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WHAT'S NEW

Survey: Many Middle Schools 'Drug Infected'

CASA data point to the need for new treatment programs for adolescents with drug problems.

BY DIANA MAHONEY

More than one-quarter of the nation's school students say drugs and gangs are rampant in their middle and high schools, and almost half report that they are aware of drugs being sold or used on school grounds, a Columbia University report shows.

The 15th annual "National Survey of American Attitudes on Substance Abuse XV: Adolescents and Parents," conducted by the university's National Center on Addiction and Substance Abuse (CASA), found that 5.7 million (27%) of the country's 12- to 17-year-old public school students attend schools where drugs are used, kept, or sold and where gangs are present.

The study also found that 32% of middle school students specifically said drugs are used, kept, or sold at their school—which represents a 39% increase since last year, when 23% of middle school students reported their schools to be "drug infected." It also found that about 66% of high school students reported attending drug-infected schools, which represents a slight but steady rise since 2006.

Gang activity, which was included in the survey for the first time this year, appears to be an important marker of drug activity. Compared with their counterparts, adolescents in schools with gangs were nearly twice as likely to report that drugs are used, kept, or sold on school grounds (30% vs. 58%), according to the report (www.casacolumbia.org/templates/publications_reports.aspx).

"These data are particularly troubling," Dr. Mark S. Gold said in an interview when asked about the CASA report. "It is difficult enough to learn and compete in this global economy without having drugs on school grounds, gangs, and likely sales

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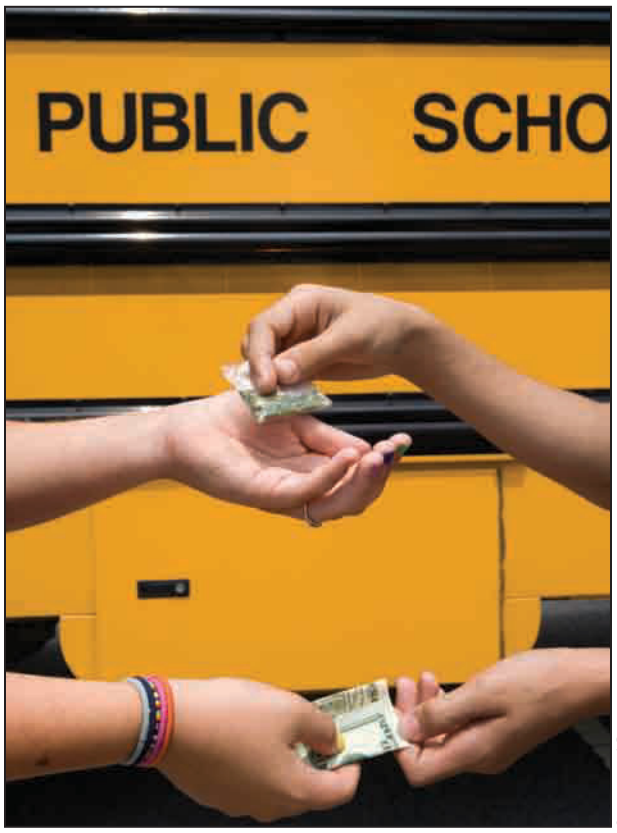

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Adolescents reporting drugs and gangs at their schools were five times more likely to have used marijuana.

PRACTICAL PSYCHOPHARMACOLOGY

Consider Carcinogenicity of Psychotropics

Preclinical and epidemiologic studies reveal sharply disparate carcinogenic profiles of drugs commonly used in psychiatry, offering some degree of reassurance about certain drugs, including many benzodiazepines, but suggesting that caution might be needed in long-term prescribing of atypical antipsychotics.

Antidepressants fall into a middle ground, with available data revealing a potentially high risk of carcinogenicity in 40% of monoamine oxidase inhibitors (MAOIs), 33% of modern antidepressants (including selective serotonin reuptake inhibitors [SSRIs]), and 22% of tricyclic antidepressants.

Dr. Juan F. Gálvez-Flórez and his associates at Tufts Medical Center in Boston reviewed available pharmacologic records and published studies from 1965 to 2009 and found that carcinogenic data exist for two-thirds of psychotropic drugs, but that the research is spotty and often inconclusive.

Despite the shortcomings underlying available data, the body of evidence is deserving of consideration by prescribers and largely unknown to clinicians, said Dr. Gálvez-Flórez at the annual meeting of the American Psychiatric Association in New Orleans.

"Our patients are chronic," he said. "Patients with bipolar disorder or schizophrenia or depression … take medications for years, for decades. This should be a great concern for everyone in this audience and all practicing psychiatrists."

Ideally, clinical trials should include carcinogenicity as a primary outcome measure, and longitudinal trials should examine carcinogenicity of classes of drugs and specific agents, in order to give clinicians a better sense of the risk/ben-

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Amphetamines Show High Risk

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efit equation when prescribing psychotropic agents, he recommended.

Dr. Gálvez-Flórez pointed to the huge Women's Health Initiative trial that was necessary to identify substantial, previously unsuspected risks of hormone replacement therapy, and suggested that a similar effort would seemingly be warranted for the most widely prescribed psychotropic drugs.

For now, preclinical data, epidemiologic studies, and a handful of case-control studies provide the only window into many drugs' potential to increase patients' risk of cancer. The few clinical trials exploring carcinogenic risks have produced mixed results and are marred by a failure to control for myriad confounding factors, he said. "This is a summary of our current knowledge," said coinvestigator Dr. Nassir Ghaemi, director of the mood disorders and psychopharmacology programs at Tufts University, Boston, in a telephone interview. "What this provides is an awareness that the medical risks of these agents cannot be taken for granted."

Before he became involved in the review, Dr. Ghaemi said he gave no consideration to carcinogenicity of antidepressants, even when prescribing to patients with a history of cancer.

Now, he said he would attempt to choose an agent with the least amount of carcinogenic potential based on preclinical data, assuming other prescribing considerations were equal.

With regard to antidepressants and breast cancer risk, conclusions about class-wide data remain murky.

A large, Canadian case-control study published in 2002 raised concerns of heightened cancer risk among patients prescribed certain tricyclic antidepressants (amoxapine, clomipramine, desipramine, doxepin, imipramine, and trimipramine) but not others (amitriptyline, maprotiline, nortriptyline, protriptyline) (Br. J. Cancer 2002;86:92-7).

In a follow-up study in 2006 by McGill University, Toronto, researchers from the same research group failed to find significant evidence of the increased risk, but nonetheless saw differences between the two groups of tricyclic antidepressants, with the group of drugs originally suspected of carcinogenicity numerically associated with higher breast cancer risk.

Dr. Gálvez-Flórez maintained that such information, while not definitive, might help to guide prescribing decisions.

No Food and Drug Administration–approved tricyclic antidepressant in the Tufts review showed a low potential risk of carcinogenicity (defined as no positive preclinical or clinical studies or only negative studies). And yet, class wide, the percentage of tricyclics with two or more positive studies of carcinogenicity was lower than that of modern antidepressants or MAOIs.

Within the SSRI class, four medications met the Tufts group's criteria of posing a low carcinogenic risk: fluvoxamine, duloxetine, venlafaxine, and nefazodone. "It was quite shocking to us that sertraline, citalopram, and fluoxetine—which are the main drugs we use in psychiatry—have a high risk of carcinogenicity [according to available data]," he said.

Mirtazapine also fit Tuft's criteria for a high risk of carcinogenicity: two or more preclinical studies with evidence of increased cancer risk.

Among older antidepressants, only moclobemide (which does not have FDA approval) had enough data to convincingly suggest a low carcinogenetic potential, although some, including doxepin and nortriptyline, demonstrated negative genotoxicity in available studies.

Among 15 epidemiologic studies of antidepressants, including 2 that assessed amphetamines, 6 had positive findings, 7 had negative findings, and 2 elicited "questionable" conclusions about carcinogenicity.

Drugs used in the treatment of attention-deficit/hyperactivity disorder also possess varying degrees of available data, and variable levels of carcinogenicity potential, based on that limited data.

Atomoxetine and modafinil both had evidence of low carcinogenic and low genotoxic potential.

Little troubling data exist to suggest that methylphenidate might be carcinogenic over the long-term, but the Tufts group rated it as "intermediate" in terms of potential risk because of the sparsity of data.

Amphetamines were categorized by the group as having high carcinogenic potential. Among antipsychotics, clozapine and mesoridazine demonstrated a low carcinogenicity risk in preclinical studies, while risperidone, olanzapine, quetiapine, aripiprazole, and to a slightly lesser degree, ziprasidone demonstrated a high risk.

Haloperidol, chlorpromazine, trifluoperazine, pimozide, and fluphenazine all were categorized as "intermediate" in carcinogenic potential based on available preclinical data. In seven epidemiologic studies of carcinogenicity of antipsychotics, five found positive evidence of carcinogenicity and two were negative, Dr. Gálvez-Flórez reported. Many benzodiazepines, on the other hand, showed little evidence of carcinogenicity in preclinical studies.

Among mood stabilizers, carbamazepine and oxcarbazepine showed a high risk of carcinogenicity, lamotrigine and lithium showed a low risk, and other agents were deemed to be of intermediate risk in preclinical studies.

"In terms of consistent results, it seems that almost all atypical neuroleptics showed a high potential risk," Dr. Ghaemi said. "This is one class that clearly needs to be studied."

The Pharmaceutical Research and Manufacturers of America declined to comment on this story.

Dr. Gálvez-Flórez has served on the speakers bureau, advisory board, or as a consultant to Eli Lilly, GSK, Pfizer-Wyeth, and AstraZeneca, and has received educational support from numerous pharmaceutical companies. Dr. Ghaemi has received a research grant from Pfizer. ■

By Betsy Bates. Send your thoughts to cpnews@elsevier.com.

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