemented with INGAP peptide (250 ng/ml) (Group 1) or maintained in basal medium (Group 2) for an additional four days. Data was compiled in triplicate from each of 4 separate islet isolations representing 4 different human donors.

Following addition of INGAP peptide, as observed under the inverted microscope, 34% of duct-like cystic structures acquired a solid islet-like appearance. In contrast, 0% of the cystic structures in Group 2 underwent this change in morphology. By IHC, 88% of the islet-like structures in Group 1 were positive for PDX-1; 83% were positive for insulin; 79% were positive both PDX-1 and insulin and all were negative for CK-19. At the cellular level, 25±5% of all cells became immunoreactive for PDX-1 (vs 8±2% in Gr. 2, p<0.01); 21±5% became positive for insulin (vs 0% in Gr. 2), 4±1% became positive for glucagon (vs 0% in Gr. 2); 1±0% became positive for somatostatin (vs 0% in Gr.2); and 19.6±6% of cells expressed both PDX-1 and insulin (vs 0% in Gr. 2).

These results support the notion that INGAP peptide is a potent inducer of islet cell neogenesis from a putative adult islet progenitor cell, and that the induction of endocrine differentiation is mediated by PDX-1, a transcription factor known to be required for pancreatic Beta-cell development. ENDO 2002 (OR30-2)

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Quote of the Week-----

----- **Vision without action is merely a dream. Action without vision just passes the time. Vision with action can change the world.** ----- Joel Barker

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([link to burke archive page](#))

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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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