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The Hyperactive Platelet in Type 2 Diabetes- sponsored by Baylor College of Medicine, Houston, Texas, offers 2 hours of AMA PRA category 1 credit To access this free on-line activity, visit <http://www.medscape.com/cmecircle/platelet>

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

July 10 2002, Issue 112

From the Editors Desk:

If you or your patient is a gadget person then the Therasense Tracker is a must have tool for managing your diabetes. [Read about my personal experience.](#)

Diabetes In Control will be giving the "Medical Professional's Choice Award" to the company with the most innovative diabetes product or service of the new millennium. Please nominate the product or service you feel has made the greatest impact on diabetes in the new millennium. Then each of our 31,000 plus readers will vote for the top product or service. Everyone who makes a nomination will be entered into a grand prize drawing. To make a nomination, just **Click Here**

Dr Jennifer Larson, MD, University of Nebraska Medical Center, gave a very informative overview of Pancreas, Islet, and Kidney Transplantation: Metabolic and Endocrine Consequences, at the Endo2002 conference. We have an overview of her presentation, **[click here](#)**

Make sure you read this weeks' feature from Kristina Sandstedt, MS, Clinical Exercise Physiologist, Diabetes Educator; The Role of Exercise in the Treatment of Arthritis, it talks about the relationship of arthritis and diabetes and how exercise can improve both conditions.

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 on new studies, new programs, new products that you can try, great prizes for you and much, much more. Make sure you put it in your calendar to stop by our booth #919 and check it out.

We put the final touches on the AADE Affiliate free Web site Program. Please visit <http://www.fwcade.org> and then if you would like a free site for your chapter visit <http://www.diabetesincontrol.com/aadeaffil.htm> to find out how

Dave Joffe
Editor-in-Chief

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Kristina Sandstedt, MS, Clinical Exercise Physiologist, Diabetes Educator
"The Role of Exercise in the Treatment of Arthritis", Why this information is important for Diabetes Educators

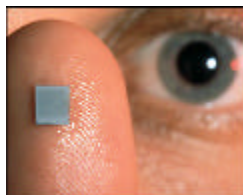
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Dr. Rosen's Feature
"Winning the Battle, but Losing the War"
The trials of trying to get your patients to achieve ADA and AACE goals.

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News Flash - News Flash

Therasense Announces Launch of *CoPilot*, A Data Management Program

Freestyle(TM) Testing Systems Can Upload to New Web Portal for More Comprehensive Data and Diabetes Management. **CoPilot will allow analysis and communication of glucose levels by healthcare providers and people with diabetes. To Learn more [Click Here](#)**

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New Product Information: **A silicon chip with 400 needles.**



400 needles that pierce the skin and let big molecules enter the bloodstream. Drug delivery with this techniques offers several advantages over pills and injections. It can ensure the steady release of medication into the patient's bloodstream over long periods, improving the efficacy of a dose. It can prevent the rapid breakdown that many drugs taken orally undergo when they pass through the digestive system. **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 9 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 [click HERE!](#)

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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!**

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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/Issue112index.htm>

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

1. 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](#)

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

3. 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**

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This Weeks Items:

1. **New Drug Restores Eyesight***
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2. **Diabetes Management Market Predicted to Explode***
[Click Here](#)
3. **Night-Light May Prevent Diabetic Eye Damage***
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14. **Early Statin Therapy After Coronary Event Does Not Appear to Improve Outcome**
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16. **Risk for Type 1 Diabetes Greater in Overweight Children**
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17. **Anti-Inflammatory Effect of Rosiglitazone in Obese Diabetic Patients**
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18. **Special Cell Prevents Diabetes**
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19. **Increasing Aspirin Use to 90% Could Save over 8,000 Lives a Year!**
[Click Here](#)
20. **Advanced Glycation End Products Associated with Endothelial Dysfunction in Type 2 Diabetes**

ITEMS For The Week:

Item #1

New Drug Restores Eyesight

New drug takes eyesight from 20-100 to 20-20

An estimated 200,000 new cases of wet macular degeneration are diagnosed in the United States annually. About 4 million U.S. diabetics have some degree of retinopathy, and 24,000 go blind each year.

Both diseases result from misguided growth of blood vessels in the eyes. Since the new drugs attack this underlying problem, doctors hope they will work for both diseases.

The need for new treatments is especially dire in wet macular degeneration, because nothing can be done for most victims. Blindness often follows within months or even weeks of the first symptoms.

It occurs when leaky blood vessels sprout behind the retina, probably in a mistaken attempt to fix the slow breakdown of light-sensitive cells that occurs with age. These vessels ooze fluid and damage the fragile tissue that controls straight-ahead vision.

To doctors' amazement, experimental new medicines are rescuing people from the brink of blindness so they can read and drive and sometimes even regain perfect vision.

Around the country, about 70 patients with wet macular degeneration have been treated with, Genentech's rhuFab. About half were treated by Dr. Jeffrey Heier of Ophthalmic Consultants of Boston, who says, "I can honestly say I have never seen anything as exciting as this."

Experts caution that most of the results from the studies on this and similar drugs will not be known for at least a year or two. And for now, the treatments are available only to study volunteers.

None of the drugs are intended for the more common but less aggressive "dry" kind of macular degeneration, nor will they work after eyesight has been gone for months.

Guessing the drugs' ultimate effectiveness based on early testing is risky. Still, doctors estimate that roughly one-quarter to one-third of people with newly diagnosed wet macular degeneration have had significant improvement in their eyesight. In most of the rest, loss of sight is stopped, at least temporarily

These lucky few are the first beneficiaries of an entirely new category of drugs that many hope will revolutionize the care of common eye diseases.

Several competing medicines are in development, all based on similar principles. They are designed to stop the two top causes of adult blindness _ the "wet" form of macular degeneration, which affects the elderly, and diabetic retinopathy, the biggest source of blindness in working-age people.

Vision loss seems halted for most if they take the drugs soon after their symptoms begin. Some experience stunning reversals of what would have been inevitable blindness.

The new drugs vary, although most of them, like rhuFab, zero in on a growth-promoting protein called vascular epidermal growth factor, or VEGF. It appears to be an especially important trigger of damaging blood vessels in both forms of blindness.

Other drugs in testing include:

--Anecortave acetate from Alcon, a new steroid injected next to the eye once every six months for macular degeneration.

--Eyetech Pharmaceuticals' EYE001, which is injected into the eyeball like rhuFab for macular degeneration.

--Bausch & Lomb's Retisert implant, which exudes a steroid into the eye for up to three years and is being used for diabetic retinopathy and macular degeneration.

--Lilly's LY333531, the only pill among the new drugs; used to prevent worsening eye disease in diabetics. *Source: American Diabetes Association*
Publication date: 2002-07-02

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(Public Service)

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

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Item #2

Diabetes Management Market Predicted to Explode

Diabetes management will grow at an annual rate of 11 percent during the next decade, according to a market research report.

Consequently, by 2010, annual sales for this market will reach \$15 billion, Medtech (Market Research Firm) said.

Because of the large and growing diabetes patient population, the larger undiagnosed population and the fact that patients are responsible for 99 percent of diabetes management responsibilities, "opportunities for device manufacturers to develop patient-friendly solutions in this market abound," said Sharon O'Reilly, Medtech's president and chief executive officer.

Among the most promising diabetes management products are oral therapies, glucose monitoring and insulin infusion products, Medtech continued. By 2005, revenues for the glucose monitoring market will surpass \$2.5 billion, and revenues for the external insulin pump market will reach \$625 million, Medtech predicted.

While inhaled insulin products have captured headlines recently, Medtech identified some roadblocks to growth in the inhaled insulin market. "Pulmonary delivery is not expected to completely replace insulin shots or insulin drugs," the company said, noting that some studies have "raised concerns about the effectiveness of inhaled insulin over time, and possible adverse effects on the lungs."

Medtech also pointed to islet cell transplantation and pancreas transplantation as promising possible cures for diabetes. However, the company conceded that a shortage of suitable organs and the risks of lifetime immunosuppression have hindered the use of such procedures

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FACT

Alternate Site Confusion?

Are you confused about when it's appropriate to use "alternate site testing" for measuring blood glucose for your patients?

Getting a blood sample from the arm or thigh is less painful. But blood flow is faster in the fingers...so rapid blood glucose changes show up in the fingers BEFORE other sites.

FDA is now allowing alternate site testing with several meters...*Accu-Chek Active, FreeStyle, Glucometer Elite* and *DEX, One Touch Ultra, InDuo, Sof-Tact*.

You should tell patients using these meters that alternate sites are okay only for ROUTINE testing of fasting and preprandial glucose levels. Then advise them to stick with fingertips when testing within 2 hours AFTER meals...exercise...or insulin dose.

Don't forget to recommend fingertip testing when checking for hypoglycemia.

[Diabetes Care 2001;24:1303-4.](#)

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Item #3

Night-Light May Prevent Diabetic Eye Damage

An illuminating theory may lead to a simple way to prevent a common cause of blindness among diabetics.

Researchers from the U.K. suggest that a condition known as diabetic retinopathy might be avoided by sleeping with the lights on. But they add that more studies are needed to prove that their bright idea can actually save sight.

New research supports the theory that hours of complete darkness increases retinal damage from diabetes--and that sleeping with some lights on could help counter the effect.

However, it's too soon to recommend diabetics keep the bedroom lights on every night to cut their risk of the eye damage--known as diabetic retinopathy. For one, chronic exposure to light during sleep could have some unforeseen effects.

Diabetic retinopathy is a common complication of diabetes that can lead to blindness. It is caused by changes in retinal blood vessels.

Drasdo, of Cardiff University in Wales, explained that some researchers believe that oxygen deprivation in the retina during dark hours promotes diabetic retinopathy.

In their study, Drasdo and his colleagues looked at seven adults with Type 2 diabetes but no apparent retinopathy, and compared them with eight non-diabetics. They found that activity in tissue near the surface of the retina was reduced after being in the dark, but was bumped up with exposure to oxygen. Healthy individuals showed no such changes.

Professor Neville Drasdo and colleagues offer direct evidence that diabetic retinopathy is caused by a lack of oxygen, occurring within the inner layers of the retina during darkness. Previous research has shown that oxygen levels in the retina of diabetics fall as the eyes adapt to dark.

The researchers tested the effect of breathing in 100% oxygen -- normal air is 21% oxygen -- on the eyes of seven people with type 2 diabetes and eight people without diabetes. The diabetics

had the disease for an average of about seven years. None of the patients had been diagnosed with retinopathy, but they all had evidence of too little oxygen within the retina during darkness.

With high oxygen treatment, the eyes of the diabetic patients returned to normal.

Drasdo stated that the findings expand on earlier research indicating a link between a lack of oxygen and diabetic retinopathy. He also suggests that it's likely that the lack of oxygen is what is causing the increase in blood vessels in the eye -- thus the retinopathy.

The researchers suggest that sleeping with the lights on could prevent retinopathy in diabetics because light through closed eyelids suppresses the eyes' ability to adapt to the dark. Drasdo says the nighttime light therapy would have to be permanent because it takes up to two decades for retinopathy to develop in diabetics. And he adds that the long-term consequences of this preventive treatment are not known.

The findings are published in the June 29th issue of *The Lancet*.

However, he added, more research is needed before diabetics start taking on a permanent, "full night-time illumination" regimen.

Drasdo also noted that sticking with a diabetes management plan aimed at controlling blood sugar levels can help ward off diabetic retinopathy. *SOURCE: The Lancet 2002;359:2251-2253.*

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Item #4

Simvastatin Lowers CV Risk and Mortality Regardless of Levels

This information could save about 50,000 lives a year — that is, a thousand each week."

Simvastatin, but not antioxidants, lowered cardiovascular (CV) risk and mortality in the Heart Protection Study (HPS), that, according to two reports in the July 6 issue of *The Lancet*. The benefit of simvastatin was proportional to the CV risk, not to the baseline cholesterol concentration.

"HPS shows unequivocally that statins can produce substantial benefit in a very much wider range of high-risk people than had been previously thought," investigator Rory Collins, from the University of Oxford in England, says in a news release. "These new findings are relevant to the treatment of some hundreds of millions of people worldwide."

The HPS randomized 20,536 adults in the United Kingdom to receive daily placebo, simvastatin 40 mg, or antioxidant supplementation with 600 mg vitamin E, 250 mg vitamin C, and 20 mg beta-carotene for five years. Subjects were 40 to 80 years of age and had coronary artery disease, other occlusive arterial disease, or diabetes.

Death from all causes was 12.9% for patients given simvastatin, 14.7% for patients given placebo, and 14.1% for patients given antioxidants ($P=.0003$ for simvastatin vs. placebo). The reduced mortality for patients receiving simvastatin was primarily related to an 18% relative reduction in the coronary death rate from 6.9% (707 deaths) for patients receiving placebo to 5.7% (587 deaths) to patients receiving simvastatin ($P=.0006$).

"If, as a result [of these findings], an extra 10 million high-risk people were to go onto statin treatment, this would save about 50,000 lives a year — that is, a thousand each week," Collins says. "In addition, this would prevent similar numbers of people from suffering non-fatal heart attack or stroke."

Relative reductions in patients receiving simvastatin were about 25% for nonfatal myocardial infarction or coronary death, for nonfatal or fatal stroke, and for coronary or noncoronary revascularization. Simvastatin was well tolerated with no major adverse effects, although the annual excess risk of myopathy was 0.01%. Its benefits did not depend on baseline lipid levels and were synergistic with those of other cardioprotective treatments including aspirin, beta-blockers, and angiotensin-converting enzyme inhibitors.

Antioxidant supplementation was not linked to any significant reductions in the five-year risk of myocardial infarction, stroke, cancer or other major outcomes.

"These findings should tear up the rule-book on statin prescribing," says Richard Horton, editor of *The Lancet*. "They are the most important and far-reaching results for the treatment and prevention of heart disease and stroke that we have seen in a generation. They should result in a dramatic change in clinical practice around the world. Previously there has been concern that statins have been used too much; after the results of HPS have been published there should be concern that they may not be used enough in the future." *Merck & Co. helped support this study. Lancet. 2002;360:7-22, 23-33*

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FACT:

Statins may cause peripheral neuropathy?

Researchers are now suspecting that. But, keep this in perspective. The risk of neuropathy from a statin is probably less than the risk of myopathy.

Researchers speculate that statins might cause neuropathy by inhibiting cholesterol synthesis and affecting nerve cell membranes. Statins might also affect nerve function by inhibiting co-enzyme Q10 which plays a role in neuron energy utilization. You don't want to let the fear of this potential side effect scare patients from using a statin. Statin's beneficial effects far outweigh the small risk of neuropathy. The data suggest that there is a strong association between statin use and neuropathy. At this point the incidence appears low. It is probably an under-recognized problem since it is not common, and clinicians may not look for it. However, it seems prudent to watch for sensory or motor changes in patients on long-term statins.

When you see a patient with unexplained neuropathy...pain, tingling, numbness, etc...check to see if they're on a statin and explain that the neuropathy is often reversible when the statin is discontinued...but it can take 3 to 12 months. [South Med J 1998;91\(7\):667-8.](#)

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Item #5

ADA: Post-Challenge Glucose Levels Correlated Directly to Cardiovascular Outcomes

Treatment of post-challenge glucose (PCG) levels may reduce cardiovascular disease and mortality associated with type 2 diabetes.

Hyperglycemia has been shown in prior research to add significantly to adverse outcomes associated with type 2 diabetes. Recent studies have indicated that higher than normal PCG may be an independent factor associated with morbidity and mortality.

The investigators undertook a review of published data to evaluate the association of elevated PCG levels with cardiovascular outcomes and all-cause mortality in type 2 diabetes and to establish the strength of this association in comparison to fasting blood glucose (FPG) levels.

They conducted a MEDLINE search of English-language articles published from 1980-2001, supplemented by a search of bibliographies and references supplied by content experts. They used specific criteria to find articles addressing the association of PCG and cardiovascular

morbidity/mortality and/or all-cause mortality.

They found 4,242 pertinent references in the literature. They finally accepted 14 studies for the review, 12 prospective and 2 cross-sectional.

Twelve of the studies (85 percent) documented a positive association between elevated PCG and cardiovascular morbidity/mortality and/or all-cause mortality in type 2 diabetes.

Seven studies provided direct comparison data on FPG and PCG levels. Five studies (71 percent) indicate that PCG is a better predictor of cardiovascular morbidity/mortality and/or all-cause mortality than FPG. The other 2 studies indicated no association between either FPG or PCG and morbidity or mortality.

"Fasting plasma glucose is an important screening tool in diabetes," said investigator Myriam Bernal, research associate at ZYNX Health in Los Angeles. "We also found that there is powerful evidence in the wider medical literature to support the belief that post challenge glucose, if it's higher, is directly correlated with cardiovascular outcomes. It should be targeted by physicians." *The study was supported by a grant from Novartis Pharmaceuticals.*

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

ADA: Metformin Decreases Cardiovascular Events in Diabetics

Metformin monotherapy results in fewer fatal and non-fatal cardiovascular (CV) events compared to sulfonylurea monotherapy in new users of these agents.

Said, investigators said at the 62nd Scientific Sessions of the American Diabetes Association (ADA).

Dr. Jeffrey A. Johnson with the University of Alberta in Edmonton, Canada, and colleagues used Databases of Saskatchewan Health to identify new users of oral antidiabetic agents, described as those with prescriptions for a sulfonylurea agent or metformin in 1991 to 1996 who had not used these agents in the prior 12 months.

The researchers defined CV events as any hospitalization or death during the follow-up period, which extended up to nine years. Causes of death or hospitalization were identified based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). They used multivariate logistic regression analysis to assess the differences between drug cohorts, after adjusting for potential confounding variables

The total study sample comprised 8,866 new users of oral antidiabetic agents with at least one

year of drug exposure and no insulin use, who were followed for an average of 5.3 years.

A CV-related event occurred in 1,216 of 3,034 (40.1 percent) subjects on sulfonylurea monotherapy, in 351 of 1,150 (30.5 percent) on metformin monotherapy, and in 1,733 of 4,682 (37.0 percent) on combination therapy.

Deaths due to CV causes were significantly lower in patients treated with metformin alone or in combination compared to the sulfonylurea monotherapy cohort.

The number of non-fatal hospital admissions for CV-related diagnoses was significantly lower in the metformin monotherapy cohort but the combination therapy cohort was not significantly different compared to the sulfonylurea monotherapy group.

The adjusted odds ratios for a CV-related event were 0.79 and 0.98 for metformin and combination therapy, respectively, compared to sulfonylurea monotherapy. .

Dr. Johnson cautioned that the study is limited by the fact that information for this analysis was taken from administrative databases and thus does not contain clinical data.

Another possible limitation involves the study's retrospective design. "As with any study using retrospective data, the observations depend on the accuracy and completeness of the records," Dr. Johnson said. "However, the Saskatchewan Health databases are recognized internationally for their accuracy and comprehensiveness of health care data for all residents of Saskatchewan."

Overall, observations from this cohort of new users of oral antidiabetic agents indicate that metformin is safe as either monotherapy or in combination with sulfonylureas, Dr. Johnson said. In addition, the use of metformin may be associated with reduced CV mortality in people with type 2 diabetes.

62nd *Scientific Sessions of the American Diabetes Association (ADA)*.

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Item 7

Orlistat Helpful for Obese Type 2 Diabetics

But lifestyle modification still needs to be the cornerstone of therapy.

Orlistat (Xenical) is beneficial for obese type 2 diabetic patients, according to results of a randomized, placebo-controlled trial reported in the July issue of *Diabetes Care*. However, the reduction in HbA_{1c} was less than 0.5%, and lifestyle modification, diet, and exercise still need to be the cornerstone of therapy. Despite significantly more adverse effects in the orlistat group, the withdrawal rate was higher in the placebo group, suggesting a perceived benefit from being on the medication.

"The results of this study show that the addition of orlistat plus a reduced calorie diet to existing metformin therapy can benefit patients by helping lower body weight and serum glucose levels," lead author John M. Miles, MD, from the Mayo Clinic in Rochester, Minnesota, says in a news release. "The combination of Xenical and metformin had a positive impact on many cardiovascular risk factors, which are among the most common and potentially serious risks associated with type 2 diabetes."

This study enrolled 516 patients at 34 centers in the U.S. and six centers in Canada who were receiving metformin, 1,000 to 2,550 mg/day for at least six weeks, or a stable dose of sulfonylureas for 12 weeks before study entry in addition to metformin. Subjects were randomized

to receive either orlistat, 120 mg three times daily, or placebo in addition to a reduced-calorie diet. Of the original study group, 311 patients completed one year of treatment.

After one year of treatment, twice as many patients in the orlistat-treated group (39.0%) as in the control group (15.7%) lost 5% of baseline body weight, and significantly more patients in the orlistat-treated group (14.1%) than controls (3.9%) lost 10% of baseline body weight.

"Patients in this study treated with orlistat plus diet also had a reduced need for one or more diabetes medications," Miles says.

Twice as many patients in the orlistat-treated group (17.1%) as in the control group (8.2%) either reduced or discontinued one or more diabetes medications, and 21.7% of patients in the control group but only 12.2% of orlistat-treated patients required either additional or increased dosages of diabetes medications.

HbA_{1c} decreased by 0.5% or 1.0% in significantly more patients treated with orlistat than in control patients, and mean decrease in systolic blood pressure was also greater in the orlistat-treated group ($P<.05$). Beneficial effects on lipids in orlistat-treated patients compared with control patients included improvements in total cholesterol (-4.1% vs. +2.6%), low-density lipoprotein (LDL) cholesterol (-2.8% vs. +3.9%) and LDL/high-density lipoprotein (HDL) cholesterol (-0.60 vs. -0.46); $P<.05$ for all.

Adverse event profiles were similar in the two groups, except for gastrointestinal symptoms, which were more common with orlistat (83% vs. 62%; $P<.05$). Because the overall rate of study withdrawal was higher in the control group than in the orlistat-treated group (44% vs. 35%; $P<.05$), gastrointestinal events do not generally seem to cause discontinuation of orlistat therapy.

"The weight loss achieved in the current study was associated with significant improvements in glycemic control and other cardiovascular risk factors," the authors write. "Although lifestyle changes to decrease energy intake and increase physical activity should remain the cornerstone of weight loss therapy, data from the present study suggest that anti-obesity medications can enhance weight loss and provide benefits in the management of patients with type 2 diabetes." *Hoffmann-La Roche Inc. supported this study. Diabetes Care. 2002;25(7):000-000*

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Item 8

Diabetics Must Control Hypertension

ABC's of controlling hypertension in people with diabetes.

Normalizing blood pressure is critical, especially in the diabetic patient. Unfortunately, many people don't realize they have hypertension until a medical catastrophe occurs, such as a major heart attack.

When treating a diabetic, physicians may prescribe one of two types of drugs: either an ACE inhibitor or an AR blocker.

An ACE inhibitor, such as Accupril, Altace, Monopril, Zestril, Prinivil, Vasotec, Lotensin or Capoten, may be prescribed for you as the first therapeutic weapon to combat vascular disease.

Of these drugs, Accupril and Altace are preferred by some doctors because of their beneficial effect on the kidneys of a diabetic.

An AR blocker may be used instead. These include Avapro, Diovan, Atacand, Cozaar and

Micardis.

These are used rather than ACE inhibitors because they stay focused on specific blood vessels, so they cause fewer side effects elsewhere in the body.

In resistant patients, other medications such as calcium-channel blockers or water pills may work. In fact, water pills (diuretics) are quite popular and sometimes used as first-line agents. It just depends. Diuretics reduce the pressure in your vascular "pipes" by causing you to urinate excessive fluid. Don't take them at night or you'll spend more time in the bathroom than in the bedroom.

Compliance is important. If you have a good health-care team and a regimen that is working, don't be distracted. Stick to it and monitor your blood pressure frequently.

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Item 9

UK Diabetes Targets Too Aggressive?

New targets set for diabetes treatment in Britain's National Health Service may be too strict to be practical, an article in Friday's British Medical Journal warns.

Many patients are unlikely to achieve the guidelines, laid out in a new National Service Framework (NSF), and meeting them will require some patients to take an array of different drugs, according to Dr. Peter Winocour of Queen Elizabeth II Hospital in Hertfordshire, England.

Targets for managing blood sugar, cholesterol, blood pressure and anticlotting medication have only been attainable in 50% to 70% of participants in well-controlled studies, meaning that even fewer could be expected to achieve them in routine practice, Winocour said.

And in trying to achieve these guidelines, as well as others, it is likely going to be necessary to give patients many different drugs, he added.

Up to 10% of patients could need to take two or three drugs to lower blood pressure, including insulin; at least three blood pressure-lowering drugs; two drugs to cut cholesterol; and aspirin, he explained. And many may need additional drugs for heart disease or other types of chronic illness.

"It is difficult to see how we can realistically expect patients to comply for long with such a draconian regimen requiring so many separate drugs," Winocour said.

Individually tailored targets that take into account factors such as estimated duration of diabetes, obesity, age and lifestyle would be preferable, he argues.

Dr. Mike Pringle, of the University of Nottingham and co-chair of the diabetes National Service Framework, argued that the framework's chief concern was to help patients manage their disease.

"Many patients are not receiving sufficient information and education about their diabetes and are not put in a position to make informed choices about their lifestyle and diet and exercise, and about treatment options," he said.

"The diabetes NSF is about systems of care and the most important standard is standard number 3, which is about empowering patients to make good decisions about how they will look after their own diabetes," he told Reuters Health.

He said the way in which the diabetes NSF is implemented was crucial. "It must recognize patients' choice; it must recognize the natural variations in performance that occur; and it must

identify and reward good practice in supporting patients to make informed choices about their care."

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Item 10

Americans Getting Fatter Faster

Overall, 26 percent of U.S. men and 28 percent of U.S. women already are obese by about age 36, according to a new University of North Carolina at Chapel Hill study of adult weight gain among different ethnic groups, races and sexes.

For still-unknown reasons, black women become obese more than twice as fast as white women, and the rate for Hispanic women is about midway between the two. U.S. men of different races and ethnic groups also put on pounds at varying rates.

"We found Hispanic men became obese 2.5 times faster than U.S. men of European ancestry," said Dr. Kathleen M. McTigue, a Robert Wood Johnson clinical scholar at the UNC School of Medicine. "We saw no difference in the rate of obesity development between black and non-Hispanic white men until after age 28 when black men in this country became obese 2.2 times more rapidly than white men."

A report on the new study appears in the June 18 issue of *Annals of Internal Medicine*, a professional journal. Besides McTigue, authors are Drs. Joanne M. Garrett, associate professor of medicine; and Barry M. Popkin, professor of nutrition of the UNC School of Public Health.

Researchers analyzed information over time on 9,179 people born between 1957 and 1964 and enrolled in the National Longitudinal Survey of Youth beginning in 1979.

More than 80 percent of those who were obese by about age 36 did not become obese until after ages 20 to 22, although many began gaining excess weight earlier, McTigue said.

"Based on their gender, ethnicity and body mass index at ages 20 to 22, we could fairly accurately predict who would be obese at ages 35 to 37," she said.

Overall, the prevalence of obesity in U.S. adults between ages 20 and 74 doubled during the past 40 years, from 13 percent to 27 percent of the population, McTigue said. Sixty-one percent of U.S. adults now are either obese or overweight.

"Obesity is important for health, and, as health-care professionals, we need to pay more attention to it," she said. "In the group we studied, there was substantial obesity at ages much younger than most of obesity's health complications tend to occur. Early intervention with such people has the potential to prevent significant illness and should not be overlooked."

Equally important, the physician said, is preventing obesity in the first place and focusing more on children and people just entering adulthood who are only slightly or moderately overweight.

"Since African-American and Hispanic young adults are at particular risk for obesity, we also need to better understand ethnic differences in weight development so that we can design effective interventions," she said.

Obesity receives increasing attention nowadays because it has become so prevalent in U.S. society, McTigue said. The condition is an important risk factor for four of the six leading causes of death in this country -- heart disease, certain cancers, stroke, and diabetes. It also contributes to less deadly but still troublesome osteoarthritis, obstructive sleep apnea. and diminished mobility.

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Item 11

New Test Predicts Which Type 2's Will Become Type 1's Within 5 Years

Islet antibody testing could prevent complications by initiating insulin treatment much earlier.

The results of a 12-year prospective follow-up study show a strong relationship between the presence of islet antibodies at diagnosis of adult-onset diabetes and future beta-cell function.

in the June issue of the journal *Diabetes*, Dr. Henrik Borg from Lund University, Malmo and Swedish colleagues write, that the study argues for repeated islet antibody testing beginning at diagnosis in patients with adult-onset diabetes,

They previously found that a group of adult diabetics with islet cell antibodies had high levels of glutamic acid decarboxylase 65 antibodies (GADA) and/or IA-2 antibodies at diagnosis, and more severe beta-cell dysfunction 5 years after diagnosis, than diabetics with lower GADA levels.

Dr. Borg's group now reports that, in 107 patients, the vast majority of those with GADA and/or islet cell antibodies at diabetes diagnosis developed complete beta-cell failure (undetectable fasting P-C-peptide) after 12 years, regardless of age.

"Patients with isolated GADA positivity had some preserved function 5 years after diagnosis of diabetes; however, most of them (80%) had developed beta-cell failure 12 years after diagnosis," the authors note.

By contrast, fasting P-C-peptide levels remained unchanged over the 12 years in antibody-negative patients indicating preservation of beta-cell function.

Only rarely did antibodies develop after diagnosis, according to Dr. Borg's team. They found that islet cell antibodies, but not GADA or IA-2 antibodies, which developed after diagnosis in roughly 5% of the originally islet cell antibody-negative, mostly overweight patients, predicted a decline in beta-cell function.

Dr. Borg's group concludes the findings strongly support islet antibody testing at diagnosis in most patients. Noting that such testing is costly, they suggest the following strategy: a primary screen for GADA followed by a second test for IA-2 antibodies in GADA-positive patients with low GADA levels "to improve the prediction of a fast progression to beta-cell failure." *Diabetes* 2002;51:1754-1762.

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Item 12

Alcohol Unlikely to Cut Diabetes Risk

A new study has found that alcohol does not appear to prevent the development of type 2 diabetes.

Although several recent studies have suggested that light to moderate drinking might protect against diabetes,

In the current investigation, lead author Dr. Goya Wannamethee of Royal Free and University College Medical School, London, UK and colleagues studied 5,221 healthy British men between the ages of 40 and 59 years. After 17 years of follow-up, 198 of the men developed type 2 diabetes.

In the study, moderate alcohol consumption was defined as consuming 16 to 42 drinks per week. The investigators report that the heaviest drinkers--more than 42 drinks per week--had the highest risk of developing type 2 diabetes, which they attributed to the additional calories consumed and resulting overweight from drinking so much alcohol.

Co-author Dr. Gerry Shaper said that "these drinkers consumed more than 42 units of alcohol per week, drinking 6 or more units a day most days in the week.

Moderate drinkers appeared to carry the lowest risk of developing type 2 diabetes, the researchers report in the June issue of the Journal of Epidemiology and Community Health.

Shaper stated that "there appears to be no justification for encouraging light or occasional drinkers to increase their intake or for nondrinkers to take up drinking." "There is no sound rationale for alcohol preventing the development of diabetes," Shaper added. "Indeed, alcohol lowers levels of blood insulin."

Moderate alcohol consumption as defined in the present study may be considered fairly heavy alcohol consumption by American standards, Shaper pointed out.

"Regular moderate drinking is certainly likely to be associated with more untoward effects than overall benefits, and is certainly not a desirable public health recommendation," Shaper concluded. *SOURCE: Journal of Epidemiology and Community Health 2002;56:542-548.*

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[BMJ 1990;300:972-5.](#), [Lancet 2002;359:1550-4.](#)

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Item #13

ADA: Nateglinide Effectively Lowers Hemoglobin A1c in Type 2 Diabetics

It is good for patients in the real world who occasionally overeat

The addition of nateglinide (Starlix; Novartis) to metformin controls postprandial surges in blood glucose in patients with poorly controlled type 2 diabetes, researchers reported at the 62nd scientific sessions of the American Diabetes Association.

Dr. Kenneth S. Hershon of Albert Einstein College of Medicine in the Bronx, New York, reported results of a study of 141 patients with poorly controlled disease. Of these, 58 had been maintained on diet alone and 83 were taking metformin. Nateglinide was added to the regimens for a 12-week study period.

Dr. Hershon reported that 78% of patients in the diet-maintained group and 70% of the metformin group responded well to the addition of the rapid-onset insulinotropic agent, with a drop of postprandial hemoglobin a1c of 0.5%.

About 10% of the diet-maintained patients and 5% of the metformin patients experienced mild symptoms of hypoglycemia. Plasma glucose levels below 60 mg/dL were confirmed in 2.9% and 1.9%, respectively.

"Nateglinide works very quickly--within 5 minutes--and the effects last about 2 hours. "This drug takes away the effects of the sulfonylureas, which cause a constant stimulation of insulin. This gives a bolus and then goes away."

"Although this is not how this trial is set up and it's not FDA-approved for this, you can use nateglinide prn. It is good for patients in the real world who occasionally overeat, such as when they go out to eat. They can take this with meals [to prevent postprandial hyperglycemia]," Dr. Hershon commented. Because of its rapid onset of action and short bioavailability, "you can use it how you see fit."

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Item #14

Early Statin Therapy After Coronary Event Does Not Appear to Improve Outcome

Physicians should use caution in starting a statin early after an acute coronary event in the absence of cholesterol measures or in patients who do not meet current treatment guidelines.

Although previous reports have suggested that starting patients on statins soon after an acute coronary event can improve clinical outcomes, findings from a new report in the June 19th issue of the Journal of the American Medical Association suggest otherwise.

"In contrast to previous reports, we found no association of starting statins early (within 1 to 3 days) after an acute coronary event with better clinical outcomes (death or the composite of death or MI) at 90 days or 1 year," said lead author Dr. L. Kristin Newb.

"In addition, we observed that if LDL cholesterol levels were below current treatment guidelines (<130 mg/dL), starting a statin early after an acute event may be associated with worse outcomes, whereas at higher levels there may be benefit," Dr. Newby, from Duke Clinical Research Institute, Durham, North Carolina, said.

Dr. Newby and colleagues looked at data from the SYMPHONY (Sibrafiban versus Aspirin to Yield Maximum Protection from Ischemic Heart Events Post-acute Coronary Syndromes) and 2nd SYMPHONY trials.

In these trials, 12,365 patients were randomized to statin therapy within 1 to 3 days of an acute coronary event or to no statin therapy. The researchers looked at a combined endpoint of the incidence of death; death or myocardial infarction (MI); or severe recurrent ischemia at 90 days and at 1 year.

At 90 days, there was no apparent benefit from statin therapy compared with no therapy, for death, MI or severe recurrent ischemia, the researchers found.

After propensity and covariate adjustment, there was no benefit found from early statin therapy at 90 days or 1 year compared with no statin therapy, the researchers note. The adjusted hazard ratio for death at 90 days was 1.08, for death or MI 1.08 and for death, MI or severe recurrent ischemia, 1.15. For 1-year mortality the adjusted hazard ratio was 0.99, they add.

Dr. Newby believes that "we need the results of randomized clinical trials of early statin initiation that are adequately powered for the hard endpoints of death and death or MI to satisfactorily address the question of the benefits and risks of early statin initiation and to guide practice."

"Until such evidence is available," Dr. Newby said, "physicians should use caution in starting a statin early after an acute coronary event in the absence of cholesterol measures or in patients who do not meet current treatment guidelines."

"The observations made within the SYMPHONY cohorts are interesting and noteworthy," Drs. Karin B. Michels and Eugene Braunwald from Brigham and Women's Hospital, Boston, comment in a journal editorial.

"The analyses by Newby et al. indicate the presence of confounding by indication in the observational data and underscore the need for well-conducted large randomized clinical trials on the benefits of early statin initiation," they add. *JAMA 2002;287:3087-3095,3130-3132.*

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FACT

Even in the absence of diabetes, even modest elevations in HbA1c, increase the risk of cardiovascular disease. Those in the highest quartile of A1c levels had almost three times the risk compared to those in the lowest group. Hoorn Study (Framingham Study of the Netherlands ADA#258)

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Item #15

Effectiveness of a Physician - Patient Education Program in Diabetes Management

Study demonstrates that physician and patient education from a Diabetes Health Educator is effective in the private practice

Management of diabetic patients is often complicated by factors such as cost, patient compliance, and physician education. This study was conducted to determine if an external Diabetes Health Educator (DHE) within a private practice could improve the health outcomes of diabetics within the practice.

A DHE working 24 hours per week using chart reviews to identify patients and perform physician-patient education programs. Variables including; hemoglobin (HbA1c), creatinine, blood pressure

(BP), lipids, micro-albumin, Body Mass Index (BMI) and compliance with other diabetic care indicators were measured at baseline, 6 and 12 months. The practice contained 476 diabetics, and were divided into Education (n=305) and Non-education (n=171) groups. Non-Equivalent Control group, significance testing included repeated measures Analysis of Variance or Analysis of Covariance (ANOVA and ANCOVA) and between group t-tests. McNemar Change Tests (MCT) were performed on stratified risk and non-risk groupings using cut-points for clinical values.

The results showed that there were no demographic differences between groups for gender, ethnicity or age (all $p > 0.30$). Baseline comparisons indicated no significant differences BMI, systolic or diastolic BP, cholesterol, HDL, LDL or, triglycerides (all $p > 0.10$). There was a baseline difference in HbA1c ($p < 0.001$) between Education and Non-education groups (8.13 ± 1.96 and 7.09 ± 1.52 , respectively, mean \pm sd). ANOVA and ANCOVA (for HbA1c) indicated significant improvement in the education group for HbA1c ($p < 0.001$), HDL ($p = 0.050$), LDL ($p < 0.001$), cholesterol ($p = 0.001$) and Diastolic BP ($p = 0.002$). MCT revealed significant that risk factor reduction for HbA1c, HDL and DBP occurred in the first six months, while cholesterol and LDL effects occurred at the end of the first year. Non-education group showed a significant improvement for HDL ($p = 0.028$) and Diastolic BP ($p = 0.043$), however MCT indicated that these effects were not sustained, nor did they improve patient condition below risk factor range.

This study demonstrates that physician and patient education from a DHE is effective in the private practice management of the diabetic population. This model of care allows for determination of program effectiveness and reports on the timing of treatment effects, allowing clinicians to know when treatment effects will occur. *ENDO 2002 [P3-674]*

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Item #16

Risk for Type 1 Diabetes Greater in Overweight Children

A disturbing rise in the incidence of overweight children has occurred along with an increase of type 1 diabetes.

In recent decades, the incidence of type 1 diabetes (DM1) in developed countries has increased for children under age 15 in general, but mostly in younger children, as reported by EURODIAB. Concurrently, a disturbing rise in the incidence of overweight children has occurred.

We therefore searched computer and clinic records of all pediatric patients diagnosed with DM1 between 1.1.98 and 12.31.01, and examined body mass index (BMI) at diagnosis (Dx), and by <3 months post-diagnosis (P-Dx) reflecting body habitus prior to any weight loss. BMI Z-scores (BMIZ) for age >2 years, were calculated per CDC 2000 data. We included patients from physicians who admit all of their newly diagnosed diabetics to Children's Hospital of San Diego, and all DM1 patients cared for at Kaiser Permanente in San Diego. Patients from physicians who primarily admit younger or sicker patients with DM1 were excluded, as were non-resident patients.

Also, we excluded obese patients initially treated as type 2, based on c-peptide, and clinical phenotype, who had DM1 antibodies, and later became insulinopenic. Of 289 patients <15 years old (yr) in age groups 0-4, 5-9, and 10-14, there were 26.0%, 35.3%, and 38.7%, respectively. Distribution by gender was 29.9%, 34.3%, and 35.8% in 137 girls, and 22.4%, 36.2%, and 41.4% in 152 boys, in the respective age groups. Mean (SD)[%] BMIZ at Dx and P-Dx were respectively -0.61 (1.6)[27%] and 1.09 (0.78)[86%] for ages 2-4, 0.03 (1.4)[51%] and 0.89 (1.0)[82%] for ages 5-9, -0.3 (1.2)[38%] and 0.64 (0.8)[74%] for ages 10-14. Height Z-score was about 0.25 for the 3 age groups [60%]. Mean weight gain was 15.2%, 12.5%, and 14.9%, respectively. Of all 321 pediatric patients <19 yr [1.2:1 M:F], 62.1% were Caucasian, 23.6% Hispanic, 3.4% African American, 2.5% Other, 0.9% Asian, 7.5% mixed ethnicities. BMIZ post-Dx was 1.09 in Hispanics and 0.7 in Caucasians ($p < 0.05$). Mean weight for height P-Dx was at 80% for patients <2yr. Mean BMIZ are high P-Dx compared to expected BMIZ=0 ($p < 0.0001$) in ages 2 to <15 yr, even though

P-Dx BMI Z-scores may be underestimated, since in some cases we only had P-Dx data at <10 days. BMIZ correlated negatively with age of Dx in ages 2 to <15 yr, with $r = -0.22$ (spearman, $p < 0.001$), and was significantly higher than BMIZ in 10-14 yr ($p = 0.01$).

Conclusions: Age of Dx of DM1 no longer shows a prominent peak after age 10.

Overweight may increase the risk of developing type 1 diabetes, especially in younger children. Endo 2002 [P2-357] The Changing Epidemiology of Childhood Type 1 Diabetes and the Obesity Epidemic

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Did You Know:

CVD is a major complication and the leading cause of premature death among people with diabetes---at least 65 percent of people with diabetes die from heart disease or stroke. Middle-aged people with type 2 diabetes have the same high risk for heart attack as people without diabetes who already have had a heart attack. *CDC Diabetes Surveillance Report 1999*

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Item #17

Anti-Inflammatory Effect of Rosiglitazone in Obese Diabetic Patients

Rosiglitazone exerts an anti-inflammatory effect at the cellular and molecular level.

We have recently demonstrated a potent anti-inflammatory effect of rosiglitazone (RSG) in obese non-diabetic subjects. We have now investigated the anti-inflammatory action in 11 obese diabetes patients who were given RSG 4 mg/day for 6 weeks. Fasting blood samples were obtained at 0, 1, 2, 4, 6 and 12 weeks.

Blood glucose concentration decreased significantly following RSG treatment, from a basal concentration of 157 ± 16 mg/dL to 127 ± 9 mg/dL at week 6 ($p < 0.05$). Insulin concentration also significantly decreased from a basal concentration of 32.6 ± 4.6 μ U/mL to 16.1 ± 2.2 μ U/mL at week 6 ($p < 0.05$). NF- κ B binding activity in MNC nuclear extract fell significantly ($p < 0.02$). This inhibition was significant by week 1 ($77 \pm 13\%$ of the basal level) and continued up to week 6 ($66 \pm 10.6\%$ of basal). There was a significant fall in ROS generation by MNC ($p < 0.05$), decreasing to $94 \pm 6\%$ by week 1 and $66 \pm 10\%$ at week 6. RSG treatment reduced plasma MCP-1 (75% of the basal level; $p < 0.05$) and CRP (70% of basal; $p < 0.05$). FMD at baseline was $3.4 \pm 1.2\%$ and this increased significantly to $8.6 \pm 1.9\%$ ($p < 0.05$) at week 6. Nitroglycerin-induced endothelium independent vasodilatation also increased from $11.8 \pm 1.4\%$ at baseline to $16.7 \pm 2.3\%$ at week 6 ($p < 0.05$).

We conclude that RSG exerts a profound ROS suppressive and anti-inflammatory effect as reflected at the cellular and molecular level, and in plasma. RSG also improves vascular reactivity. These observations may have implications for atherogenesis in the long-term in patients treated with RSG.

Endo 2002 [P2-376]

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Item #18

Special Cell Prevents Diabetes

In studies they have found a special type of dendritic cell that kills the T cells and appears to prevent diabetes in mice.

In preclinical studies, a special type of dendritic cell that promotes the swift death of T cells appears to prevent diabetes in mice. A genetically engineered version of these dendritic cells may serve as a potential therapy for diabetics.

In diabetes, the T cells of the patient's own immune system invade and destroy the body's insulin-producing cells, the islets of Langerhans. Usually, T cells do not attack a foreign antigen unless dendritic cells first identify and present the antigen to the T cells.

Unlike most dendritic cells, which originate in bone marrow, the special dendritic cell, B220+, originates in the liver. It causes T cells to die by apoptosis instead of causing them to proliferate.

Researchers at the University of Pittsburgh (PA, USA) treated diabetic-prone laboratory mice with B220+ dendritic cells, while a group of control mice received no treatment. The untreated mice all developed diabetes within 20 weeks. In contrast, those mice treated with the B220+ dendritic cells had still not developed diabetes.

"These results are very exciting, but perhaps it may not be so feasible to develop a therapy for humans that involve cells obtained from the liver," said Lina Lu, M.D., research associate professor of surgery at the Thomas E. Starzl Transplantation Institute at the university. "So, in other studies we are using a gene therapy approach to see if we can give bone marrow-derived dendritic cells the same qualities as the B220+DC." Thus far, the results of those studies indicate the modified dendritic cell can significantly delay the onset of diabetes in diabetes-prone mice

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Did You Know?

If we could get 90% of patients with type 2 diabetes to take aspirin, we would save more than 8,000 lives and prevent more than 11,000 MI's a year

See Below: Item #19

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Item #19

Increasing Aspirin Use to 90% Could Save over 8,000 Lives a Year!

Increasing daily aspirin use to 90% of those with Type 2 diabetes could prevent an additional 11,000 MIs and potentially save >8,000 lives.

Despite being a safe, effective therapy for lowering cardiovascular risk, only 20% of diabetic patients were using aspirin in the early 1990s. This study examines current physician practices and the use of aspirin therapy by individuals with diabetes.

A random sample of diabetic patients receiving care in the Department of Veterans Affairs health care system were surveyed during January-March 2000. The association between aspirin counseling, aspirin use, and reported coronary vascular disease (CVD) and classical CVD risk factors were examined using logistic regression. The effect of increasing aspirin use on risk of myocardial infarction (MI) and cardiovascular mortality was demonstrated by simulation.

Results of the study showed that seventy-one percent of respondents reported being counseled about aspirin use, and 66% were taking daily aspirin. Individuals with known CVD were more likely to be counseled (odds ratio [OR] 4.9, 95% CI 2.9–8.1) and to use aspirin (2.1, 1.2–3.7). The factor most strongly associated with aspirin use was having been counseled about aspirin therapy by a doctor. We estimate that for this population, increasing daily aspirin use to 90% could prevent an additional 11,000 MIs and potentially save >8,000 lives.

It was concluded from the study that compared with previous reports, a substantial proportion of these diabetic patients have been counseled about and use aspirin. Most clinicians recognize aspirin as an important treatment for patients with preexisting coronary disease. However, since diabetes is now considered a CVD equivalent, it is imperative that clinicians include counseling

about aspirin therapy as a care priority for all their diabetic patients, as this simple intervention may prevent many cardiovascular events and deaths. *Diabetes Care, 2002 25/6 (965-970)*

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Item #20

Advanced Glycation End Products Associated with Endothelial Dysfunction in Type 2 Diabetes

Can treating AGEs lead to a reduction of endothelial dysfunction?

Data from experimental studies have suggested that the increased formation of advanced glycation end products (AGEs) is one of the causes of endothelial dysfunction in diabetes.

This study was performed to investigate whether changes in endothelium-dependent vasodilation, a marker of endothelial function, were related to serum AGEs concentrations in patients with type 2 diabetes.

For this study, 170 patients with type 2 diabetes and 83 healthy nondiabetic control subjects of similar age were recruited. Serum AGEs were assayed by competitive enzyme-linked immunosorbent assay. Endothelium-dependent and -independent vasodilation of the brachial artery was measured by high-resolution vascular ultrasound. RESULTS—Serum AGEs were increased in diabetic patients compared with control subjects (4.6 ± 0.7 vs. 3.1 ± 0.8 unit/ml; $P < 0.01$), and both endothelium-dependent (5.1 ± 2.5 vs. $9.1 \pm 4.1\%$; $P < 0.01$) and endothelium-independent vasodilation (13.2 ± 4.6 vs. $16.4 \pm 5.5\%$; $P < 0.01$) were impaired. On univariate analysis of all subjects, serum AGEs correlated with endothelium-dependent vasodilation ($r = -0.51$, $P < 0.01$); a weaker association was found with endothelium-independent vasodilation ($r = -0.24$, $P < 0.01$).

On multiple regression analyses including age, sex, smoking status, and plasma lipids, only serum AGEs remained a significant independent determinant of endothelium-dependent vasodilation ($r^2 = 0.34$, $P < 0.01$).

In conclusion, it was shown that Increased serum concentrations of AGEs in patients with type 2 diabetes is associated with endothelial dysfunction, independent of other cardiovascular risk factors. Further studies to determine whether treatment targeting AGEs will lead to an amelioration of endothelial dysfunction are warranted. *Diabetes Care, 2002 25/6 (1055-1059)*

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Quote of the Week-----

-----"Optimism is the one quality more associated with success and happiness than any other."

-----*Brian Tracy*

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