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

June 19 2002,Iissue 109

From the Editors Desk:

The ADA conference is over and they are setting up for the Endo 2002 conference.

We have seen a lot of research about diabetes and related conditions. In addition all the Manufacturers were there with new product ideas and medication programs. The new *FreeStyle Tracker* is available and they have a great new system from iControl Diabetes so you and your patient can check glucose records anytime, anywhere.

If you want to learn about my real world experiences with the new GlucoWatch®, check out our special feature The GlucoWatch® Biographer—A Personal Experience

Kristina Sandstedt, MS, Clinical Exercise Physiologist, brings us Exercise Consultation: An Empirically Validated Approach

Steve and I are at the ADA and Endo 2002 conferences in San Francisco. If you would like to read all our daily news releases **Click here**

Dave Joffe
Editor-in-Chief

News Update: June 10, 2002
Metrika receives NGSP Certification for their A1cNow instant A1c test.
The A1cNow test is the first and only A1c test that is instant and disposable with NGSP certification. For more info on the NGSP certification and how you can now use it in your office practice click HERE!

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"*Tools*" for Your Practice:
Stayed tuned next week for an exciting new program from **Pritchett & Hull**, They will be providing you with a series of Printed handouts for your patients. You will be able to sign up for these to be mailed to you
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Monthly Feature On Nutrition:

How Sweet It Is: A Look at Sugars and Sweeteners
Sherri Shafer, R.D., CDE

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News Flash - News Flash
Flying With Diabetes: New Precautions
8 Tips to prevent problems
Click HERE

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Product information:

Read the GlucoWatch® Biographer – professional report
By Gina Gilbert, RN, BSN, CDE Sr. Manager, Training and Education, Cygnus, Inc.

Dr. Richard Bernstein's Corner:
Check out Dr. Bernsteins Corner for Insights for Controlling Blood Sugars
http://www.diabetesincontrol.com/bernsteinarchive.htm

A Bit of History on the need for tight control:
This week you view the Rejection Letters from ADA, NEJM, AMA and Lancet, stating that there was not a preponderance of knowledge demonstrating a need for tight control

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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/Issue108index.htm

OPEN STUDIES:

1. Gym Study II: Gymnemosupium II, a combination of the extracts of Gymnema sylvestre, Pterocarpus marsupium, Diachrome and Vanadium

2. RELAXATION – WarmFeet® study Version II Open For Registration (less labor intensive version**)** Learn More: Click here

3. PATIENT EXPERIENCE PROGRAM (PEP) Open For Registration Learn more...>

SOON TO OPEN STUDIES for your participation

1. **A new feedback study for you and your patients- Using a medical/nutritional assessment survey**
2. **Medical Professional evaluation study—Educational tear-sheets for your patients**
3. **The S.T.E.P. study, 10,000 Steps To Enhanced Prevention**

The Abstract from our study "**THE EFFECT OF LOW GLYCEMIC FOODS ON BLOOD GLUCOSE IN NIDDM AND IDDM PATIENTS"** is now available. Thanks to all our readers who participated. Click here

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This Weeks Items:

1. **Education Helps Reduce Elevated Glycosylated Hemoglobin Levels**
Click Here
2. **ADA: Better Lipid Management Needed in Patients with Diabetes and Heart Disease**
Click Here
3. **Item Revisited**:
Click Here
4. **Postprandial Insulin Deficiency Major Factor Of Deteriorating Glucose Control**
Click Here
5. **Intestinal Cells Can Be Stimulated To Make Insulin**
Click Here
6. **Fasting Glucose Inadequate in Screening for CV Risk**
Click Here
7. **ADA: Pramlintide Decreases Glucose Fluctuations in Diabetics Using Pumps**
Click Here
8. **ADA: Acarbose May Delay Development Of Type-2 Diabetes**
Click Here
9. **Dentists Need to Discuss Glycemic Control Vs.Periodontal Disease**
Click Here
10. **Those with Normal Blood Pressure can Decrease Risk of Stroke and Mortality**

Click Here
11. **Cardiac Events Increased With High-Normal BP**
Click Here
12. **Diabetes Risk in Middle-Aged Men Predicted with C-Reactive Protein**
Click Here
13. **Predictors of Acute Complications in Children With Type 1 Diabetes**
Click Here
14. **Microvascular Processes Plays A Role in Development of Diabetes**
Click Here
15. **Cost-effectiveness of Intensive Glycemic Control**
Click Here

ITEMS For The Week:

Item #1
Education Helps Reduce Elevated Glycosylated Hemoglobin Levels
A trial comparing intensive and passive education in patients with diabetes.

Both intensive and passive education methods seem to work equally well in improving glycemic control in patients with elevated glycosylated haemoglobin [HbA(1C)] levels.

Patients who are receptive to education can substantially improve their levels after either type of educational intervention, say researchers from the Veterans Affairs Healthcare System and Brigham and Women's Hospital, Harvard Medical School in Boston, Massachusetts, United States.

They found a decrease in HbA(1C) level of approximately 2.0 percent after one year in 106 patients randomised to either intensive or passive education groups. Such a decrease is significant, investigators add. "Maintaining this mean decrease in HbA(1C) level would represent a significantly reduced lifetime risk for microalbuminuria, retinopathy and neuropathy."

They concluded that the results reinforce the need for and benefits of incorporating educational interventions into the management of diabetic patients: "Any educational method that provides instruction in the core content areas, particularly when delivered to patients who are interested and receiving ongoing care, can be an effective means for reducing HbA(1C) levels."

The investigators say they were surprised to find no significant difference in the metabolic control achieved in the two educational intervention groups.

They suggest participants who enrolled were highly motivated. Regardless of their group assignment, these patients were prepared to make change in their diabetic control.

Because of this, the researchers compared the outcomes in both groups of participants with those of patients who refused to participate. The patients who refused also had a decline in HbA(1C) level, but that it was significantly less than that of the intervention groups.

Participants had HbA(1C) levels greater than 8.5 percent. A total of 50 were randomised to intensive education and 56 to passive education.

Intensive education included 3.5 days of structured curriculum taught by five staff: a doctor, a nurse, a pharmacist, an exercise physiologist and a social worker. Passive education participants received basic diabetes information by mail every three months.

Participants in both groups continued to see their primary care providers. Investigators measured their levels of HbA(1C) at three, six and 12 months. Patients who declined participation were measured at baseline and 12 months.

Researchers found intensive-education participants had a mean decline of 2.0 percent in HbA(1C) level at 12 months. The mean decline for passive-education participants was 1.9 percent.
Archives of Internal Medicine, 2002; 162: 1301-1304.

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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: Better Lipid Management Needed in Patients with Diabetes and Heart Disease

Study shows that CAD patients with diabetes are under-tested and under-treated.

As a result of these findings, the researchers called for interventions to help physicians improve their use of lipid testing and drug therapy for patients with diabetes and coronary artery disease (CAD).

The findings were presented here Friday at the 62nd Scientific Sessions of the American Diabetes Association (ADA).

Dr. Mark Massing, with Medical Review of North Carolina in Cary, North Carolina, United States and co-workers studied trends in lipid management from 1996 to early 1998 among CAD patients with and without diabetes mellitus (DM) seen at 295 outpatient practices in the US by 1,540 physicians participating in the Quality Assurance Program. About 23 percent of the 47,813 CAD patients included in their analyses had diabetes.

During the study period, lipid profile testing rates among patients with DM increased dramatically from 28 percent to 50 percent. Even so, rates of lipid profile testing were 20 percent lower among patients with DM compared to those without DM (odds ratio 0.8 , 95 percent confidence interval: 0.7, 0.8).

Prescriptions for cholesterol-lowering drugs among patients with DM increased form 33 percent to 50 percent.

While trends in cholesterol lowering drug prescriptions were similar for those with and without DM, those with DM were 20 percent less likely to receive a prescription than those without the condition.

As lipid treatment improved, the mean low-density lipoprotein (LDL)-cholesterol values declined for patients with and without diabetes. Among patients treated with cholesterol-lowering drugs, the percent decline over time for mean LDL-cholesterol was greater for those who did not have DM (15 percent) compared to those with DM (7 percent)

Overall, the data indicate that lipid management improved markedly for CAD patients with and without diabetes during this time period, Dr. Massing observed. However, despite their high-risk status that requires more aggressive treatment, there was no evidence of such treatment in patients CAD patients with DM compared to those who did not have DM.

Dr. Massing said that the study is limited by the fact that individual patients were not followed over time, which means that trends comparing different populations over time may be misleading. Also, patient information from physicians in non-participating practices was not available. On the other hand, he said, an important strength of the study is that it included a very large cohort of patients seen at some of the largest medical practices in the US.

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Item #3 Item Revisited**: June 12, 2000 Issue 4** two years ago

AVANDIA MAY SLOW TYPE 2 PROGRESSION

(Watch for Actos to make same claim to fame)

It only makes sense that all the insulin sensitizers will slow the progression of type 2 diabetes.
If you make the cells more sensitive to the bodies own insulin, it doesn't have to produce as much and you won't overwork the pancreas as much, therefore helping to prevent beta cell depletion.

Avandia(r) (rosiglitazone maleate) may improve beta cell function in the pancreas, according to data presented at the American Diabetes Association (ADA) 60th Scientific Sessions meeting.

Improving beta cell function may enhance long-term blood sugar control in type 2 diabetes patients, thereby slowing the progression of type 2 diabetes. Leading diabetes experts say that if this data is supported in long-term studies, improved beta cell function could have profound implications for preventing the complications of type 2 diabetes.

The United States Department of Veterans Affairs Health Administration (VA) is conducting a long-term nationwide study to determine the impact of intensive drug therapy with Avandia in combination with other type 2 diabetes drugs on preventing the life-threatening, long-term complications of type 2 diabetes. SmithKline Beecham is announcing at the ADA meeting that Avandia will be a key antidiabetes treatment investigated in this study.

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FACT:

Physicians rank diabetes as higher risk factor for cardiovascular disease than smoking, that according ADA and ACC survey.

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Item #4

Postprandial Insulin Deficiency Major Factor Of Deteriorating Glucose Control

Postprandial insulin deficiency is the most powerful explanatory factor of deteriorating glucose control in newly presenting type 2 diabetes.

"Indices of insulin sensitivity and pancreatic beta-cell responsiveness explain fasting glucose and HbA_{1c} (glycated hemoglobin) well but fail to explain postprandial glucose," add investigators from City University in London and the University of Wales College of Medicine, United Kingdom.

The investigators examined the ability of indices of insulin sensitivity and pancreatic beta-cell responsiveness to explain interindividual variability of glucose control measures in 65 patients with newly presenting type 2 diabetes.

Minimal model-derived insulin sensitivity, glucose effectiveness, first-phase insulin secretion and disposition index were determined using an insulin-modified iv glucose tolerance test.

Fasting/basal and postprandial pancreatic beta-cell responsiveness was measured by a standard meal tolerance test.

Stepwise linear regression was used with these indices to explain the interindividual variability of fasting and postprandial concentrations of plasma glucose, plasma insulin and HbA_{1c}.

Results showed a negative correlation between measures of pancreatic beta-cell responsiveness and fasting plasma glucose. Pancreatic beta-cell responsive measures were positively correlated with fasting plasma insulin and insulin response to the meal tolerance test.

Minimal model-derived insulin sensitivity was found to be negatively correlated with fasting plasma insulin but was not correlated with any glucose variable.

Postprandial beta-cell responsiveness and disposition index were the "most informative in explaining interindividual variability," according to the investigators.

J Clin Endocrinol Metab 2002; 87(1): 198-203

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Item #5

Intestinal Cells Can Be Stimulated To Make Insulin

A new source of beta cells can provide an answer to the shortage in Edmonton Protocols

An international research team has discovered a new source of cells to combat diabetes. Scientists at the University of Calgary and Japan's Shiga University find that intestinal cells produce insulin.

Dr. Norman Wong, a University of Calgary physician-scientist, and his colleagues, Drs. Takaaki Nakamura and Atsunori Kashiwagi, clinician-scientists of Shiga University in Japan, have completed studies which demonstrate that intestinal cells can be stimulated into producing insulin –- a hormone that millions of diabetics are lacking.

The team's findings are published in the May edition of *Diabetes*, a prestigious international research journal.

"Scientists the world over are studying how to manipulate cells in order to convert them into pancreatic cells, which may be used to treat diabetes mellitus," says Wong, professor, medicine, and biochemistry & molecular biology, University of Calgary Faculty of Medicine, and director, Libin Gene Therapy Unit. "My colleagues and I decided to investigate whether we could make islet cells by altering intestinal cells so that they would transform into pancreatic islet cells and produce insulin."

Type 1 diabetes mellitus, previously known as juvenile diabetes mellitus, is caused by the destruction of insulin-producing beta cells in the pancreas. This destruction occurs when the immune system mistakenly attacks the beta cells. The absence of insulin means that people with diabetes have high blood glucose and associated complications that affect vital organs including: kidney, eye and nerve conditions as well as heart and vascular disease.

This research stems from the understanding that pancreatic cells and intestinal cells share a common origin in the embryo. Armed with that knowledge, the team began exploring whether conducting a series of experiments on intestinal cells would stimulate those cells into performing the functions normally provided by pancreatic cells.

The scientists first exposed the intestinal cells of rats to a transcription factor called PDX-1. This factor has been previously shown to be important for insulin gene expression. Secondly, the team exposed the PDX-1 expressing intestinal cells to a growth factor called Betacellulin. "We discovered that the combination of those two steps enabled us to fire up the intestinal cells so that they produced insulin," says Wong.

"The advantage of using intestinal cells to perform the work of pancreatic cells is that people have available to them a nearly limitless supply of their own intestinal cells -– whereas pancreatic cells are extremely scarce," says Wong. "That's what's so exciting about these results –- we have taken the first step in finding a man-made way to produce pancreatic cells. These findings may provide an important source of cells for the Edmonton islet cell transplantation protocol."

Wong's research is supported by: Canadian Diabetes Association, Alberta Heritage Foundation for Medical Research, and Canadian Institutes of Health Research. - By Karen Thomas

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Item #6

Fasting Glucose Inadequate in Screening for CV Risk

Two-thirds of subjects with cardiovascular risk factors remain undetected using fasting glucose testing as a screening method, say researchers.

Fasting glucose inadequate in screening for CV risk

The researchers used a two-step strategy to compare metabolic risk profiles in subjects with impaired glucose fasting (IFG) and those with impaired glucose tolerance (IGT). They identified 1,855 people without diagnosed diabetes with fasting plasma glucose of between 5.6-7.8 mmol/l. Those patients were asked to complete an oral glucose tolerance test (OGTT; n=1,456).

The results between the two measurements only agreed in 20.8% of the subjects. Those with isolated IFG did not have clinical features associated with cardiovascular risk, whereas subjects with IGT had associated cardiovascular risk profiles. The researchers commented that if IFG were used for glucose intolerance screening about 66.6% of subjects with IGT with cardiovascular risk would not have been detected.

Li CL et al. Comparison of metabolic risk profiles between subjects with fasting and 2-hour plasma glucose impairment: The Kinmen Study. J Clin Epidemiol 2002; 55: 19-24.

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Did you know?

According to recent survey by IDF and Lyons, The majority of people with diabetes are not worried about long-term complications of the disease, even though 74 percent of people with diabetes may suffer diabetic microvascular complications.

Item #7
ADA: Pramlintide Decreases Glucose Fluctuations in Diabetics Using Pumps
Replacement of amylin with pramlintide reduces excessive glucose fluctuations in patients with type 1 diabetes.

In the setting of intensive insulin therapy, replacement of amylin with pramlintide reduces excessive glucose fluctuations in patients with type 1 diabetes, according to results reported here Friday at the 62nd Scientific Sessions of the American Diabetes Association (ADA).

Dr. Claresa Levetan with MedStar Clinical Research Center in San Diego, California, and colleagues used a continuous glucose monitoring system (CGMS) to evaluate the effect of pramlintide on glucose fluctuations in patients with type 1 diabetes intensively treated with insulin pumps (CSII).

They enrolled 24 patients with type 1 diabetes with a mean age of 42 years who were being treated with CSII. Twenty-two evaluable patients were randomized to receive preprandial injections for four weeks -- six of them with placebo and 18 with 30 µg pramlintide TID. Preprandial insulin doses were initially decreased by 10 percent to 20 percent. CGMS was used to measure interstitial glucose concentrations every five minutes over 24 hours at baseline and week 4, and two weeks after the end of the treatment period.

At enrollment, patients had excessive glucose fluctuations, spending on average 59 percent of the 24-hour period with a glucose value above 140 µg/dL, 13 percent below 80 µg/dL, and 28 percent in the euglycemic target range (80 to 140 µg/dL).

After four weeks on pramlintide, the time spent above the target range decreased to 48 percent, while time spent within the target range increased by 32 percent (to 37 percent). This shift from the hyperglycemic to the euglycemic range occurred without a relevant increase in the time spent below the target range (15 percent), without any severe hypoglycemic events, and with sustained preprandial insulin dose reductions of approximately 20 percent. At week six (off treatment), the 24-hour glucose profile reverted toward pre-treatment values.

Pramlintide was generally well tolerated, and nausea was the most common adverse event reported.

Dr. Levetan said the results show that the addition of pramlintide to insulin therapy in patients with type 1 diabetes intensively treated with SCII reduces excessive 24-hour glucose fluctuations by shifting glucose values from the hyperglycemic into the euglycemic target range, without increasing the time spent below the euglycemic range.

The addition of pramlintide to insulin therapy may therefore help patients more safely achieve their glycemic goals, he said.

Excessive 24-hour glucose fluctuations are a common abnormality in patients with type 1 diabetes, are comprised of hyperglycemic peaks and often unrecognized nocturnal hypoglycemia, and can hinder the attainment of glycemic targets. They have been demonstrated in both adult and adolescent patients with type 1 diabetes using continuous glucose monitoring technology and are present even in intensively treated patients who are in seemingly good overall glycemic control.

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Item #8
ADA: Acarbose May Delay Development Of Type-2 Diabetes
An international study indicates acarbose could be used to delay the development of Type II diabetes in patients with impaired glucose tolerance.

A randomized placebo controlled trial directed by Dr Jean-Louis Chiasson, Research Centre, Centre Hospitalier de l'Université de Montréal, Hôtel-Dieu, Montreal, Quebec was carried out among 1,429 patients with impaired glucose

tolerance. Patients were from Canada, Austria, Denmark, Finland, Israel, Germany, Norway and Sweden.

They were recruited to the Study To Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) trial, mainly through screening of high-risk populations, especially first-degree relatives of patients with Type II diabetes. Men and women were screened who were between the ages of 40 to 70 and who had a body-mass index of between 25 and 40 kg/m.

Researchers assigned 714 patients with impaired glucose tolerance to acarbose (100 mg) and 715 to placebo three times daily. The primary endpoint was the development of diabetes on the basis of a yearly oral glucose tolerance test. Overall, 211 (32 percent) of 682 patients in the acarbose group and 130 (19 percent) of 686 on placebo discontinued treatment early.

Investigators found that 10 percent fewer patients given acarbose developed diabetes: 221 (32 percent) of patients randomized to acarbose and 285 (42 percent) randomised to placebo. This is a relative reduction in risk of 25 percent.

At the same time, acarbose significantly increased reversion of impaired glucose tolerance to normal glucose tolerance. The main side effects of acarbose were flatulence and diarrhoea.

Dr Chiasson and colleagues conclude: "Lifestyle modification has already been shown to prevent Type II diabetes. Our results show that intervention with acarbose is also effective. Whether these two treatment options can be used together remains to be determined. Nevertheless, recommendations for screening and treatment of impaired glucose tolerance should now be reassessed." *Lancet 2002; 359: 2072-77*

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Did You Know:

According to the results of the recent LCIF survey: More than 40% of people with diabetes surveyed feel that problems due to diabetes will occur no matter what they do. They believe that they will experience complications regardless of what precautions they take.

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Item #9

Dentists Need to Discuss Glycemic Control Vs.Periodontal Disease

Poor Glycemic Control Directly Related to Severe Periodontal Disease

The study investigated the association between glycemic control of type 2 diabetes and severe periodontal disease in the US adult population ages 45 years and older.

Data on 4343 persons ages 45–90 years from the National Health and Nutrition Examination Study III were analyzed using weighted multivariable logistic regression. Severe periodontal disease was defined as 2 + sites with 6 + mm loss of attachment and at least one site with probing pocket depth of 5 + mm. Individuals with fasting plasma glucose > 126 mg/dL were classified as having diabetes; those with poorly controlled diabetes (PCDM) had glycosylated hemoglobin > 9% and those with better-controlled diabetes (BCDM) had glycosylated hemoglobin ≤9%. Additional variables evaluated in multivariable modeling included age, ethnicity, education, gender, smoking status, and other factors derived from the interview, medical and dental examination, and laboratory assays.

The results showed that individuals with PCDM had a significantly higher prevalence of severe periodontitis than those without diabetes (odds ratio = 2.90; 95% CI: 1.40, 6.03), after controlling for age, education, smoking status, and calculus. For the BCDM subjects, there was a tendency for a higher prevalence of severe periodontitis (odds ratio = 1.56; 95% CI: 0.90, 2.68).

These results provide population-based evidence to support an association between poorly controlled type 2 diabetes mellitus and severe periodontitis. *Community Dent Oral Epidemiol 2002; 30: 182–92.*

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Item #10

Those with Normal Blood Pressure can Decrease Risk of Stroke and Mortality

ACE inhibitors cut the incidence of stroke, decrease stroke mortality, and reduce functional impairment following stroke in high-risk patients who have relatively normal blood pressure, reported Dr. Jackie Bosch and associates in the Heart Outcomes Prevention Evaluation (HOPE) study.

Their findings show that patients at high risk of stroke should be treated with ACE inhibitors, even if they have normal blood pressure, and in addition to other preventive treatments they may be taking such as aspirin therapy, lipid-lowering agents, antiplatelet drugs, and antihypertensive medications, the researchers said (BMJ 324[7339]:699-702, 2002).

The benefit of ACE inhibitor therapy in preventing cardiac events has been documented in previous reports from the HOPE study, a randomized trial involving 267 hospital clinics in 19 countries in which ramipril was compared with placebo. In the latest analysis of HOPE study data focusing on stroke outcomes, 9,539 high-risk patients were followed at 6-month intervals for an average of 4.5 years.

The number of strokes and stroke fatalities were significantly lower in subjects taking ramipril. Among subjects who developed stroke, significantly fewer of those on ramipril showed cognitive, motor, or speech impairment, compared with those on placebo.

Although ramipril decreased blood pressure modestly (an average of 3.8 mm Hg systolic and 2.8 mm Hg diastolic), the drug's beneficial effect occurred across a range of blood pressure levels. This confirms that the benefit of ACE inhibitors isn't confined to hypertensive patients and that their action in preventing stroke is independent of their antihypertensive effect, said Dr. Bosch of McMaster University, Hamilton, Ont., and associates.

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Item #11

Cardiac Events Increased With High-Normal BP

Framingham study finding

Even normal blood pressure may boost a person's risk of cardiovascular disease if the pressure hovers near the upper limit of normal.

“When a person's blood pressure is below 140/90 mm Hg, most people think that's fine and there's no need to pay attention to cardiovascular risk,” Dr. Donna S. Hanes said at the annual meeting of the American College of Physicians–American Society of Internal Medicine.

But the results of a recently reported epidemiologic analysis documented the risk from high-normal pressure, when the systolic pressure is 130-139 mm Hg and the diastolic is 85-89 mm Hg.

People with blood pressures at this level need to work on lowering their pressure, not with drugs but with lifestyle modifications like diet, exercise, and weight loss, said Dr. Hanes of the University of Maryland, Baltimore.

The study cited by Dr. Hanes involved 6,859 people who participated in the Framingham Heart Study.

All of these people entered the study free of hypertension and cardiovascular disease.

The study participants were divided into three groups according to blood pressure: People with optimal blood pressure, less than 120/80 mm Hg; those with normal pressure, 120-129/80-84 mm Hg; and those with high-normal pressure, 130-139/85-89 mm Hg.

The incidence of cardiovascular disease events was tracked in the study participants during an average follow-up of 11 years.

During the follow-up period, the incidence of cardiovascular disease events in men was 30% higher in those with normal blood pressure and 60% higher in those with high-normal pressure, compared with the men who had optimal blood pressure, investigators reported in a journal article that was published last November (*N. Engl. J. Med. 345[18]:1291-97, 2001*).

The increased risk of the high-normal group was statistically significant and took into account the between-group differences in age and other cardiovascular risk factors such as serum lipid levels and diabetes.

Among the women in the study, those with high-normal pressure had a risk-adjusted, 80% increased risk of developing cardiovascular disease, compared with women who started with an optimal blood pressure.

A goal blood pressure of less than 140/90 mm Hg was established for certain high-risk patients, such as those with diabetes, in the most recent U.S. recommendations on blood pressure treatment by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

But these findings from the Framingham Heart Study are the first to document a substantial risk from high-normal blood pressure in people without any other risk of cardiovascular disease, according to Dr. Hanes.

Although the recent Framingham analysis presents compelling evidence on the danger of high-normal blood

pressure, the data do not justify changing the threshold for starting antihypertensive drug treatment since the evidence is entirely epidemiologic.

For this reason, Dr. Hanes only felt comfortable recommending lifestyle interventions to lower blood pressure in these people.

It's unlikely that a study will be done to test the benefits of drug treatment for otherwise healthy adults with high-normal blood pressure, because the study would require either a huge number of subjects or a very long follow-up period, said Dr. Hanes.

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Item #12

Diabetes Risk in Middle-Aged Men Predicted with C-Reactive Protein

Elevated C-reactive protein (CRP) levels are associated with an increased risk of developing type 2 diabetes in middle-aged men independently of established risk factors,

British investigators report. This finding supports the theory that low-grade inflammation contributes to the pathogenesis of type 2 diabetes.

Dr. Dilys J. Freeman, of the University of Glasgow and members of the West of Scotland Coronary Prevention Study Group obtained plasma samples at baseline from 5245 men, mean age 55.6 years. According to their report in the May issue of Diabetes, 127 subjects developed diabetes during 5 years of follow-up.

The mean natural logarithm of sensitive CRP was 1.05 among those who developed diabetes versus 0.53 for the remainder of subjects, indicating its strong predictive value ($p < 0.0001$). Individuals with CRP greater than 4.18 mg/L had more than six times the risk of diabetes compared with those with CRP levels 0.66 mg/L or lower.

After adjustment for baseline body mass index, natural log triglyceride, blood glucose, systolic blood pressure, total and HDL cholesterol, and natural log white cell count, log CRP level remained a significant predictor of diabetes ($p = 0.0075$).

According to the authors, these findings complement a similar observation of elevated risk for diabetes in women with higher CRP values. The association is strengthened by the ability of weight loss, thiazolidinediones, statins, and ACE inhibitors to decrease insulin resistance while exerting significant anti-inflammatory effects. Dr. Freeman's team suggests that inflammatory cytokines may produce insulin resistance through their effect on insulin receptors or by stimulating adipocyte lipolysis.
Diabetes 2002;51:1596-1600.

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FACT

In the recent LCIF survey, the results suggest that people with diabetes are not worried about long-term complications and in fact, 30 percent find it hard to control their diabetes and just 25% feel guilty about not taking proper care of themselves. Yet as many as 70 percent of people with diabetes were unable to provide their last hemoglobin HbA1c level.

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Item #13

Predictors of Acute Complications in Children With Type 1 Diabetes

Study determines the factors that predict the incidence of ketoacidosis and severe hypoglycemia in children.

Diabetic ketoacidosis and severe hypoglycemia are acute complications of type 1 diabetes that are related, respectively, to insufficient or excessive insulin treatment. However, little is known about additional modifiable risk factors.

The Objective was to examine the incidence of ketoacidosis and severe hypoglycemia in children with diabetes and t determine the factors that predict these complications.

A cohort of 1243 children from infancy to age 19 years with type 1 diabetes were followed up prospectively for 3994 person-years from January 1, 1996, through December 31, 2000.

Main Outcome Measures were Incidence of ketoacidosis leading to hospital admission or emergency department visit and severe hypoglycemia (loss of consciousness, seizure, or hospital admission or emergency department visit).

The Results showed the incidence of ketoacidosis was 8 per 100 person-years and increased with age in girls. In multivariate analyses, sex-adjusted and stratified by age, the risk of ketoacidosis in younger children increased with higher hemoglobin A_{1c} (HbA_{1c}) and higher reported insulin dose . In older children, the risk of ketoacidosis increased with higher HbA_{1c} and higher reported insulin dose. The incidence of severe hypoglycemia was 19 per 100 person-years and decreased with age in girls. In younger children, the risk of severe hypoglycemia increased with diabetes duration. In older children, the risk of severe hypoglycemia increased with duration, lower HbA_{1c}, and presence of psychiatric disorders. Eighty percent of episodes occurred among the 20% of children who had recurrent events.

The Study reached the conclusions that some children with diabetes remain at high risk for ketoacidosis and severe hypoglycemia. Age- and sex-specific incidence patterns suggest that ketoacidosis is a challenge in adolescent girls while severe hypoglycemia continues to affect disproportionally the youngest patients and boys of all ages. The pattern of modifiable risk factors indicates that underinsured children and those with psychiatric disorders or at the extremes of the HbA_{1c} distribution should be targeted for specific interventions. *JAMA. 2002;287:2511-2518*

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Item #14

Microvascular Processes Plays A Role in Development of Diabetes

Microvascular damage may play a role in the initial development of diabetes.

Retinal arteriolar narrowing is independently associated with the risk of diabetes, according to results of the prospective Atherosclerosis Risk in Communities study, which suggests that microvascular damage may play a role in the initial development of the disease.

Dr. Ronald Klein, of the University of Wisconsin-Madison, and associates obtained retinal photographs from 7993 study participants between 1993 and 1995. High-resolution scanners measured the diameter of individual arterioles and venules surrounding the optic disk, which were then used to express arteriole-to-venule ratios (AVR).

Within a median follow-up period of 3.5 years, 3.6% of participants developed diabetes. The incidence increased from 2.4% to 5.2% with decreasing quartiles of AVR. The relationship remained significant after adjustment for age, sex, race, fasting glucose and insulin levels, and family history of diabetes, with an odds ratio of 1.71 for those in the lowest quartile versus those in the highest quartile of AVR.
The association remained when individuals with signs of diabetic retinopathy, such as microaneurysms and retinal hemorrhages, were excluded, and was similar for those stratified according to risk. The authors of the study, published in the May 15 issue of the Journal of the American Medical Association, suggest that "arteriolar narrowing precedes the onset of diabetes," and when "resulting from hypertension, cigarette smoking, inflammation, and other unmeasured processes, may be a common pathophysiological link to diabetogenesis."

"The fact that microvascular changes precede the onset of diabetes is surprising," co-author Dr. A. Richey Sharrett, of the National Heart, Lung, and Blood Institute in Bethesda, Maryland," stated. "However, there have been a number of things that previously were thought to be markers of the presence of diabetes that are now known to be predictors, for example, lipid abnormalities and low HDL cholesterol."
"It's as if part of the metabolic syndrome appears first," he added.

In the article, the authors suggest that microvascular changes may reduce the ability of insulin to mediate glucose uptake by skeletal muscles. However, Dr. Sharrett pointed out, the arteriolar narrowing "is a finding that begs explanation." He noted that researchers involved in the MESA (Multiethnic Study of Atherosclerosis) study should extend the findings by also evaluating retinal photographs.
JAMA 2002;287:2528-2533.

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Item #15

Cost-effectiveness of Intensive Glycemic Control

Controlling blood pressure, blood glucose and cholesterol reduces costs and improves the quality of life.

The Objective of this study was to estimate the incremental cost-effectiveness of intensive glycemic control (relative to conventional control), intensified hypertension control, and reduction in serum cholesterol level for patients with type 2 diabetes.

Design, Setting, and Patients Cost-effectiveness analysis of a hypothetical cohort of individuals living in the United States, aged 25 years or older, who were newly diagnosed as having type 2 diabetes. The results of the United Kingdom Prospective Diabetes Study (UKPDS) and other studies were used to create a model of disease progression and treatment patterns. Costs were based on those used in community practices in the United States.

Interventions Insulin or sulfonylurea therapy for intensive glycemic control; angiotensin-converting enzyme inhibitor or Beta-blocker for intensified hypertension control; and pravastatin for reduction of serum cholesterol level.

Main Outcome Measures Cost per quality-adjusted life-year (QALY) gained. Costs (in 1997 US dollars) and QALYs were discounted at a 3% annual rate.

Results The incremental cost-effectiveness ratio for intensive glycemic control is $41 384 per QALY; this ratio increased with age at diagnosis from $9614 per QALY for patients aged 25 to 34 years to $2.1 million for patients aged 85 to 94 years. For intensified hypertension control the cost-effectiveness ratio is -$1959 per QALY. The cost-effectiveness ratio for reduction in serum cholesterol level is $51 889 per QALY; this ratio varied by age at diagnosis and is lowest for patients diagnosed between the ages of 45 and 84 years.

Conclusions Intensified hypertension control reduces costs and improves health outcomes relative to moderate hypertension control. Intensive glycemic control and reduction in serum cholesterol level increase costs and improve health outcomes. The cost-effectiveness ratios for these 2 interventions are comparable with those of several other frequently adopted health care interventions. *JAMA. 2002;287:2542-2551*

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Quote of the Week--------

Perseverance is not a long race; it is many short
races one after another. -- Walter Elliott

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