



screen large numbers of compounds for biological activity, but we've gotten to the point where we've studied most of the molecular entities," Nissen said. "So now we're shifting to drug discovery based on gene products, proteins, and what they can do for targeted therapy."

In any case, the reporting of negative findings from clinical trials at major meetings is to be welcomed, regardless of their implications about the state of the field, Gardner said.

Researchers sometimes "get invested in their own theories and hate

to give up on them, and sometimes even overlook or downplay the negative findings because it diminishes their whole body of research," he noted. "But the importance of a negative study is to have it out in the open so we can learn from it and move on." □

## UNDERSTANDING GENES

Nissen estimates that it may take a decade before researchers have a good enough understanding of the workings of genes to design new approaches for reducing cardiovascular disease risk.

"The problem is that while we've mapped the genome, we don't know how it works exactly," he said. "So we develop a new compound that affects maybe 50 genes, but we don't know what all those genes do, and we're seeing a lot of off-target effects."

As an example, Nissen noted his recent study on the peroxisome proliferator-activated receptor agonist, muraglitazar (Nissen SE et al. *JAMA*. 2005;294:2581-2586). This agent was awaiting approval by the US Food and Drug Administration for controlling blood glucose levels in patients with type 2 diabetes. But Nissen and colleagues found muraglitazar was associated with an excess incidence of death, major adverse cardiovascular events, and congestive heart failure. "We don't know exactly which genes are responsible, and this compound was off target."

But while some in the cardiovascular research community may be turning to gene-based research, Timothy Gardner, MD, chairman of the AHA's scientific program committee for the annual meeting, said the negative trial findings presented in November do not signal the end of positive results for conventional therapeutic studies.

"I totally disagree that [these negative trials] are a sign that we've reached an end," said Gardner, who is also the medical director, Center for Heart and Vascular Health, Christiana Care Health Services in Wilmington, Del. "We may have reached the limit with certain types of drugs, but we're still making new observations and creating therapeutic strategies with conventional methods."

# Shift Seen in Patterns of Drug Use Among Teens

Bridget M. Kuehn

**T**HE LATEST DATA ON ADOLESCENTS' attitudes about and use of drugs suggest a decline in the abuse of illicit drugs by older teens. But it also offers some indications that declines in drug use may be slowing among the youngest teens and that many teens continue to abuse prescription drugs.

Results from the annual Monitoring the Future survey, which each year collects data on the attitudes and drug use habits of a nationally representative sample of about 50 000 students in grades 8, 10, and 12 at public and private schools, provide a nuanced picture of drug use patterns among teens. About 16% of students in grades 8, 10, and 12 reported abusing illicit drugs in the past month compared with 19.4% in the 2001 study. But the trend of declining use may be ending for the younger students, reported the researchers from the University of Michigan who conducted the study. For example, 2005 was the first year since 1999 that the reported rate of illicit drug abuse among 8th graders during the past 30 days did not decline from the previous year, with 8.4% reporting such use in 2004 and 8.5% in 2005.

Smoking rates among 10th and 12th graders reached an all-time low since the survey's inception in 1975, although declines in smoking among 8th graders seem to have leveled off. A little more than 23% of 12th graders reported using cigarettes in the past 30

days and 13.6% reported daily use. The number of 8th graders who reported use of cigarettes in the past 30 days was 9.3% in 2005, which was a tenth of a percentage higher than in 2004, and only 4% reported daily use in 2005, which was down a few tenths of a percentage from the previous year.

Alcohol use among adolescents also has declined over the last several years, although it remains the most widely used drug represented in the survey, with 50% of all 12th graders, 33% of all 10th graders, and 17% of all 8th graders reporting alcohol use at least once in the preceding month. Rates of abuse of prescription drugs remain high,



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Alcohol use and smoking have declined among US adolescents but remain the drugs that are most frequently used by teens.



particularly among 12th-grade students. For example, 1 in 11 high school seniors reported they had taken hydrocodone for nonmedical purposes in the past year.

#### GETTING THE MESSAGE

Nora D. Volkow, MD, director of the National Institute on Drug Abuse (NIDA), which funds the study, attributed the declines in illicit drug abuse among adolescents to a variety of factors, including campaigns aimed at educating youths about the dangers of using such drugs, as well as research that has provided more information about the effects of drugs on the developing brain. Decreased availability of some drugs, such as LSD, also was a factor, she said.

In particular, research on the consequences of repeated drug administration and how these effects are different in adult and adolescent brains has helped provide young people with information that is salient to them, Volkow explained.

"It has made these kids realize it's not just someone telling them 'don't take drugs,' but someone telling them in an objective way why they shouldn't be taking drugs," she said.

Still, half of all students will have tried an illicit drug by the time they finish high school, so there remains room for improvement, according to Lloyd Johnston, PhD, a researcher at the University of Michigan Population Studies Center and the survey's principal investigator. Also, according to Johnston, there are some indications that the declines may represent a cohort effect, in which a particular birth or class cohort continues to have a higher or lower rate of abuse than other cohorts as it ages. The observation that the declines in illicit drug use seen among the older teens in the current survey were present as they moved through grades 8 to 12, as well as the finding that the rate of illicit drug use among 8th graders in 2005 was not lower than that seen among 8th graders the previous year, suggests that a cohort effect may explain the declines in drug abuse among teens in recent years.

The fact that cigarette smoking has reached an all-time low among these adolescents is also a notable public health achievement. Volkow explained that this is important because individuals who initiate smoking in adolescence are more likely to become addicted than those who first smoke as adults, so even if these teens try smoking later in life they are less likely to become hooked.

#### PRESCRIPTION ABUSE

While illicit drug use has declined, abuse of prescription drugs, particularly painkillers, has remained high. Nearly 10% of high school seniors reported taking hydrocodone during the past year and 5.5% reported taking oxycodone.

Volkow noted that adolescents may perceive these drugs as safer than illicit drugs, in part because physicians prescribe them. Also advertisements for pharmaceuticals and portrayals of the use of prescription medications in movies and on television may leave young people with the impression that all prescription drugs are widely used.

"We are giving that false security and kids are struggling with this notion that these are safer drugs," she said.

The drugs are also easy to come by. In some cases, adolescents themselves may have a prescription for these drugs or access to drugs prescribed to their parents. However, Volkow said, she believes most of the prescription drugs being abused come from Internet pharmacies that provide them without prescription to the adolescents themselves or to drug dealers. Volkow said the National Institute on Drug Abuse will support or conduct future studies aimed at learning precisely where students are getting the drugs.

In the meantime, she urged physicians to be alert for the potential diversion of painkillers. They should warn parents who are being prescribed painkillers to destroy leftover pills. They also should consider signs of vulnerability to addiction—such as a personal or family history of drug or alcohol abuse—when they weigh the costs and benefits of prescribing these drugs.

Information about the NIDA-funded survey, *Monitoring the Future*, is available at <http://www.monitoringthefuture.org>. □

## Group Launches Peripheral Arterial Disease Guidelines

Mike Mitka

**M**ORE TIMELY DIAGNOSIS IS needed for patients with peripheral arterial disease (PAD), a condition that can lead to disability and is associated with an increased risk of stroke, myocardial infarction, and death. But the condition is frequently overlooked due to subtle physical findings and a lack of classic symptoms. To aid in diagnosis, new PAD guidelines were issued in December by the American Heart Association and the American College of Cardiology.

PAD, as defined by the guidelines, encompasses "the vascular diseases caused primarily by atherosclerosis and throm-

boembolic pathophysiological processes that alter the normal structure and function of the aorta, its visceral arterial branches, and the arteries of the lower extremity." Untreated, PAD, which affects more than 12 million people in the United States, can lead to amputation, aortic aneurysm rupture, severe hypertension, and kidney failure. A substantial number of patients also have claudication, which can at times be nearly disabling. Another important reason for physicians to test for PAD is that it frequently serves as a marker for widespread atherothrombotic disease. Not surprisingly, the major causes of death in PAD patients are myocardial infarction and stroke.