

Most Think Obesity is Serious Problem

A poll by the Harvard School of Public Health found that most Americans think that obesity is a serious problem, and they do not believe that health risks associated with obesity are overestimated. In addition, people are no less likely than 1 year ago to be keeping track of calories, fat content or the amount of carbohydrates they eat.

Three-fourths of Americans rated obesity as an “extremely” (34%) or “very” (41%) serious public health problem in the United States. In addition, the majority of Americans believed that scientific experts have accurately portrayed (58%) or even underestimated (22%) the health risks of being obese. Very few Americans reported believing that scientific experts overestimate the health risks of obesity (15%).

“Even after all the criticism that too much attention is being paid to obesity, Americans still see this as a very serious problem for the country,” said Robert J. Blendon, Professor of Health Policy and Political Analysis at the Harvard School of Public Health.

The poll also finds approximately the same number of Americans in 2005 as in 2004 reported that they keep track

of calories (32% in 2005 vs 35% in 2004), fat content (47% vs 46%) and carbohydrates (36% vs 36%) in their daily diet. In addition, the survey found a small increase in the number of Americans who reported trying to lose weight (32% vs 27%). Of people surveyed, 54% considered themselves to be overweight.

Forty-one percent of Americans reported believing that the same number of people in the United States die from the effects of being seriously overweight as from the effects of smoking/tobacco. In addition, 51% thought that someone who is moderately overweight would be more likely than someone who is not overweight to die prematurely. However, 73% thought that a moderately overweight person would be more likely than someone at the recommended weight to develop a chronic illness such as diabetes or high blood pressure.

“Americans are pretty certain that being moderately overweight leads to serious health problems,” Professor Blendon said. “But, they are not convinced that it leads to premature death.”

Gene Linked to Type 2 Diabetes, Obesity

Scientists in France and the United States have reported that a variant of a common protein plays a primary role in type 2 diabetes and obesity, key features of the metabolic syndrome that affect more than 50 million people in this country and a similar number in Europe.

The research is based on a large genetic study of French families and is published in *Nature Genetics*. The study identified a target protein for potential drugs to restore the body's ability to respond to insulin, said Ira Goldfine, MD, a co-author of the study. His University of California-San Francisco (USCF) research team first detected the protein, PC-1, in abnormally high amounts in diabetes patients 10 years ago.

That same 1995 paper showed that the PC-1 protein inactivated the insulin receptor that binds insulin. Other work in the lab showed that when this inactivation occurred, it prevented insulin from regulating

metabolism of glucose in diabetic patients.

The discovery opens up the possibility of developing drugs to prevent or reverse the potentially deadly insulin resistance syndrome, said Dr. Goldfine, professor of medicine at UCSF.

The research was led by David Meyre and Philippe Froguel, leading French scientists in research on the genetics of obesity and diabetes, based at the Pasteur Institute's CNRS Institute of Biology, in France.

The human genetics study involved an extensive analysis of the variations in the PC-1 gene in a family population study of >3,000 people. The scientists found that a common variant of the PC-1 gene, when coupled with other small changes in the PC-1 gene, was very strongly associated with insulin resistance, type 2 diabetes, childhood obesity, and adult obesity.

The genetics researchers zeroed in on single changes in the sequence of letters that make up the DNA coding for the PC-1 gene. In a variant called the q allele, they found that two such mutations, known as SNPs, increased production of the protein in both cells and in the blood.

The finding is the strongest evidence yet that PC-1 is a cause of insulin resistance, type 2 diabetes and obesity, according to Dr. Goldfine and the French scientists.

Smoking Linked to Metabolic Syndrome in Teens

Teenagers who smoke or are exposed to secondhand smoke – especially those who are overweight – are at increased risk for developing metabolic syndrome.

According to researchers from the University of Rochester who reported their findings in *Circulation*, nearly 25% of all overweight teens who smoked had the metabolic syndrome versus 5% of those who did not smoke nor were exposed to secondhand smoke.

Michael Weitzman, MD, of the University of Rochester and executive director of the American Academy of Pediatrics Center for Child Health Research said having any exposure to smoke increases the risk of developing metabolic syndrome by fivefold. Being an active smoker increases the risk by at least sixfold.

In an interview, Dr. Weitzman said: “The obesity epidemic is a truly worrisome and consuming issue, and these data demonstrate that there are certain subsets of overweight young people who are especially at risk for premature morbidity and mortality for cardiovascular and diabetic related complications.”

The study of 2,273 adolescents aged 12 to 19 years, found that metabolic syndrome risk increased in relation to the amount of cigarette smoke adolescents were exposed to. The investigators used data from the National Health and Nutrition Examination Survey III. Overall, 5.6% of the patients in the study had the syndrome. Those teens who did not smoke had a 1.2% occurrence of metabolic syndrome versus 5.6% for those with some smoke exposure and 8.7% for those who were current smokers ($P < .001$).

The researchers found that the effects of cigarette smoke were even more dramatic in overweight teens. Among this group, 5.6% of nonexposed adolescents had metabolic syndrome versus 19.6% of exposed teens and 23.6% of active smokers ($P < .01$).

Many CKD Patients do Not get Recommended Care

Many older adults with chronic kidney disease (CKD) do not receive the screening tests and basic preventive care rou-

tinely recommended for patients with this condition, according to a report in the *Journal of the American Society of Nephrology*.

Research led by Annamaria T. Kausz, MD, of Tufts-New England Medical Center obtained data from 2,500 elderly Medicare recipients with CKD who eventually required dialysis. The investigators reviewed records to evaluate routine medical care the patients received 2 years before dialysis.

The results showed that there were shortcomings in general health and CKD care. For example, many diabetic patients did not receive routine tests to detect diabetic complications. Specifically one-third did not have an eye exam in the 2-year study period and another one-third did not have cholesterol and other lipid levels checked. One-quarter of the diabetic CKD patients did not have their HbA1c levels checked.

According to a news release from the American Society of Nephrology, rates of other important tests were also low, including screening for various cancers. Only half of patients had recommended tests for anemia and 15% had testing done of parathyroid hormone levels. CKD patients were less likely than other patients to receive common vaccines.

According to the report, overall medical care for patients with CKD was similar to that for a comparison group of about 1 million Medicare patients without CKD. It wasn't that health care was neglected for the CKD patients, the investigators said, it was that their suboptimal care reflected a “generalized lack of implementation of recommended health care measures” for elderly Medicare recipients. The researchers noted that because both groups were Medicare patients, the shortcomings did not reflect issues with health care access.

Genetic Regions Determine Response to Exercise, Linked to Prediabetes

The response to exercise is not the same in every person, and genetic makeup may be partly responsible.

People differ in how exercise alters their blood sugar equilibrium, an effect demonstrated in a study by researchers at Washington University School of Medicine in St. Louis and other institutions in the HERITAGE Family Study. The divergence in exercise response allowed researchers to identify regions on

chromosomes 6, 7, and 19 that are linked to prediabetes. Their report appeared in *Diabetologia*.

"There's no question that prediabetes and type 2 diabetes have a genetic basis," said lead author Ping An, MD, research assistant professor in genetics and biostatistics, in a news release. "The rising incidence of type 2 diabetes makes it more important to locate the genes so they can lead to effective intervention and treatments."

A total of 441 nondiabetic, sedentary parents and offspring in 98 white and 90 black families participated in supervised aerobic exercise for 20 weeks. Researchers measured insulin action and glucose metabolism at baseline and endpoint.

"At the end of the exercise program, the insulin sensitivity of the participants had improved overall – they needed to produce less insulin to handle the same amount of glucose intake," Dr. An said. "But, the amount of improvement varied across families and family members. This variation allowed us to locate sites on the chromosomes associated with dynamic prediabetes traits."

An area on chromosome 19 showed the strongest link to training response among black participants. That link was revealed by the effect of exercise on glucose metabolism and indicated that chromosomal location is likely to contain gene variants that influence the propensity for prediabetes. Very close to the area identified, a vital gene for storing glucose in the form of glycogen within skeletal muscles is located. Patients with type 2 diabetes often have impaired glycogen storage.

Although not as strong, other links to prediabetes traits were found on chromosomes 6 and 7 among the white participants in the study. These locations have been shown to contain several genes related to fat and glucose metabolism, insulin sensitivity and glucose-induced insulin secretion.

Coffee Drinkers Have Lower Type 2 Diabetes Risk

A review into the effects of coffee on type 2 diabetes has shown that those people who drink coffee as a habitual action have a lower risk of developing the disease.

Reported in the *Journal of the American Medical Association*, American and Dutch investigators performed a systematic review of literature and found 15 epidemiological studies and nine cohort studies that dealt with habitual coffee consumption in type 2 diabetic patients. These studies accrued data from 193,473

participants, 8,394 of whom had diabetes.

Patients were categorized by the amount of coffee they drank. The first group drank zero to two cups per day, the second drank four to six cups of coffee and the third group drank between six and seven cups of coffee each day. In the second and third groups, the relative risk (RR) of developing type 2 diabetes was 0.72 and 0.65 compared to the first group of coffee drinkers. When data was adjusted for obesity, sex or region, results were similar. "In the cross-sectional studies conducted in northern Europe, southern Europe and Japan, higher coffee consumption was consistently associated with a lower prevalence of newly detected hyperglycemia, particularly postprandial hyperglycemia," they wrote. Investigators concluded that habitual coffee consumption may lower the risk for type 2 diabetes by a significant amount.

Active People Who Slow Down are at Risk for Diabetes

Veterans who are returning home from active duty service may be at an increased risk for diabetes because of the change from an active to sedentary lifestyle.

This is most likely to occur in veterans who have a high-fat diet, investigators from Ohio University have suggested. These people should avoid foods high in fats, limit carbohydrates and continue to exercise regularly. Veterans face a high risk of diabetes because of the dramatic changes in lifestyle that often follow military service, and there is speculation that type 2 diabetes may be connected to military service, especially in Vietnam vets, the investigators noted.

"After serving in the military, many veterans want to come home and relax," said Andrew Razzano, undergraduate researcher at Ohio University. "The trouble is that these are precisely the kinds of behaviors that can pave the way for type 2 diabetes."

John Kopchick, MD, professor of molecular biology at Ohio University is heading up a study to determine the risk factors associated with sedentary lifestyles of veterans. Dr. Kopchick and colleagues are looking at specific genes in blood serum that may activate or become inactive to cause type 2 diabetes.

From this study, investigators hope to develop better diagnostics and therapies. The study is being performed in conjunction with the America's Armed Forces, AMVETS.

Diuretics Effective for People with Diabetes, Hypertension

In people with diabetes, diuretics work as well as angiotensin-converting enzyme (ACE) inhibitors and calcium channel antagonists in protecting against myocardial infarction (MI) and improving survival. They also offer more protection against congestive heart failure.

The latest findings from ALLHAT, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial, were published in the *Archives of Internal Medicine*.

ALLHAT, sponsored by the National Heart, Lung, and Blood Institute (NHLBI), is the largest study to compare these three major classes antihypertensives. The study originally reported in 2002 that diuretics were more beneficial as initial treatment for high blood pressure for protecting against adverse cardiovascular outcomes. This latest analysis shows that even among diabetic patients and those with mildly elevated fasting glucose, the less costly diuretics are at least as effective, and may be more beneficial for some people, according to a NHLBI news release.

About 73% of adults with diabetes have hypertension, which in diabetic patients is defined as $\geq 130/80$ mm Hg or use of prescription medications for their hypertension.

"Controlling high blood pressure is an urgent concern especially for people with diabetes. Our findings demonstrate the advantages of diuretics in diabetic [patients] as well as in those with impaired and normal fasting glucose levels," said NHLBI director Elizabeth G. Nabel, MD. "As a physician, I have seen the consequences of poorly controlled hypertension and diabetes. These results show many people and their families can be spared that devastation."

ALLHAT was a randomized double-blind trial involving 42,418 participants with high blood pressure, aged ≥ 55 years. Of those, 31,512 participants were randomized to a diuretic, a calcium channel antagonist or an ACE inhibitor. In the group, 13,101 had diabetes, 1,399 had elevated fasting glucose and 17,012 had normal glucose levels.

Compared with the ACE inhibitor and the calcium channel antagonist, the diuretic was:

- more protective against congestive heart failure in patients both with and without diabetes;
- more effective in lowering systolic blood pressure among those with and without diabetes;
- at least equally protective against fatal coronary heart disease or non-fatal MI in people with diabetes, those with elevated fasting glucose and nondiabetic patients;
- equally protective against death from all causes, end-

stage kidney disease, or cancer in people with diabetes, those with elevated fasting glucose, and nondiabetic patients; and

- more protective in black patients, against stroke in people with and without diabetes (compared with ACE inhibitor).

"This study shows the advantage of diuretics for preventing congestive heart failure in most people with high blood pressure, regardless of diabetes status," said Jeffrey Cutler, MD, NHLBI senior adviser.

Diabetic Patients at Increased Risk of Common Infections

Both type 1 and 2 diabetic patients are at higher risk of contracting respiratory, urinary tract and skin infections than people without diabetes.

Previous studies have indicated a possible relationship between diabetes and infections, but most of the studies have been retrospective and analyzed previously collected data, according to a study published in *Clinical Infectious Diseases*. This research prospectively compared about 7,500 diabetic patients with 19,000 control patients to examine the link between diabetes and infections.

The researchers found that compared to patients in the control group, the odds were significantly higher that both type 1 and type 2 diabetic patients would develop infections of the respiratory and urinary tracts, skin and mucous membranes. In fact, patients with type 1 diabetes were twice as likely to develop a urinary tract infection as nondiabetic patients. Diabetic patients risk for recurring infection was also higher.

"Physicians should be aware of the fact that diabetes patients have an increased risk of common infections," said Leonie Muller, MSc, of the University Medical Center Utrecht, in the Netherlands and lead author of the study. "Further research should focus on the prognosis of common infections in patients with diabetes, thereby providing physicians tailored information on which patients are at high risk."

Americans' expanding waistlines carry a heightened risk for diabetes, which could also mean heightened risk for infections, according to a news release from the Infectious Diseases Society of America.

"With increasing rates of type 2 diabetes patients, some common infections of the lungs, bladder and skin will also be more common in this group," Ms. Muller said, but more research is needed on obesity as an isolated risk of

infections resulting from diabetes.

Diabetic patients “should realize that they are at increased risk of common infections,” said Ms. Muller, so that they can take preventive measures, including influenza vaccination, drinking plenty of fluids and leading a generally healthy lifestyle. “Moreover, they might pay attention to signs indicating an infection at an earlier stage and contact their physician for advice.”

Fracture Risk Increases With Diabetes

Because older adults with diabetes are at a higher risk for bone fractures, there is a need for fracture prevention programs, wrote investigators reporting in the *Archives of Internal Medicine*.

Elsa S. Strotmeyer, PhD, and colleagues conducted the Health, Aging and Body Composition Study to evaluate the association of type 2 diabetes in older black and white individuals to bone fracture. They also studied bone fracture incidence in patients with impaired fasting glucose.

Patients were aged between 70 and 79 years, and were assessed for the difference in bone mineral density (BMD) between those with and without fractures and with and without diabetes. Within patients that had the same BMD, incidence of fracture was more persistent in patients with diabetes. The elevated risk of fracture in diabetic patients was RR 1.64, and patients with a fracture were also inclined to experience a loss of peripheral sensation. Those patients with impaired fasting glucose did not have an increased risk for fracture (RR 1.34).

“Fracture prevention needs to target specific risk factors found in older adults with diabetes mellitus,” investigators concluded.

Very Early Premies Face Risk of Adult Kidney Failure

Babies born before the 32nd week of pregnancy and small for their gestational age may be at increased risk of reduced kidney function in young adulthood.

A Dutch collaborative study group, led by Mandy G. Keijzer-Veen, MD, assessed various kidney function measures in 422 young adults born very prematurely and reported the results in the *Journal of the American Society of Nephrology*. The patients studied had an average birth time of 30 weeks into the pregnancy and an average birth weight of 2.9 lbs. About half of the patients were

considered small for gestational age at birth. The average birth weight in this group was 2.5 lbs, compared to 3.3 lbs in babies born appropriate for gestational age.

At 19 years, kidney function test results were within the normal range for all of the former premature infants. Several measures of kidney function were significantly related to birth weight, where kidney function was lower for subjects with lower birth weights, according to a news release from the American Society of Nephrology.

However, the link between birth weight and kidney function was significant only for patients who were small for gestational age. For patients appropriately sized for gestational age group, birth weight was unrelated to kidney function. None of the kidney function measures was related to adult weight.

Microalbuminuria was found in nearly 3% of the patients. This finding was more than twice as common in subjects born small for gestational age: 3.8% versus 1.6% in the appropriate for gestational age group.

The researchers said that previous studies have linked low birth weight to problems with kidney development. Low birth weight may lead to a reduced number of nephrons, meaning that the remaining nephrons must work harder, eventually leading to reduced kidney function. Kidneys continue to develop until the 36th week of pregnancy. The combination of prematurity and being born small for gestational age – also known as intrauterine growth retardation – may increase the risk of kidney failure even further.

Kidney function normally begins to decrease after age 20 years. The new results suggest that this process may be accelerated in very premature babies who are born small for gestational age. If so, then these babies may be at increased risk of kidney failure later in life.

Oral Contraceptives May Increase Nephropathy Risk

According to a study published in *Diabetes Care*, people who use oral contraceptives may be at risk of developing macroalbuminuria and diabetic nephropathy.

Sofia B. Ahmed, MD and colleagues studied the renin angiotensin system (RAS), which is activated by oral contraceptives. Women who are using oral contraceptives, including healthy women, may experience RAS. Furthermore, if RAS is activated, it may be a risk factor for nephropathy and/or diabetic nephropathy. The goal of the study was to assess the correlation between oral contraceptive use and the risk for nephropathy.

Investigators enrolled nondiabetic and diabetic women and followed them for 20.7 years. Patients were split into four groups: nondiabetic patients not on an oral contraceptive, nondiabetic patients on an oral contraceptive, diabetic patients not on an oral contraceptive and diabetic patients on an oral contraceptive.

The renal plasma flow was calculated with captopril to determine RAS activity in all four groups. It was determined that nondiabetic patients not taking a contraceptive did not have a significant response of renal plasma flow in response to captopril, but the response experienced by nondiabetics taking an oral contraceptive was significant. The most significant renal plasma flow and RAS activity was seen in the group of diabetic patients using oral contraceptives. Investigators reported that macroalbuminuria developed in 18% of the patients on an oral contraceptive versus 2% in those who did not take an oral contraceptive. They noted that its use may be considered as a risk factor for developing diabetic nephropathy.

Anti-CD3 Antibody Preserves Beta-Cell Function in Type 1

Short-term treatment with an anti-CD3 antibody (ChAglyCD3) can preserve residual beta-cell function and decreases the insulin need for at least 18 months in people with recent-onset type 1 diabetes, according to the Juvenile Diabetes Research Foundation (JDRF).

The phase 2 clinical trial was reported in the *New England Journal of Medicine*. It involved 80 newly diagnosed patients and was conducted in collaboration with a team of clinicians and researchers from France, Belgium, Germany and England.

The team found that patients who received the antibody over 6 days immediately following their diagnosis continued to produce their own insulin and needed less supplemental insulin to maintain normal blood glucose levels versus patients who received placebo. This benefit was apparent at 6, 12 and 18 months after treatment, suggesting that the protective effect is lasting, according to a JDRF news release. Side effects were minor and short-lived.

"These exciting results provide enormous hope that we can preserve residual beta-cell function by modulating the autoimmune attack and in fact change the clinical course of type 1 diabetes," said Richard Insel, MD, JDRF executive vice president for research. "There is no other current treatment that can actually change the clinical course once the disease has begun. This study shows we

are on the right track, and opens the door for researchers to target this treatment specifically to individuals who would receive the most benefit."

This clinical trial extends a JDRF study that used a similar antibody. It was published in 2002. The current study takes the previous research — as well as anti-CD3 research overall — a step further by involving a much larger group of patients and recording how much residual beta-cell function each patient had at the beginning of treatment. This allowed the investigators to track and compare ChAglyCD3's effect on patients who had high and low residual beta-cell function initially to see how well the drug worked with patients in both categories.

The team observed that ChAglyCD3's protective effect was more pronounced in patients who had higher beta-cell function at the time they received the drug. Interventions that can preserve endogenous insulin production are expected to result in better metabolic control of diabetes, and thus delay or reduce the risk of microvascular complications.

New-onset Diabetes in Older Patients Could Signal Cancer

In nearly 1% of patients aged ≥ 50 years diagnosed with new onset diabetes, the underlying cause of diabetes was pancreatic cancer.

According to Suresh Chari, MD, of the Mayo Clinic College of Medicine, this is nearly eight times the rate that is expected in the normal population. Dr. Chari and colleagues published their findings in *Gastroenterology*.

This finding, based on a retrospective study of 2,122 Rochester, Minn residents, added to the increasing evidence that diabetes may be a consequence of pancreatic cancer, Dr. Chari said. It also suggests that testing for hyperglycemia may be able to detect this type of cancer early and at a potentially curable state. Pancreatic cancer rarely exhibits physical symptoms until it is advanced and most often incurable. Of the 32,000 patients diagnosed yearly, almost all die.

According to Dr. Chari and colleagues, key questions have to be addressed by prospective studies before diabetes or hyperglycemia tests could be used to identify pancreatic cancer in its early stage.

"The success of the strategy to use hyperglycemia as a screening tool to identify subjects with a high likelihood of having underlying undiagnosed pancreatic cancer will depend largely on our ability to differentiate pancreatic-cancer induced diabetes from type 2 diabetes using a serological marker," the researchers concluded. ■