

## Getting an Edge — Use of Stimulants and Antidepressants in College

Richard Kadison, M.D.

A college student sought help at our health center because he was having social anxiety and difficulty participating in class discussion. He said he had used an antidepressant drug to combat his social fears when he was in high school but had stopped taking it because he wanted to make a fresh start in college — and because he'd noticed that the medication affected his libido. Now, however, because he was painfully aware that class participation counted for half his grade, he wanted a new prescription for his old medication.

Around the same time, I saw another student who, he told me, had always been distractible, even while in his academically nonrigorous high school. When he started college, he found that he had trouble managing his time and maintaining his focus. When his roommate offered him some methylphenidate to help him study for an exam, however, he discovered that he could stay up much later than usual and concentrate on his work. He looked up the symptoms of attention deficit-hyperactivity disorder (ADHD) online, believed he had several of them, and came into the health center wanting to try medication to help him study more effectively.

Like most students, these two young men were probably fed the usual clichés before they left home — among them, cherish your college years; they're the best years of your life. Unfortunately, for many college students, the reality does not live up to the promise. In fact, the current rates of

depression, stress-related symptoms, insomnia, and eating disorders in U.S. colleges and universities are staggering; not surprisingly, so are the rates of substance abuse. In a recent national survey of 13,500 college students, nearly 45 percent reported being so depressed that they had difficulty functioning, and 94 percent reported feeling overwhelmed by everything they had to do.<sup>1</sup> Various studies have shown that about 45 percent of college students intermittently engage in binge drinking.<sup>2</sup>

Some of these students no doubt meet the criteria for therapy with effective, new psychotropic medications. The trouble is that many more of them, affected by the increased stress of college life — overextended by extracurricular activities taken on in order to build their résumés, sleeping even less than their predecessors, and worrying more than ever about financial, social, and academic pressures — are at risk for misusing or abusing these drugs, which can have serious adverse effects.

The emergence of the selective serotonin-reuptake inhibitor (SSRI) antidepressants and a variety of drugs for treating ADHD has changed the landscape of prescribing for the college-age population. Unfortunately, beyond the legitimate prescription of such medications lies new territory marked by illegitimate, or at least inappropriate, uses of stimulants and antidepressants — practices that are often not even covert. Increasing numbers of students,

and sometimes their families, request medication to provide an “edge,” even if the students have no clinically significant impairment of functioning. They think of such drugs as safe “brain steroids” that help to maximize performance with minimal risk, and they know the symptoms to describe in order to persuade a doctor to write a prescription. Thus, the number of prescriptions has increased dramatically over the past decade; it is estimated, for example, that 25 to 50 percent of U.S. college students who are seen in counseling and at student health centers are taking antidepressants.

At least in part, such consumer demand reflects our bombardment with advertisements imploring us to “ask your doctor if this pill is right for you.” This type of marketing is a double-edged sword, not only raising awareness of common problems such as depression and attention deficits but also implying that there is a magic bullet for complex problems and enticing some healthy people to seek their own magical boost. The challenge for physicians is to determine which patients have a legitimate need for psychotropic medication, particularly given recent warnings about the safety of some of these compounds.

It is true that late adolescence is a common time for the onset of a first episode of depression and that ADHD is the most common childhood psychiatric disorder, affecting 4 to 10 percent of young people in the United States, with as many as half of them

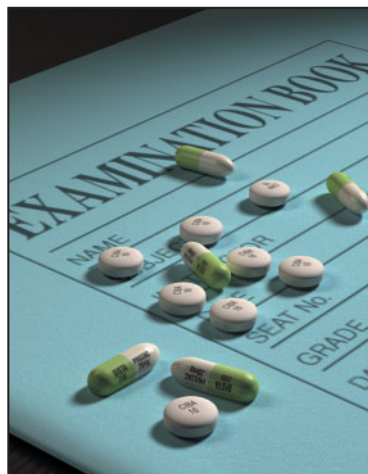
continuing to have symptoms into adulthood. Moreover, many bright students find ways to compensate for the symptoms of ADHD in their early years, so that the disorder reveals itself only with the increased intellectual and organizational demands of college. Depression follows a parallel path, often appearing in late adolescence and worsening during the transition to college. Students with diagnosed ADHD are also three times as likely as their peers to abuse other substances, partly in an effort to ameliorate their attention problems, and students with depression may self-medicate with alcohol or other drugs.

Yet more and more students with symptoms that do not clearly reach the threshold for depression or ADHD have begun seeking psychotropic drugs. When the first SSRI, fluoxetine (Prozac), was released in 1987, it heralded a new age of effective treatments for depression with far fewer side effects than with the older tricyclic drugs. But the SSRIs also quickly came to be viewed as a means of evoking an “improved self,” better than the original, and they began to be prescribed for mild symptoms, to reduce social and generalized anxiety and unproductive obsessive thinking, thereby allowing students to improve their class participation and feel more comfortable in social situations (similar to the use of beta-blockers to reduce performance anxiety).

More recently, stimulants have begun to be used in a similar way — to improve concentration, focus, and alertness. Many students report what they call “pharming”: using stimulants for recreation and to work more efficiently (with

a reduced need for sleep). They may get medications from friends or over the Internet, but many also obtain prescriptions from physicians.

Some studies estimate the frequency of such abuse at 3 to 10 percent among U.S. college students, with a higher frequency among men than women. Most commonly, students use the medications in order to stay up later or study harder before tests. Some



users crush the pills and snort or smoke the powder or, in extreme cases of recreational abuse, inject it intravenously to achieve a more rapid, intense effect. The goal of this approach is to get an intense “buzz,” an effect heightened by the simultaneous use of alcohol or other drugs. This sensation is often the first step on the road to dependence and addiction.

SSRI antidepressants and stimulants affect different neurotransmitter systems and therefore have different therapeutic and side effects. The SSRIs are thought to act, in part, by blocking the presynaptic reuptake of serotonin. Their therapeutic effects include improved mood, social functioning, energy, sleep, and concentration and (often at higher doses)

reduced obsessive thinking and urges to binge on food. In most people, the side effects are minimal. They include mild nausea, headaches, odd dreams, sleep disturbance, decreased libido, and delayed orgasm. Occasionally, there are more serious side effects, especially during the first few weeks of treatment. They can induce anxiety and agitation and, albeit rarely, increase obsessive thinking about suicide.

The stimulants, for their part, appear to affect both dopaminergic and noradrenergic pathways in the brain, with methylphenidate and its siblings blocking reuptake and the amphetamines increasing their availability. Common side effects include sleep problems, jitteriness, abdominal pain, anorexia, and irritability, and the drugs can, in rare cases, cause more serious side effects such as paranoia and psychosis. Stimulants are usually prescribed for ADHD, which is believed to involve impaired function of frontal or frontal-striatal networks, as well as diminished behavioral inhibition.

Since the potential for abuse is high, diagnosing true ADHD requires careful history taking and collateral data from family and teachers, whenever possible, including a detailed assessment of drug and alcohol use. It is crucial to distinguish ADHD from early-onset bipolar disorder, since stimulants can markedly worsen the symptoms of the latter. If the patient is deemed to be at high risk for abusing the medication, it may be prudent to consider the use of a long-acting formulation such as Concerta (methylphenidate), which is difficult to crush and use effectively through the intranasal or intravenous route, or alternative

classes of drugs; Strattera (atomoxetine), a presynaptic norepinephrine-reuptake inhibitor, and antidepressants such as Norpramin (desipramine), Effexor (venlafaxine), and Wellbutrin (bupropion) may be effective, and in patients with concomitant depression or substance abuse, they may be better choices than a stimulant.

College students — and their families — tend to have polar-

ized views about medication: either they embrace these types of drugs as a way of improving their performance or even their lives, or they shun medications as a “crutch” and fear becoming dependent on them. A student’s last visit to a primary care physician before departing for college may offer an ideal opportunity to provide education about medication, warning signs of

common problems, and the need for a balanced lifestyle.

Dr. Kadison is the chief of mental health at the University Health Services, Harvard University, Cambridge, Mass.

1. National College Health Assessment: reference group report. Baltimore: American College Health Association, 2004.

2. Wechsler H, Lee JE, Kuo M, Nelson TF, Lee H. Trends in college binge drinking during a period of increased prevention efforts: findings from four Harvard School of Public Health college alcohol study surveys: 1993–2001. *J Am Coll Health* 2002;50:203-17.

## Wall Street and Clinical Trials

Robert Steinbrook, M.D.

Should physicians sell their expertise and knowledge about clinical research to Wall Street? In recent months, financial relationships between some physicians and the investment industry have come under scrutiny.<sup>1-3</sup> Physicians have been paid to provide investors with general information about therapeutic problems, the mechanism of action of drugs, and the regulatory process. Some of these activities may ultimately have benefit to society. However, some physicians have also allegedly been paid to reveal specific confidential data.

In August 2005, the *Seattle Times* reported that it had found “at least 26 cases in which doctors have leaked confidential and critical details of their ongoing drug research to Wall Street firms.”<sup>2</sup> In 24 cases, according to the newspaper, investment firms had used the information to issue detailed reports to select clients, advising them whether to buy or sell a drug-company stock. In some cases, trading stock on the basis of secret information purchased from medical researchers is illegal. The person who provides the information — an act known

as “tipping,” in legal parlance — may also be breaking the law, even if he or she does not actually buy or sell stock (see box).

One of the reported cases involved a pulmonologist at the University of Pennsylvania who was a member of the data and safety monitoring board for the clinical trial of a drug for pulmonary hypertension. During a conference call in February 2005, before the trial’s results had been announced, he discussed the safety data with analysts. The physician has denied revealing nonpublic information. In July 2005, an oncologist from the University of California, Los Angeles, allegedly discussed nonpublic information about two investigational drugs for kidney cancer during a recorded conference call.

The *Seattle Times* report also described how Smith Barney Citigroup acquired information about a study of a macular-degeneration drug this past spring. The financial firm systematically interviewed study investigators in order to predict the results before they were announced. Many of these investigators subsequently acknowledged accepting money

to talk to investment companies, although none specifically recalled talking to Smith Barney.

Although unlawful insider trading related to biomedical research is not new,<sup>4</sup> the recent allegations point to novel types of wrongdoing. Senator Charles Grassley (R-Iowa), chairman of the Senate Finance Committee, has expressed his outrage about “selling drug secrets” and has asked the Justice Department and the Securities and Exchange Commission to investigate.

The increasing opportunities for physicians to make money by advising not only drug companies but also Wall Street are a response to the rapid growth of private funding for pharmaceutical research and development (see graph). The billions of dollars that may be at stake dwarf the size of the consulting payments, which are typically in the range of thousands to tens of thousands of dollars. One of the complexities is that some financial relationships between physicians and investors are perfectly legal, even if they are ethically problematic.

If investors know what they are doing, they can make money