

Secondhand Smoke and Glucose Intolerance Might Be Linked

For the first time, researchers in the *British Medical Journal* have reported a possible link between second-hand cigarette smoke and impaired glucose tolerance.

Thomas Houston, MD, MPH, of Alabama's Birmingham Veterans Affairs Medical Center, and colleagues investigated whether active and passive smokers are more likely than nonsmokers to develop clinically relevant glucose intolerance or diabetes as part of the Coronary Artery Risk Development in Young Adults (CARDIA) prospective cohort study.

Patients included were recruited from Birmingham, Alabama; Chicago; Minneapolis; and Oakland, California. They were black and white men and women aged 18 to 30 years with no glucose intolerance at baseline, including 1,386 current smokers, 621 previous smokers, 1,452 never smokers with reported exposure to secondhand smoke (validated by serum cotinine concentrations 1 ng/mL to 15 ng/mL), and 1,113 never smokers with no exposure to secondhand smoke.

At baseline, the mean age was 25 years, 55% of the

patients were women and 50% were black. During 15 years of follow-up, 16.7% of the participants developed glucose intolerance. The investigators found a graded association between smoking exposure and the development of glucose intolerance. The 15-year incidence of glucose intolerance was highest among smokers (21.8%), followed by never smokers with passive smoke exposure (17.2%), and then previous smokers (14.4%).

The 15-year incidence of glucose intolerance was lowest for never smokers with no passive smoke exposure (11.5%). Current smokers and never smokers with passive smoke exposure remained at higher risk than never smokers without passive smoke exposure after adjustment for multiple baseline sociodemographic, biological, and behavioral factors, but risk in previous smokers was similar to that in never smokers without passive smoke exposure.

Dr. Houston and colleagues concluded that the findings support a role of both active and passive smoking in the development of glucose intolerance in young adulthood.

UN to Consider Diabetes Epidemic Resolution

Diabetes has become an international problem with the number afflicted expected to surpass 334 million, according to the International Diabetes Federation (IDF).

In response to this crisis, the IDF has initiated an effort to develop and promote a United Nations (UN) resolution on diabetes. In an IDF news release, the organization said it has gathered leaders in the areas of diabetes care, advocacy and industry, including the World Health Organization, American Diabetes Association (ADA) and the Juvenile Diabetes Research Foundation to cooperate on the resolution. "Above all, unity is required in the fight against this pandemic," the IDF said in a news release.

Two tactics are required to make an impact on the crisis worldwide: To create a UN resolution acknowledging diabetes as a serious problem and to develop an extensive public relations campaign highlighting the need for action,

according to the news release. The project will span several years. "The aim is to run the largest global awareness campaign ever held for diabetes with the goal of reaching 1 billion people," said IDF President-elect Professor Martin Silink.

The goal of the campaign is to empower, energize and educate those living with and affected by diabetes. An important component of the campaign is to involve young people by engaging them as advocates through the Youth Ambassadors program. Youth Ambassadors must be between the ages of 18 and 25 years and will be nominated by each of the IDF member associations. Twenty-five ambassadors will be chosen to attend training at the upcoming IDF meeting in Cape Town, South Africa, in December.

The resolution is a declaration only and as such does not include any financial support. "The IDF hopes that by voting for this resolution, countries within the UN will be motivated to become involved in other efforts to affect the condition," the IDF news release said.

American Program for Teen Weight Loss Launches Camp in UK

US-based Wellspring Camps has established Wellspring UK, Britain's first comprehensive, scientifically based summer weight-loss camp for teens ages 12 to 17 years. The program focuses on weight loss through diet and activity management, as well as the psychological and emotional issues that often prevent successful weight loss by sustaining problematic eating and inactivity.

Through a combination of cognitive-behavioral therapy, an introduction to healthy eating habits and daily exercise and adventure activities, campers at Wellspring's US programs typically lose 4.4 lbs per week during camp and continue to lose weight after leaving the program.

The camp, located in the Lake District and based on the Cumbria campus of the University of Central Lancashire, is the first program to be established outside the United States for Healthy Living Academies, the organization that manages Wellspring Camps. Healthy Living Academies is America's leader in the treatment of obesity in young people.

"Obesity and excess weight are the most serious health issues facing British children," said Deb Sweeney Whitmore, director of Wellspring UK. "In fact, a recent study by the Health and Social Care Information Centre revealed that in 2004, 24% of 11- to 15-year-old boys were obese, along with 25% of 11- to 15-year-old girls — nearly double the rate of 10 years earlier. Up until now, treatment options for significantly overweight children and teens have been limited and rarely effective," Ms. Whitmore added. "Wellspring UK was designed by top researchers as a healthy lifestyle immersion program that introduces both the teen and his or her family to a new lifestyle and a new way of thinking."

Breastfeeding Helps Prevent Obesity in Kids

Breastfeeding for longer than 3 months can reduce a child's risk of becoming overweight or obese later in life by more than 40%, if the child was born to an overweight mother diagnosed with diabetes during her pregnancy, according to a study published in *Diabetes Care*.

Researchers in Germany found that the longer a woman breastfed, the less likely her child was to become overweight or obese before the age of 8 years. The study included 324 children born between 1995 and 2000 to women with gestational diabetes. Gestational diabetes affects

roughly 4% of all pregnant women; it goes away after the baby is born. Both mother and child are at increased risk (later in life) for type 2 diabetes.

In the study, more than 37% of those children who were never breastfed had become overweight by the age of 8 years. Of those who were breastfed for up to 3 months, 32.5% became overweight children. Of those who were breastfed longer than 3 months, only 22% became overweight.

The study also found, however, that women who were obese (and whose children were therefore at greater risk for obesity) were less motivated to breastfeed than nonobese women. Obese women were twice as likely to forego breastfeeding their children as women of healthier weights, the researchers noted.

"It's important to find out why these women resist breastfeeding and help them overcome whatever barriers there are," said Ute Schaefer-Graf, MD, lead researcher for the study. "We know that obesity and overweight contribute to numerous health problems in adults, and we are increasingly seeing these problems in children. Since the children of obese parents and, in particular, of women who are diagnosed with gestational diabetes, are at greater risk for gaining excessive amounts of weight as they grow up, breastfeeding becomes more important than ever as a means of getting children started on a path to good health. We strongly encourage anyone diagnosed with gestational diabetes to breastfeed for as many months as possible."

Vegetarian Diets: Weight Loss Without Exercise or Calorie Counting?

A scientific review in *Nutrition Reviews* showed that a vegetarian diet is highly effective for weight loss.

People who are vegetarian tend to be slimmer than those who eat meat, and they experience lower rates of heart disease, diabetes, high blood pressure and other life-threatening conditions linked to overweight and obesity.

In the March/April 2006 issue of DIABETIC MICROVASCULAR COMPLICATIONS TODAY, there was an error in the article, "Podocytes Play Critical Role in Nephropathy," by Fuad N. Ziyadeh, MD. The caption for Figures 2 and 3 should have read, "VEGF164 protein level is increased in the nondiabetic d/m mouse. Figure 2 is a normal glomerulus from the nondiabetic d/m mouse." We apologize for the error and regret any confusion it may have caused.

The review compiled data from 87 previous studies and showed that weight-loss effect does not depend on exercise or calorie counting, and it occurs at a rate of approximately 1 pound per week.

Rates of obesity in the general population are rapidly rising, while in vegetarians, obesity prevalence ranges from 0% to 6%, according to study authors Susan E. Berkow, PhD, CNS, and Neal D. Barnard, MD, of the Physicians Committee for Responsible Medicine.

The authors found that the body weight of both men and women vegetarians is, on average, 3% to 20% lower than that of meat-eaters. Vegetarian and vegan diets have also been put to the test in clinical studies, the review notes. The best of these clinical studies isolated the effects of diet by keeping exercise constant. The researchers found that a low-fat vegan diet leads to weight loss of about 1 lb per week, even without additional exercise or limits on portion sizes, calories or carbohydrates.

“Our research reveals that people can enjoy unlimited portions of high-fiber foods such as fruits, vegetables and whole grains to achieve or maintain a healthy body weight without feeling hungry,” said Dr. Berkow, the lead author.

“There is evidence that a vegan diet causes an increased calorie burn after meals, meaning plant-based foods are being used more efficiently as fuel for the body, as opposed to being stored as fat,” said Dr. Barnard. Insulin sensitivity is increased by a vegan diet, allowing nutrients to more rapidly enter the cells of the body to be converted to heat rather than to fat.

A team of researchers led by Tim Key of Oxford University, found that meat-eaters who switched to a plant-based diet gained less weight over 5 years. Articles reviewed by Drs. Berkow and Barnard include several published by Dr. Key and his colleagues, as well as a recent study of more than 55,000 Swedish women showing that meat-eaters are more likely to be overweight than vegetarians and vegans.

Congress Should Increase CDC Diabetes Prevention Funding by \$20.8 Million, ADA Urged

The ADA has urged the US Congress to ensure that the government does not shortchange its commitment to diabetes research and prevention. Appearing before the US House Subcommittee on Labor, Health and Human Services and Education Appropriations, L. Hunter Limbaugh, Chair of the ADA Advocacy Committee, stressed the need for federal funding to keep pace with the growing diabetes epidemic.

Specifically, Mr. Limbaugh, a South Carolinian whose daughter has type 1 diabetes, urged the committee to increase fiscal year 2007 funding for the Centers for Disease Control and Prevention’s (CDC) Division of Diabetes Translation by \$20.8 million — or \$1 for every American with diabetes — and to increase funding at the National Institutes of Health (NIH) by 5% (\$92 million).

Despite the growing nationwide diabetes epidemic — which increased by 14% since 2003 estimates — the Bush administration recently proposed a budget that would cut funding for diabetes prevention at the CDC for the second straight year. This would significantly weaken the efforts of the the CDC’s Division of Diabetes Translation, which runs state-based Diabetes Prevention and Control Programs. Because of funding shortfalls, the CDC can only provide comprehensive prevention in 28 states, leaving 22 states with basic monitoring programs. The administration also proposed in its budget an \$11 million cut to the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK), an NIH research division.

“Rather than recognizing the scope and cost of the diabetes epidemic and investing the resources necessary to address it, we are doing backflips to redesign our health insurance system in ways that will make it nearly impossible for people with diabetes to find coverage,” said Mr. Limbaugh. “Instead, we should spend the relatively small amount of money that we know it would take to slow the growth of the epidemic and reduce the costly complications among those who are already living with diabetes.”

In fiscal year 2006, the Division of Diabetes Translation at the CDC is funded at \$63.1 million. This fiscal year marked the first time that the division received a federal funding cut, and this year’s proposed cut would be an even larger reduction. The division takes the research that is conducted at the NIH and translates it into proven educational programs, best practice guidelines and prevention, detection and management supplies. It works in partnership with state and local governments to direct funds to the areas where they will have the most impact.

Thousands to Get Diabetes Drug in Alzheimer’s Study

In 2004, an NIH study found diabetes was linked to a 65% increased risk of developing Alzheimer’s disease. A genetic link between the two diseases was recently reported in *Alzheimer’s & Dementia* by Allen Roses, MD. This link will now be tested in thousands of Alzheimer’s patients who will be given rosiglitazone maleate (Avandia; GlaxoSmithKline, Philadelphia) in hopes of

slowing cognitive function decline.

According to an *Associated Press* report, the number of people with Alzheimer's is expected to skyrocket as the population ages, growing from 4.5 million today to 14 million by 2050. If the diabetes-Alzheimer's link is correct, the obesity-fueled type 2 diabetes epidemic may compound the situation.

Three phase 3 trials will test if rosiglitazone is protective against Alzheimer's. Dr. Roses' research proposes that changes in the way brain cells use sugar to generate energy eventually lead to impaired brain cell function and cell death. These are also the key elements that lead to the development of plaques, tangles and brain atrophy seen in Alzheimer's.

Preoperative Glycemic Control May Decrease Complications

Research reported in the *Archives of Surgery* suggests that if patients have good control glycemic control preoperatively, the chance of postoperative infection is reduced.

Annika S. Dronge, MD, and colleagues tested the hypothesis that HbA1c levels <7% would decrease the rate of infection postoperatively. A total of 647 patients with diabetes were enrolled through the Veterans Affairs Connecticut Healthcare System; however, only 490 patients were included in the retrospective observational study. Patients (median age, 71 years) had a major noncardiac surgery between Jan. 1, 2000, and Sept. 30, 2003. The investigators obtained data through the Veterans Affairs National Surgical Quality Improvement Program.

The investigators reported primary outcomes including infectious complications, wound infection, urinary tract infection and sepsis. Each category was analyzed in accordance with bivariate analysis to determine association between the outcome and the following factors: age, race, diabetic treatment, American Society of Anesthesiologists classification, Activities of Daily Living assessment, elective versus emergent procedure, wound classification, operation length and HbA1c levels. The investigators concluded that when HbA1c was <7%, patients experienced a decreased rate of infections complications. This was statistically significant (OR, 2.13; 95% CI, 1.23-3.70, $P=0.007$).

Countries Must Develop Individual Priorities

Reporting for the International Diabetes Attitudes Wishes and Needs Program (DAWN) Advisory Panel, repre-

sentative physicians from the United States, Denmark, the Netherlands, the United Kingdom and Germany have reported that individual countries should devise their own priority structure for improving the chronic-care model and diabetes care. The report, published in *Diabetologia*, urges countries to compare their priorities with those of other countries in order to identify strengths and weaknesses of their plan.

A total of 5,104 patients with type 1 or 2 diabetes, 2,070 primary-care physicians, 635 diabetes specialist physicians and 1,122 nurses were questioned via face-to-face or telephone interviews in order to establish country-level and individual-level patterns of perceived diabetes care. Participants were from 13 countries in Asia, Australia, Europe and North America.

The following were results from each interview set:

- All patients with type 1 or 2 diabetes said that access to care was easy, however, there is a presence of financial barriers. They also indicated that collaboration with health care providers was moderate and high collaboration with providers of their own care.
- Patients who had a lower level of socioeconomic resources (and also a higher rate of diabetes complications) said that their access to care was lower and experienced a higher rate of barriers to care. They indicated an experience of lower collaboration with health care providers.
- Health care providers indicated a mediocre chronic-care system. They also shared that access to certain specialist disciplines was not easily achieved.
- Each country experienced a significant difference in outcomes, as reported by the investigators.

Self-Monitoring of Glucose, HbA1c Useful

Assessing glycemia in diabetes can be a challenge, but approaches are available that promote successful management of blood glucose and may lead to a significant reduction in morbidity and mortality related to the disease, according to a report in the *Journal of the American Medical Association*.

Christopher D. Saudek, MD, and colleagues from Johns Hopkins University School of Medicine, wrote that, with the increasing prevalence of diabetes, successful management of blood glucose control is more and more important. Current approaches to assessing glycemia include the use of self-monitoring of blood glucose and HbA1c.

The investigators undertook a review in order to assess the evidence underlying the use of blood glucose and

HbA1c self-monitoring, to evaluate confounders and sources of error in each test, to describe upcoming developments, and to reach evidence-based conclusions on their optimal use.

They used Medline to identify relevant studies, paying special attention to those with large cohorts, meta-analyses and established recommendations. They found that, if used properly, self-monitored blood glucose gives an acceptably accurate reflection of immediate plasma glucose levels. They wrote, "Study results vary, but in general, the evidence supports a positive effect of regular [self-monitored blood glucose] for improving glycemia, particularly in individuals treated with insulin."

The best timing of monitoring one's own glucose and its frequency are controversial issues, they added, but the clinical recommendation is for regular monitoring with frequency depending on the treatment and the instability of glycemia.

"In the relatively near term, [self-monitored blood glucose] could gradually be replaced by continuous glucose monitoring," Dr. Saudek and colleagues wrote.

With regard to HbA1c, there are a number of physiologic and methodologic confounders that can affect it, but standardization of assays has been well established. "The main value of HbA1c is its use as a predictor of diabetic complications and the proven effect of improved control of HbA1c on complication risk," they wrote. A reasonable target value for HbA1c is <7%.

Most Obese People Do Not Consider Themselves to Be Obese

Apparently, obese people do not know they are obese, according to a study by University of North Carolina (UNC) scientists.

Obese men and women are reasonably accurate when it comes to reporting their own weight, said the researchers, but they are much more likely than normal-weight people to misjudge how much weight falls into the obese category and therefore do not consider themselves to be obese.

Kimberly Truesdale, MD, a research associate in the laboratory of Dr. June Stevens, UNC at Chapel Hill, presented the study results at the Experimental Biology 2006 meeting in San Francisco. The presentation was part of the scientific program of the American Society of Nutrition, according to a UNC news release.

One hundred and four men and women, white and black, between the ages of 45 and 64 years, were asked to:

- Report their weight in pounds;
- Categorize themselves as either underweight, normal weight, overweight or obese; and
- Estimate how much they would need to weigh to be considered obese.

The researchers then collected weight, height and other measures for each person. Body mass index (BMI) was calculated as normal weight (BMI 18.5 kg/m² to 24.9 kg/m²); overweight (BMI 25.0 kg/m² to 29.9 kg/m²) or obese (BMI >30.0 kg/m²).

According to BMI, there were 31 normal weight, 40 overweight and 33 obese adults in the group. About 90% of normal-weight adults and 85% of overweight and obese adults accurately self-reported their weight and height such that the BMI calculated using those self-reports fell in the same category as actual BMI.

That accuracy changed, however, when researchers asked participants about their perceived weight status; that is, would they consider themselves now to be underweight, normal weight, overweight or obese. Seventy-one percent of normal-weight and 73% of overweight adults classified themselves correctly, compared to only 15% of obese adults who correctly considered themselves to be obese.

The researcher then asked participants how much they would need to weigh to be classified as either underweight, normal weight, overweight or obese, and again the results varied depending on current weight status. On average, normal-weight participants were reasonably accurate in these estimates, but obese participants overstated how much they could weigh for every weight status category, from underweight to obese. For example, if a participant was 5 feet 7 inches and normal weight, they would estimate normal weight as 143 lbs (BMI = 22.4 kg/m²) and obesity as 189 lbs (BMI = 29.6 kg/m²), but an obese participant the same height would estimate normal weight as 164 lbs (BMI = 25.7 kg/m²) and obesity as 233 lbs (BMI = 36.5 kg/m²).

These findings have important public health implications, said Dr. Truesdale and Dr. Stevens. If obese adults do not consider themselves to be obese, they are not likely to pay full attention to public health messages about the consequences of being obese. More research is needed as to why obese adults do not consider themselves to be obese, with two possibilities being perception and denial.

Bristol Myers Squibb has Stopped Marketing Tequin

Bristol-Myers Squibb (Princeton, NJ) will no longer manufacture or sell Tequin (gatafloxacin), an antibiotic that has

been linked to both hyperglycemia and hypoglycemia in diabetics and elderly patients. The company is not pulling the agent from pharmacy shelves; a company spokesperson urged patients taking Tequin to consult their physicians before stopping the drug.

A spokesman for Bristol-Myers Squibb said that the company will return rights to the drug to Kyorin Pharmaceutical Company (Japan). The Bristol-Myers Squibb action coincided with a petition by Public Citizen Health Research Group, the watchdog group, to the Food and Drug Administration (FDA) to ban the drug, which it said was linked to 20 deaths and 159 hospitalizations since 2000. Tequin was approved in 1999 and marketed for treatment of chronic bronchitis, sinusitis, pneumonia and urinary tract infections.

In February, the FDA issued an alert concerning Tequin and strengthened the warning label on the drug. Also in February, Bristol-Myers Squibb sent a *Dear Doctor* letter warning that the drug was contraindicated for diabetic patients and reported increased risks observed among elderly patients and patients with renal insufficiency using Tequin.

A study reported in the *New England Journal of Medicine* found that patients aged in their 70s treated with Tequin were four times more likely to develop hypoglycemia and 17 times more likely to be hospitalized for hyperglycemia than similar patients treated with clarithromycin or azithromycin.

In an e-mail to DIABETIC MICROVASCULAR COMPLICATIONS TODAY, an Allergan (Irvine, Calif) representative said the adverse events with blood sugar levels associated with Tequin were linked to dosing and systemic absorption. Allergan's topically applied ophthalmic drug Zymar contains gatifloxacin and there have been no confirmed cases of hypo/hyperglycemia directly associated with that agent. The topically applied dose of gatifloxacin in Zymar is approximately 1,700 times smaller than the 200-mg oral dose of Tequin, which is a systemic therapy.

In clinical trials, the serum levels of gatifloxacin following ocular use were undetectable in the bloodstream after topical dosing. Even when Zymar was administered at twice the recommended dosage and at up to a 67% higher concentration (ie, gatifloxacin ophthalmic solution 0.5%) than Zymar's commercial formulation (gatifloxacin ophthalmic solution 0.3%), there were no detectable blood levels following single or multiple administration.

Zymar has been used safely and effectively by an estimated 4 million adults and children aged 1 year and older in clinical trials and in physicians' practices to eradicate certain harmful bacteria in the eye that can cause bacterial conjunctivitis.

Macugen Linked to Rare Hypersensitivity Reactions

The US FDA and Pfizer Pharmaceuticals (New York, NY) have notified health care professionals regarding revisions to the safety labeling for pegaptanib sodium injection (Macugen; OSI/Eyetech and Pfizer). The revisions address rare postmarketing reports of anaphylaxis/anaphylactoid reactions, including angioedema, in patients receiving the drug along with other medications administered as part of the injection procedure, according to a MedWatch alert.

The alert said that because these reactions are reported voluntarily and from a population of an uncertain size, it is not possible to reliably estimate their frequency or establish a direct relationship to pegaptanib or other concurrently administered medications.

Physicians are advised to evaluate a patient's medical history for hypersensitivity reactions. Pegaptanib is contraindicated in patients with known hypersensitivity to the active ingredient or any product excipients.

The agent is indicated for the treatment of neovascular (wet) age-related macular degeneration.

Neuropathic Pain Evaluation Specialist Sues Pfizer

David Longmire, MD, filed a lawsuit against Warner-Lambert and parent company Pfizer for fraudulent misrepresentation, concealment and deceit, according to a Boston law firm. Dr. Longmire is an Alabama neurologist and specialist in neuropathic pain evaluation and management.

The lawsuit, filed in the Circuit Court of Franklin County Alabama, arises out of a May 13, 2004 prosecution in which Warner-Lambert and its Parke-Davis division pled guilty to charges that it violated the Federal Food, Drug and Cosmetic Act associated with its marketing and sales practices for the epilepsy drug Neurontin. Pfizer acquired Parke-Davis in 2000.

Related to the 2004 case, Dr. Longmire's lawsuit charges that Warner-Lambert defrauded him by exploiting his medical expertise and reputation and lured him unwittingly to participate in a deceptive scheme to market Neurontin for off-label uses. As a result of the fraud, according to the news release, Dr. Longmire's name has been included in multidistrict litigation.

According to the plaintiff's attorneys, Warner-Lambert tried to avoid the federal statutes and regulations that make it illegal to promote off-label uses by engaging in a number of fraudulent schemes to promote sale and use of the drug for off-label indications. ■