

Diabetes 2008

From the 68th Annual Scientific Sessions of the
American Diabetes Association ■ San Francisco, CA

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Important data on diabetes presented at the 68th Annual Scientific Sessions of the American Diabetes Association come to you in **Diabetes 2008**, a newsletter CME program that is being offered to you by Yale University School of Medicine. Fax or e-mail delivery to your office of **Diabetes 2008** will be followed by a **Diabetes 2008** booklet (ACC and ADA newsletters) in the mail. After successfully completing the quiz and evaluation therein contained, you will qualify for up to 5.5 Category 1 credits towards the Physician's Recognition Award of the American Medical Association to be issued by Yale University School of Medicine.

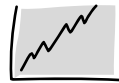
Diabetes 2008 is being offered to physicians practicing in the United States. After successfully completing this program, participants will be able to:

- Explain the pathogenesis of Type 2 diabetes, especially the coexisting roles of insulin resistance and insulin secretion.
- Recognize the clinical manifestations of the macrovascular and microvascular complications of diabetes and describe appropriate therapeutic interventions.
- Recognize the important association between insulin resistance/metabolic syndrome and atherosclerosis in patients with Type 2 diabetes.
- Identify evolving and emerging management strategies for diabetes (e.g., combination antihyperglycemic therapy, new insulin delivery systems, new glucose monitoring techniques, novel drugs).
- Describe the approach to managing dyslipidemia, hypertension, and cardiovascular risk factors in patients with diabetes.

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ADVANCing Our Understanding of the Clinical Impact of Glycemic Control



Before a packed lecture hall, the long awaited results of the ADVANCE (Action in Diabetes and Vascular Disease) trial were revealed during the opening session of the 68th Scientific Sessions of the American Diabetes Association.

The United Kingdom Prospective Diabetes Study (UKPDS) was, previously, the largest randomized clinical trial in patients with Type 2 diabetes (n=5,102) to explore the effects of more intensive blood glucose lowering on patient outcomes. In that study, in which a strategy of sulfonylurea or insulin therapy was compared to conventional diet therapy, statistically significant reductions in mainly microvascular outcomes occurred with the more aggressive approach. With a difference in HbA1c of 7.9% vs. 7.0% between groups, the investigators reported a 12% relative risk reduction for any diabetes-related outcome (p=0.029) and a 25% reduction in microvascular endpoints (p<0.01), including the development of albuminuria and retinopathy requiring photocoagulation. There was no significant reduction, however, in all-cause mortality, diabetes-related death, myocardial infarction, or stroke.

These important findings led to the teaching that glucose control in Type 2 diabetes reduces microvascular but not macrovascular disease risk. A number of explanations have been proposed for these observations. Clearly, these two types of vascular complications have divergent pathophysiologies. Endothelial dysfunction and altered capillary permeability are blamed for the former, and atherosclerosis responsible for the latter. Hyperglycemia is linked to microvasculopathy through well-documented effects on polyol flux, protein glycation, oxidative stress, and activation of the inflammatory cascade. In contrast, however, the contribution of glucose to atherogenesis is less clear, in light of the myriad other cardiovascular risk factors that are frequently present in our Type 2 diabetes patients. Some have argued that to achieve a reduction in atherosclerotic events, blood glucose must be completely normalized, something never achieved by any study. Or, perhaps, the methods by which blood glucose was lowered

in the UKPDS (focusing on 'insulin supply' as opposed to insulin action) was the problem. In this light, and notably, in a small substudy within the UKPDS, metformin, an insulin sensitizing drug, did reduce macrovascular events.

A passionate debate evolved, and from this controversy emerged several clinical trials, including three to be revealed at this week's ADA Scientific Sessions: ADVANCE, an international study; ACCORD (Action to Control Cardiovascular Risk in Diabetes), based in the US & Canada, and the VADT (VA Diabetes Trial), involving American veterans. The opening day's session focused on ADVANCE, a study involving 11,140 patients from more than 200 sites in 20 countries. The organizing center was the George Institute in Australia. Dr. Steve McMahon opened the symposium by describing the background of the study and its aims. The study examined the effects of reducing HbA1c to less than 6.5% and routine use of a fixed-dose angiotensin converting enzyme (ACE) inhibitor-thiazide combination (perindopril-indapamide) in Type 2 diabetes patients, aged 55 years or older with additional cardiovascular risk factors. Using a 2 X 2 factorial design, 25% of recruited subjects received either aggressive glucose lowering, the fixed-dose combination antihypertensive, both, or neither.

The glucose lowering strategy was sulfonylurea-based, using a controlled-release formulation of gliclazide—similar in structure to glipizide used in the US. Additional therapies (metformin, thiazolidinediones [TZDs], alpha-glucosidase inhibitors, insulin) were then added, at the discretion of the local investigators, to achieve the glycemic target.

The mean age of ADVANCE participants was 66 years, with a diabetes duration of about eight years; the gender mix was 4:6, female:male. Approximately one-half had established macrovascular disease and about 10% exhibited at least one microvascular complication. The mean HbA1c at baseline was 7.5% and the mean blood pressure (BP) was 145/81 mmHg. Median follow-up duration was five years.

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ADVANCing Our Understanding ...

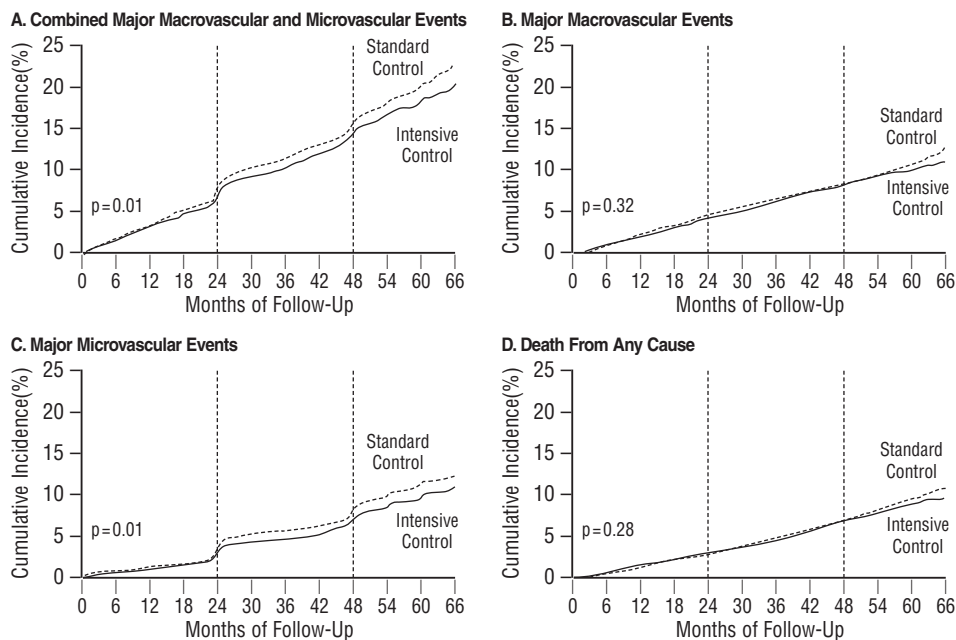
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Dr. John Chalmers next reviewed the outcomes of ADVANCE's BP arm, published late last year (*Lancet* 2007). Those randomized to fixed-dose combination therapy (initially 2.0 mg/0.625 mg, increased to 4.0 mg/1.25 mg after three months) experienced a greater reduction in BP (-5.6/-2.2 mmHg) than the control group, whose BP was managed per routine care. The BP achieved in the treatment group was 135/75 mmHg (vs. 140/77 mmHg with standard care). The primary endpoint, major microvascular or macrovascular events, was reduced by 9% in the intervention group (hazard ratio [HR] 0.91 [95% CI 0.83-1.00]; $p = 0.041$); all cause mortality was reduced by 14% (HR 0.86 [0.75-0.98], $p = 0.025$). There were also reductions in cardiovascular death (-18%), total coronary events (-14%), and total renal events (-21%). The ADVANCE hypertension management arm data would therefore appear to support the current BP target of <130/80 mmHg in diabetic patients, although the treatment strategy was based not on any specific BP target but instead on the method of BP reduction.

Dr. Anushka Patel next presented the anxiously anticipated glucose control findings. At baseline, the patients were on a variety of anti-hyperglycemic agents, with 71% taking sulfonylureas, 61% metformin, and less than 2% on insulin. By the end of the study, 92% of patients assigned to aggressive control were using the sulfonylurea, gliclazide, 74% metformin, 17% a TZD, 19% an alpha-glucosidase inhibitor, and a full 40% were on insulin. During the trial, the mean HbA1c was 7.3% in the standard care group and 6.5% in the intensive control group, with a mean difference of -0.67%. Corresponding fasting plasma glucose means were 139 and 112 mg/dl, respectively (difference, -27 mg/dl).

In reference to the primary endpoint of total microvascular and macrovascular events, patients randomized to the intensive care group experienced 10% less events (HR 0.90 [0.82-0.98], $p = 0.01$) (Figure 1). This was primarily due to a 14% reduction in major microvascular events ($p = 0.01$), which was exclusively driven by a 21% ($p = 0.006$) reduction in new or worsening nephropathy, defined as the development of macroalbuminuria, a doubling of serum creatinine to above 2.3 mg/dl, or the need for renal replacement therapy. There were no changes in retinopathy rates. Notably, microvascular complications were very low overall, with only about 6% experiencing new or worsening retinopathy. Moreover, the improvement in nephropathy exacerbation consisted of a very modest absolute risk reduction of 1.1% (event rates of 5.2% in the control group and

Figure 1. Cumulative Incidences of Events, According to Glucose-Control Strategy



4.1% in the intensive care group). Subgroup analyses did not reveal any heterogeneity of response for microvascular outcomes.

For the all-important macrovascular outcomes, there were no significant changes in event rates (10.0% with intensive management and 10.6% in controls; HR 0.94 [0.84-1.06], $p = 0.32$), including its components of non-fatal MI, non-fatal stroke, and death from cardiovascular causes. Neither was there any effect on all-cause mortality (HR 0.93 [0.83-1.06], $p = 0.28$). Subgroup analyses were similarly unremarkable for macrovascular outcomes. Of note, a potentially confounding decrease in blood pressure of 1.6/0.8 mmHg of uncertain origin was found in the intervention group. In addition, the lack of an effect of more rigid glucose control was despite the fact that, on average, ADVANCE patients had suboptimal implementation of evidence-based cardiovascular risk reduction strategies. For example, less than half of the participants were taking a statin by the end of the trial and approximately 40% were not using any anti-platelet therapy.

Other clinical outcomes were presented by Dr. Bruce Neal. Surprisingly, weight was increased in the aggressive control group by only 0.7 kg, as compared to standard care, despite more aggressive glucose lowering. There was a 7% increase in the relative risk of hospitalization (intensive group, 44.9% vs. standard care group, 42.8%; HR 1.07 [1.01-1.13]). The investigators ascribed this to closer contact between the patients and the study personnel. Hypoglycemia was relatively uncommon,

but did occur more often in the aggressively managed group (150 patients vs. 81 patients with severe events; 0.7 events per 100 patient-years with intensive management and 0.4 event per 100 patient-years with standard care; HR = 1.86 [1.42-2.40], $p < 0.001$). One of these episodes was fatal, but that occurred in the control group and one episode resulted in permanent disability in each group.

Dr. Mark Cooper then provided independent commentary and a panel discussion ensued. The general consensus was that a more aggressive glucose-lowering strategy may benefit renal outcomes, but without any effect (either positive or negative) on macrovascular events. Many questions obviously remain: How important were the specific pharmacological strategies used in ADVANCE? (At the very least, it would appear that the sulfonylureas—at least gliclazide—are reasonably safe and effective antihyperglycemic agents.) Would a benefit on cardiovascular events have been demonstrated had ADVANCE been continued for another five years? What if the therapy had been started at an earlier stage in the course of the diabetes? How will the ADVANCE data contrast with those from two other key trials to be revealed later in the week—VADT and ACCORD? *Diabetes 2008* will be providing coverage of both of these presentations as they occur in San Francisco. We hope to be able to provide some practical recommendations to our readers regarding the intensiveness of glucose management by the end of this week's Scientific Sessions.



Insulin in Type 2 Diabetes

With more convenient and perhaps safer insulin formulations now available, the precise role of insulin therapy in the care of the Type 2 diabetes patient is evolving—the topic of a symposium at this week's Scientific Sessions. Proponents of earlier insulin therapy suggest that it may not only improve glucose control but also may actually preserve β -cell function over time. Dr. Peter Butler of the University of California, Los Angeles presented data from investigations of pancreatic tissue obtained from patients at autopsy. These indicated that patients with Type 2 diabetes have a significantly reduced β -cell mass as compared to their non-diabetic peers, regardless of body weight. This difference appeared not to be due to a difference in β -cell replication (with slightly higher replication rates actually observed in the diabetes patients) but rather to higher rates of apoptosis (programmed cell death). He theorized that insulin therapy may decrease β -cell apoptosis, but admitted that designing a study to demonstrate this point would be exceedingly difficult.

In the second presentation of the symposium, Dr. Rory Holman of the University of Oxford discussed the clinical pros and cons of early insulin therapy in Type 2 diabetes. His key points are summarized in Table 1. In the third presentation of the symposium, Dr. Mayer Davidson, also of the University of California, Los Angeles, presented an oral agent therapeutic algorithm successfully employed by his institution. Given the lack of compelling evidence-based outcome data, he added that he is generally reluctant to initiate insulin therapy early in the course of a patient's diabetes care unless it is absolutely necessitated by clinical circumstances.

The Future of Insulin Therapy?

At this week's meeting several investigators reported on novel delivery methods of insulin, which may render many of the patient concerns in Table 1 a thing of the past. Smith and colleagues of Georgia examined the pharmacokinetics and pharmacodynamics of a daily transdermal insulin patch in five male and three female patients (mean age 35.4 ± 10.8 years, BMI 27.3 ± 3.7 kg/m²) with Type 1 diabetes for at least 10 years and HbA1c $\leq 9.0\%$ (abstract 309-OR). The use of intermediate or long-acting basal insulin was stopped 48 hours prior to treatment, with those on continuous subcutaneous insulin infusion having their pump turned off on arrival to the study center. Immediately following the run-in period, during which IV insulin lispro was administered to

Table 1. Using Insulin Earlier in Type 2 Diabetes Therapy

Pros

- No limit to potential glycemic lowering.
- Virtually 100% responder rate.
- Large doses can overcome insulin resistance.
- Addresses only one of the two underlying endocrinologic defects in those with Type 2 diabetes, but can overcome the other.

Cons

- Patients may be reluctant to initiate insulin earlier in the course of therapy due to their fear of injections and concerns about hypoglycemia and weight gain.
- Patients may view their transition to insulin as a signal that they have 'failed' and/or that their diabetes has worsened.
- Physicians and nurses need to spend considerable time teaching patients about the various types of insulin, how to mix and administer the agents, how to recognize and manage hypoglycemic events, as well as the intensive monitoring required to attain target goals.
- More difficult to understand and comply with an insulin regimen vs. oral medications.

achieve a glucose clamp target of 100 mg/dl, the skin site was prepared and the insulin patch applied for 12 hours. Mean serum levels of insulin increased over the first four hours following the patch application and rose to a mean steady insulin level of 23.7 μ U/ml, with this level being maintained until removal of the patch. Following removal of the transdermal insulin patch, the serum insulin levels declined with an elimination half-life of approximately 45 minutes. If further successfully developed, such a patch may provide patients with a convenient form of basal insulin. Clearly, the inter-patient reliability of absorption needs to be fully understood. In addition, we would estimate that higher insulin levels would be required in patients with Type 2 diabetes.

The antihyperglycemic effect of a novel intranasal insulin formulation was compared to that of a rapidly acting insulin analog and placebo in a Phase 2 study by Brandt and coworkers of Switzerland (abstract 424-P). Patients enrolled in the study had Type 2 diabetes treated with oral medications with or without basal insulin, and had an HbA1c $< 8\%$ and fasting plasma glucose < 140 mg/dl. Each patient remained on their usual

regimen and ate a standardized breakfast. They then underwent placebo nasal administration, dose titration phases for both the intranasal and the rapid acting insulin analog, and a randomized phase to compare the two insulin preparations at the optimized doses. The target was to achieve a post-prandial glucose increase < 60 mg/dl at one hour following a meal. In their presentation of pharmacokinetic data from the first five patients, the investigators reported that, as compared to placebo, the intranasal insulin formulation decreased glucose mean maximum concentration (C_{max}) and area under the curve (AUC) by 54% and 64%, respectively, while the rapid acting insulin analog decreased these parameters by 35% and 38%, respectively. However, a significantly higher rate of hypoglycemia occurred during treatment with the injected insulin as compared to the intranasal formulation (20.7% [6/29] vs. 3.4% [1/29], $p=0.025$).

A new oral insulin formulation directed primarily at the liver—hepatic-directed vesicle-insulin (HDVI)—significantly reduced post-prandial glucose excursions when added to standard antihyperglycemic therapy as reported by Schwartz and colleagues from Texas and Pennsylvania (abstract 426-P). Six patients (mean age 56 ± 7 years, HbA1c $8.6 \pm 2.0\%$, BMI 27.6 ± 3.6 kg/m²) receiving oral anti-diabetic therapy with suboptimal control were entered into a single-blind, placebo-controlled, dose-escalating trial. Each dosing day was preceded by an overnight euglycemic low-dose insulin infusion that was stopped one hour prior to dosing. Patients continued to receive their oral regimen plus add-on treatment each day at 30 minutes prior to breakfast, lunch, and dinner. On day 1, patients received placebo; on days 2 through 5 they received HDVI at doses of 0.05, 0.1, 0.2, and 0.4 U/kg, respectively. Venous blood sampling was done between 30 minutes before the breakfast dose and until 4.5 hours following the dinner dose. As compared to placebo, significant ($p \leq 0.011$) dose-related reductions in blood glucose AUC were observed with HDVI.

Back From the Future

As noted above, both patients and their physicians are often reluctant to initiate insulin therapy because of weight gain. However, according to interesting findings by Nieznaj and colleagues of Poland (abstract 462-P), not all patients initiated on insulin actually experience an increase in body weight. Their observational study was designed to identify factors associated with weight gain after the initiation of insulin in

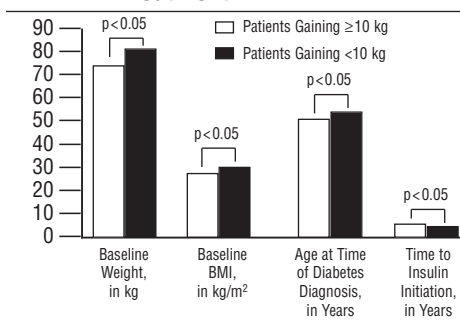
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Insulin in Type 2 Diabetes

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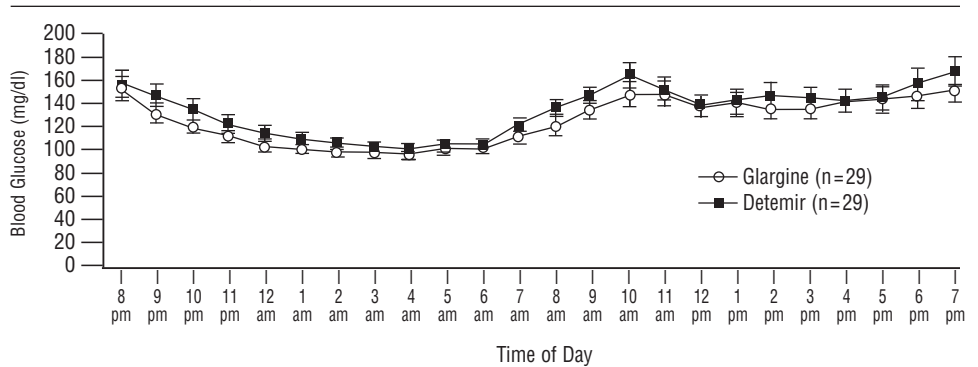
269 patients (155 women and 114 men, mean age 60.3 ± 11.6 years, mean diabetes duration 4.9 ± 3.2 years) with suboptimally controlled Type 2 diabetes ($HbA1c > 8.0\%$ despite maximum oral treatment). The investigators found that while 66% gained weight, 34% did not or actually lost weight after one year. Weight gain after one year of insulin therapy was significantly and negatively correlated with baseline body weight ($r = -0.16$, $p < 0.01$). Those who gained ≥ 10 kg during one year of insulin were less overweight at baseline, younger at the time of their diabetes diagnosis, and had a longer duration of diabetes before insulin initiation as compared to those who gained less than 10 kg ($p < 0.05$ for each comparison) (Figure 2).

Figure 2. Baseline Characteristics of Patients by Change in Weight Over One Year of Insulin Treatment



The use of long-acting insulin analogs may increase patients' acceptance of insulin therapy. In a randomized, crossover, double-blind comparison of insulin detemir and insulin glargine given once daily (at 8 pm) in 35 patients with Type 2

Figure 3. Daily Blood Glucose Measured by Continuous Glucose Monitoring (Mean \pm SE): Insulin Glargine vs. Insulin Detemir



diabetes, King and California colleagues reported that 24-hour glycemic control, assessed by continuous glucose monitoring, was essentially identical with the two agents (Figure 3) (abstract 436-P). Basal blood glucose targets of < 120 mg/dl without $> 5\%$ of readings < 70 mg/dl during the basal period (12 pm to 6 am) were achieved in all study patients at a mean of approximately 3.5 days. During this basal period as well as the entire 24-hour period there was only one timepoint (2 am) at which there was a significant ($p < 0.05$) difference in blood glucose levels between the detemir and glargine treatments.

Several studies reported on the effects of premixed insulin—typically involving a 70/30 formulation of intermediate and rapid-acting insulin analogues—on glycemic control and risk for hypoglycemia in Type 2 diabetes patients. Kim and colleagues of China and the Republic of Korea switched 329 patients who did not achieve adequate blood glucose control with long-acting insulin to biphasic insulin aspart (70/30 neutral protamine aspart/aspart) (abstract 544-P). After

six months, improvements in glucose control were demonstrated, including $HbA1c$ (from 9.5 to 7.9%) mean fasting glucose (from 217 to 147 mg/dl), and postprandial glucose (from 300 to 190 mg/dl) (each $p < 0.001$). The investigators also reported a decrease in the incidence of major hypoglycemic events (from 1.1 to 0.03/patient-years), as well as overall (from 3.5 to 2.1/patient-years) and nocturnal hypoglycemia (from 0.91 to 0.33/patient-years). In a related meta-analysis of nine randomized, parallel, or crossover trials comparing biphasic insulin aspart to a regular human premixed insulin (conventional 70/30 NPH/regular), Davidson and international colleagues reported that while there were no differences in overall and minor hypoglycemia, the likelihood for major hypoglycemic events (odds ratio [OR] 0.45, [0.22, 0.93], $p < 0.05$) and for nocturnal hypoglycemic events (relative risk [RR] 0.50, [0.38, 0.67], $p < 0.01$) were significantly lower with the biphasic analog (abstract 575-P). No significant differences were observed between the insulin groups in $HbA1c$ or body weight change.



Something to Sink Your Teeth Into: “Bridging” the ADAs



In a first-ever joint symposium of the two ADAs—that is, the American Diabetes Association and the American Dental Association—the links between periodontal disease and diabetes were characterized by a series of speakers. After presenting a fascinating overview of the history of tooth extraction as both a cure for common maladies such as arthritis, as well as a preventative measure against future illness (a practice fortunately abolished about 50 years ago), Dr. Ray C. Williams of the North Carolina School of Dentistry, defined the most common periodontal disorders for the non-dentist. *Gingivitis* presents as red and/or bleeding gums

and, if not treated, may progress to *periodontitis*, which is characterized by pockets of alveolar bone loss around a tooth. Periodontal disease is a common dental disorder, affecting more than 30% of the adult population and represents a serious public health concern due to significant associated morbidity. Of the two disorders, periodontitis is the more devastating, with gums receding (hence, the term “getting long in the tooth”) and teeth eventually loosening.

Medical dogma once held that all people—indeed all teeth—were similarly susceptible to periodontitis; however, emerging evidence indicates that there are factors that increase one's risk for

periodontal disease. Diabetic patients, especially those who are poorly controlled and/or with a longer duration of diabetes are clearly at increased risk (Table 2). Also, investigators have found that specific bacteria may increase the risk for periodontitis, with gram-negative anaerobes isolated from approximately 50% of periodontitis sites. Rather than causing the destruction, these bacteria trigger an inflammatory response that ultimately drives the progressive bone loss.

Emerging research now suggests that the relationship between periodontal disease and diabetes may actually be a reciprocal one. That is,

Continued on page 5

Something to Sink Your Teeth Into...

Continued from page 4

those with periodontal disease may be at greater risk for developing diabetes, demonstrating both poorer glycemic control and increased risk of complications. Of note, periodontal pathology has been associated with increased risk for several conditions in addition to diabetes, including cardiovascular disease, adverse pregnancy outcomes, and pulmonary, renal, and pancreatic diseases.

Conceptual models for the relationship between periodontitis and diabetes have implicated a proinflammatory state, with increased levels of the cytokines, IL-6, IL-1 β , and TNF- α triggered by low-grade infection. These, in turn, may decrease insulin sensitivity, and conceptually, worsen glucose control. Published studies have revealed that those with diabetes and severe periodontitis are at increased risk for macroalbuminuria as well as cardiovascular and renal-associated mortality.

While there is no real cure for periodontal disease, it is both preventable and treatable with good oral hygiene, specifically. In diabetic patients, evidence now indicates that treating periodontitis is beneficial to both dental health as well as glycemic control. In an analysis of NHANES III population data adjusted for demographic factors, Dr. George Taylor of the University of Michigan School of Dentistry reported that in diabetic patients the risk for poor glycemic control is nearly five-fold higher in those with severe periodontitis compared to those with healthier gums. He then presented preliminary findings from his pilot clinical trial of 46 patients with periodontal disease and Type 2 diabetes. The patients were followed for 15 months and the intervention group received aggressive non-surgical periodontal treatment and maintenance, which was accompanied by a significant decrease in HbA1c from 8.7 to 8.0%.

Dr. Maria E. Ryan from the School of Dental Medicine at Stony Brook University in New

Table 2. Risk Factors for Periodontitis

Strong Risk Factors

- Diabetes
- Presence of specific gram-negative anaerobic bacteria in the mouth
- Smoking
- Genetics

Other Risk Factors

- Poor oral hygiene
- Stress
- Advancing age
- Race (*ie*, African-American, Mexican-American have higher incidence than Caucasians)
- Gender (*ie*, women have greater incidence than men)
- Immune dysfunction, including HIV
- Certain drugs (calcium channel blockers, phenytoin, cyclosporin)
- Existing bone loss
- Poor nutrition
- Obesity

York also presented an overview of some unpublished data suggesting a correlation between the severity of periodontal disease and the degree of insulin resistance. She also reviewed studies indicating that good oral hygiene practices plus the use of sub-antimicrobial doses of doxycycline are associated with improved control of HbA1c, along with decreased levels of C-reactive protein and other cytokines.

In the concluding presentation of the symposium, Dr. Louis Rose of the University of Pennsylvania offered clinical recommendations as developed during the Scottsdale Project, which brought professionals from all branches of

healthcare together to highlight the importance of dental health in diabetes. Importantly, all patients with diabetes should be asked if they've seen a dentist in the past year, their oral health should be assessed, and treatment plans initiated and maintained, as summarized in Table 3. In addition, there is also a need to develop guidelines to assist dental providers in identifying patients with periodontal disease who are likely at increased risk for diabetes.

Table 3. Dental Management Plan for Patients with Diabetes

1. Patients should be medically managed as recommended by current American Diabetes Association guidelines.
2. Patients should have a dental examination at a minimum of twice a year, or more frequently if advised by the dental provider, and receive appropriate dental/periodontal care.
3. There should be close communication between the primary care physician and the dentist.
4. Medical providers should advise the patient with periodontal disease that it is a chronic infection of the gums and an important complication of diabetes.
5. Medical providers should also advise patients that periodontal disease has been associated with significant health problems, including worse metabolic control and complications of diabetes such as coronary artery disease and stroke.
6. Medical providers should advise the patient that periodontal disease can be treated by a dentist and dental hygienist.
7. If the patient has not seen a dentist within the last year or if there are signs of periodontal disease, the patient should be advised to make an appointment to see a dental provider as soon as possible.



So Many Posters, So Little Time....



'Double Diabetes'

The prevalence of 'double diabetes', characterized by hyperglycemia in overweight/obese children and youths with the combination of markers of both Type 1 diabetes (autoantibodies to islet cell antigens) and Type 2 diabetes was evaluated in 101 consecutive (unselected) Caucasian patients, aged 5-30 years, who were attending diabetes clinics in Italy and England (abstract 948-P). Markers typical of Type 1 and Type 2 diabetes were seen in 19.7% of the diabetic patients (16.2% of those aged 16-30 years and 23.6% of those aged 5-15 years). Previously noted in African- and

Hispanic-Americans, double diabetes is apparently also affecting Caucasians, likely the result of increased obesity among youths in all races. The genetic, immunological, and metabolic features of this emerging form of diabetes require study.

Fatty Hearts

Snel and Dutch coworkers reported that prolonged calorie restriction (450 kcal/day x 16 weeks) combined with lifestyle intervention in 12

obese, insulin-treated Type 2 diabetic patients decreased myocardial triglyceride content (by 27%, $p=0.019$), improved diastolic function (by 16%, $p=0.019$), and decreased both systolic (from 147 to 119 mmHg, $p<0.001$) and diastolic blood pressure (from 81 to 70 mmHg, $p<0.001$), and improved gluoregulation (HbA1c from 7.9% to 6.2%, $p=0.006$) (abstract 571-P). Hepatic triglyceride content also decreased markedly with calorie restriction (by 86%, $p<0.001$).

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