Talking With Alan I. Leshner, PhD, National Institute on Drug Abuse Director

Brian Vastag

BETHESDA, MD—Since Alan I. Leshner, PhD, took the helm of the National Institute on Drug Abuse (NIDA) in 1994, the agency's annual budget has nearly doubled, to $781 million, supporting much of the world's research on the biology of addiction, genetic and environmental risk factors, and addiction prevention and treatment.

Of the two dozen institutes that comprise the National Institutes of Health (NIH), NIDA is in a unique position. Addiction is, arguably, more politicized than any other medical issue, putting Leshner and his views under a spotlight. He is quoted almost weekly in major newspaper and magazine articles as *the* authority on the subject. Such visibility comes with a price, though, as Leshner has been attacked on all fronts—for being both too soft and too harsh on drug issues.

Before joining NIDA, Leshner enjoyed a highly regarded research career, which largely focused on the biology of behavior. He has also served as acting director of the National Institute of Mental Health (NIMH) and earlier worked at the National Science Foundation, Bucknell University, the Postgraduate Medical School in Budapest, Hungary, and the Wisconsin Regional Primate Research Center in Madison. He has a PhD in physiological psychology.

JAMA: I've heard you say that one of the things you'd like to do is "change the national discourse" about illicit drug abuse and addiction. Does this mean making addiction more of a medical problem and less of a criminal problem?

Dr Leshner: No, no. I am ferociously against polarizing the debate. I think that's one of the terrible problems we've made with this issue. People say that it's either a public health or a public safety issue. The truth is, it's both. And it begins with a voluntary behavior: people choose to use drugs. I don't call it morality, but I call it voluntary. And there's no question it's a medical illness and once you have it, it mandates treatment. It's a myth that millions of people get better by themselves.

National Institute on Drug Abuse

Alan I. Leshner, PhD

But having said that, my own view is that this tendency to polarize the issue has stalled the issue. Now whether you can stop [illegal drugs from] coming across the border or not, I would not pull the plug and increase the [disease] vector. But on the other hand, you've got to worry about the victim, the patient, the collateral damage to society. I try to keep in mind the complexity of the issue because we'll never have a simple solution. And everybody wants to polarize the issue.

JAMA: How does that make your job harder?

Dr Leshner: I hate the fact that people say [illicit drug use] is either a brain disease or an issue of behavior. That's ridiculous. You don't have a separate mind and body; it can be a brain disease and an individual is going to have to be involved in his or her own treatment. That means they have to learn personal responsibility, and that's a behavior. So until we understand this in its complexity, we aren't going to get a handle on it.

JAMA: How far are we from getting a full handle on the biology of addiction?

Dr Leshner: That depends on what you mean by "full handle." Is it the case that the act of engaging in drug use and the contextual cues that surround it become embedded in the addiction? Sure. Do we know that? Absolutely. Do we know a lot of the brain circuits and mechanisms? Absolutely. Do we know all the nitty-gritty about the brain changes? Absolutely not. But we are starting to see how prolonged drug use changes the brain at the level of gross circuit changes, responsivity of the brain, and a whole series of molecular changes that go on with prolonged drug use. To understand that switch mechanism that moves you from being a voluntary drug user to an addict, a compulsive drug user, is to understand the molecular mechanisms. We're getting there; we have a lot of research going on, and it's very rapidly productive.

JAMA: It sounds as if there are specific targets for drug development. There's been a lot of research directed at a dopamine receptor called D_1. Is this a promising target? What are some others?

Dr Leshner: I like the D_1 agonist notion, but I don't think that's the only target. The two big targets for [treat-

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ing cocaine addiction] have been D_1 agonists and substances that block the dopamine reuptake transport. But there are a lot of other targets that may turn out to be very important that go to the common essence of addiction, as well as ones that go to specific mechanisms for specific drugs. We have 60 compounds [for cocaine addiction] in clinical trials, targeting 10 different mechanisms.

JAMA: Which are most promising?

Dr Leshner: One of them that's very promising is disulfiram, Antabuse. There have been a few positive clinical trials that look very impressive. Disulfiram blocks cocaine craving in people. We also have a multisite trial with selegiline [Eldepryl], an antidepressant and anti-Parkinson drug. For a subset of patients, desipramine may be useful; it's also an antidepressant.

JAMA: The drug ecstasy (3,4-methylenedioxymethamphetamine, or MDMA) has been getting a lot of press lately. What specifically should physicians be doing about ecstasy?

Dr Leshner: First of all, they need to understand that it's not a benign substance at all. It's not harmless. It's an incredibly potent stimulant; that's why people love it. It's both a stimulant and a hallucinogen. It causes tremendous increases in blood pressure, heart rate, et cetera. It has a dramatic hyperthermic effect; it increases body temperature tremendously. So it's dangerous in raves [extravagantly energetic dance parties] and situations like that. And it's been shown from a decade of animal research, which is now being confirmed in humans, that ecstasy is toxic to serotonin-containing neurons.

What physicians need to know is that it's dangerous, and that when people come in [with questions about using it], it has to be taken seriously. More and more people are losing control over their ecstasy use. Whether it's truly addicting or not, we don't know. But the fact that they are coming to treatment programs saying, "I can't get control over this" means it has to be taken seriously.

One of the things I'm most interested in is distinguishing between when a compound is a medicine and when a compound is an abusable substance. It can be both, and that is very important for physicians to understand. Morphine is my favorite example, but it's also true of cocaine historically, and it's true of Ritalin [methylphenidate hydrochloride] and a lot of other medications. When used properly under controlled conditions, they're incredibly effective medicines. When misused, they're incredibly addicting.

Now, drugs like ecstasy have been purported to have clinical use, but there's never been a clinical trial demonstrating the efficacy of ecstasy for anything. And the fact that four psychiatrists claim it was useful for them is not evidence (*J Nerv Ment Dis*. 1992;180:345-52). The plural of anecdote is not evidence.

JAMA: Would NIDA support a clinical trial of ecstasy for depression or anything else?

Dr Leshner: We've never received a proposal. If [such a trial] were for a psychiatric therapeutic indication, it would have to go to the NIMH for support. The NIH supports studies on marijuana as a medicine; we support studies on all kinds of things as medicines. There's an awful lot of hype that ecstasy is a medicine, but there's no evidence. And the assertions are not dissimilar to [those made about] LSD [lysergic acid diethylamide] in the '60s and cocaine in the '70s.

JAMA: What you're saying is that the substance itself is not bad, not evil . . . .

Dr Leshner: That's right. It's the way the substance is used. That doesn't mean drug abuse is not bad. The war is not on drugs, the war is not on drug addicts. The war is on drug abuse and addiction, right? That's very important. The reason you want to keep the supply down and the reason you want to control the demand is because you're concerned about the health aspects of it, not because there's something intrinsic in the substance itself. And that nuance, I think, has been hard for people to understand.

If ecstasy turns out to be a wonderful psychotherapeutic drug, let science show that. The assertion that "it saved my life because it gave me great insight" doesn't mean it's true. And the insight could be wrong. The assertion that the insight was terrific is an assertion; it's empirically untestable.

JAMA: Overall drug use has been relatively stable during the past 10 years. What does that say about the nation's entire drug control policy?

Dr Leshner: If you look at national drug policy over the past 5 years, it's certainly moved toward a blending of public health and public safety approaches. We have advocates for treatment in prison, which we've never had before. We have national figures in the new administration advocating for more emphasis on [reducing] demand, but without giving up the emphasis on controlling the border flow and controlling the sales. That's vitally important. We know that availability is a tremendous stimulus to use. So why would we, as public health officials, advocate anything that would increase availability or increase use? But the discourse is moving more and more in the direction [of focus on reducing demand].

JAMA: I recently read that 80% of people arrested for drug crimes are arrested for possession. Is prison the right place for them?

Dr Leshner: I'm the wrong person to ask. Do I think drugs should be legalized? Absolutely not. That's my personal view; it's not a scientific question. It really isn't. The last time we legalized a substance, or manipulated its legality, it did decrease use.

JAMA: You mean alcohol?

Dr Leshner: Absolutely. [Prohibition] had collateral damage, but it did decrease use. And it's very different. If we knew 5000 years ago that alcohol would cause all the havoc it's caused, would we have made it legal? Would we have made nicotine legal if we knew [what we know now] 400 years ago? I don't have an answer.

JAMA: You've talked about making drug treatment part of the medical mainstream. What does that mean?

Dr Leshner: One of the things that's come up five times in the last 2 weeks

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is how few primary care physicians understand addiction as a health issue and how infrequently they discuss it with their patients. We're not asking physicians to become treatment experts, but we want them to see this as a health issue. We want them to talk with their patients, assess their patients, and refer them for specialty treatment just like they would for any other illness. That's what "making it part of the mainstream" means. It means medical schools and residencies giving people enough training that they're comfortable discussing it. The fault does not lie with individual physicians, but with the training that has not included this issue that has tremendous health consequences. So, we want people to understand that [drug abuse] is an illness, to view it as one of the illnesses to screen for in the primary care setting, and to know [where to refer patients].

JAMA: What happens if a physician finds a candidate for treatment but there aren't any treatment slots available?

Dr Leshner: It's conceivable that would happen, but it's not an excuse. Many people who are addicted are privately insured. So they could go to a private treatment program. They could be referred to a treatment provider. It's a myth that all of the addicts are poor Medicaid patients. There are poor Medicaid patients, but there are an awful lot of addicted individuals who can afford treatment.

JAMA: What are the characteristics of good addiction treatment?

Dr Leshner: We've published a paper in *JAMA* on this [*JAMA*. 1999;282: 1314-1316]. We know what makes bad treatment, what makes good. One of the issues is that focusing on drug use per se is too limited a view. This is a whole-person illness and it requires whole treatment. There is no magic bullet. On the other hand, it doesn't mean we don't know how to treat it, either. There's no magic bullet for strokes, for asthma. And these are chronic, relapsing conditions that require management over time; they require compliance by the patient. They require an array of rehabilitative techniques.

JAMA: Does the fact that it often takes more than one pass through treatment before people give up drug use make it harder to argue "We need more treatment"?

Dr Leshner: One of the problems is that people misunderstand treatment. They misunderstand the target of treatment and they think it's just drug use, but it has to be the total functioning of the individual. The goal of drug treatment is to restore functioning, not just to manage somebody's drug use. Being an addict is a way of life and it affects every aspect of life. The problem with the capacity issue is that people don't have great confidence in drug treatment because they think that a single momentary relapse is a failure of treatment, whereas we don't think that if somebody's blood pressure or diabetes relapses. But good drug treatments, that is, successive drug treatments, should increase the interval between episodes until [the user] gets to full abstinence, and then it may have to be maintained over time. That's the treatment approach we advocate.

JAMA: How do you see NIDA informing the overall national drug policy?

Dr Leshner: We're the science guys. Our role is to generate information, and 99.8% of our energy goes toward science, just like any other NIH institute. But what we can do is also educate the public and professionals about the nature of drug abuse and addiction and what to do about it based on that science. We believe that taking a scientific approach to this problem will inform policy. It won't set policy; policy is made on value plus facts. We're just the fact guys. But we are called upon frequently to provide factual information, and we never violate the scientific data.

JAMA: Do you get political pressure to produce certain kinds of facts?

Dr Leshner: Yes, sure. But the thing with us is, don't ask a question you don't want an answer to. Because, from us, as from any other NIH institute, if you ask a question you get a factual answer. So if you're looking for a specific answer, don't come here.

JAMA: Any examples you care to share?

Dr Leshner: No. We have tried very hard—because there are data that show that hyperbole and exaggeration are the enemy of getting a handle on this problem—we have tried to stick to the facts, and I have been accused of being excessively honest. That is, we really draw the line on what we know and what we don't know. And we try not to be hyperbolic. But we are accused, by advocates of a substance, of being exaggerators. And we are accused, by people who hate the substance, of understating the dangers. And so I must be about in the right balance if both sides think we're doing the wrong thing.

JAMA: How does a culture that stigmatizes drug abuse make your job harder?

Dr Leshner: It really is a big issue. Stigma overlays not only addiction itself, but people who work with addicts and people who study people who work with addicts. When I came to NIDA 7 years ago I declared as a goal to have science replace ideology as a foundation for how we approach this topic. And I actually think we're beginning to take a nick at it, partly because people are so frustrated with purely moralistic views on the issue that they're beginning to look to science as a way to help solve the problem.

JAMA: What are some top areas on your research agenda for the next few years?

Dr Leshner: Some of the big stuff has been our treatment initiative. We declared as our millennial goal improving the quality of drug abuse treatment nationwide using science as a vehicle. So that will continue to be a big push. We decided we're going to crank up our emphasis on prevention research, what actually works in preventing drug use. We've had a big portfolio that we're going to increase in intensity and try to hone it down. And we'll keep working at developing new medications. And we'll continue to use the science to inform the public discussion about the issue, in the hope that we can move it forward. ☐

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Immediate Prescription Coverage in Doubt for Medicare Recipients

Rebecca Voelker

CHICAGO—President George W. Bush's plan to offer immediate assistance to help low-income Medicare recipients receive prescription drug coverage is likely to be scuttled in favor of a more comprehensive plan that could take a year to hammer out.

Bush's "Immediate Helping Hand" program, announced during his second week in office, would offer federal subsidies to state programs to help low-income recipients pay for prescription drugs. The president has proposed sweeping Medicare reforms that would cover prescription drugs, but enactment could take years.

Instead of a quick remedy for low-income elderly persons, a more likely scenario is the emergence of a plan by March 2002 that will offer prescription drug coverage for all Medicare recipients, said Ed Howard, JD, executive vice president of the Alliance for Health Reform in Washington, DC.

"I think it will be universal and voluntary, and it may or may not be accompanied by structural reform to the [entire Medicare] program," Howard said during a recent news briefing held at Northwestern University Medical School and sponsored by the university's Medill School of Journalism. The briefing allowed Howard and two other health care advocates to forecast how several pressing health care issues will unfold under the new administration.

"We have a radically altered landscape in Washington," Howard noted.

PROGRAMS ARE SPARSE

Health care was not a decisive issue in the last election, but the debate over Medicare prescription drug coverage captured national attention. About one third of Medicare beneficiaries have no prescription drug coverage. Aside from partisan politics, Howard said one reason Bush's plan for immediate assistance isn't likely to succeed is that state drug assistance programs designed to help the elderly are sparse. Fewer than two dozen states have programs; in all, they cover less than a million people. "Some cover just a few chronic-care drugs," he added.

Another crucial aspect is how coverage would be offered—through the Medicare program or with separate insurance policies. Howard said drug makers are "fearful" of federal price-setting through Medicare, especially with the market for some pharmaceuticals set to burgeon as the oldest baby boomers approach age 65. Democratic leaders favor coverage through Medicare, but Bush supports federally subsidized prescription drug coverage through insurance plans.

Another uncertainty under the new administration is the future of stem cell research. President Bush has said he opposes federal funding of research using stem cells derived from induced abortions. Under current regulations, scientists can conduct research using stem cells but federal funds cannot be used to obtain the cells from human embryos. Biomedical researchers are concerned that Bush may ban federal funding of any research using stem cells derived from induced abortions.

Even so, some research advocates are optimistic. Tommy Thompson, the new Secretary of the Department of Health and Human Services, has openly commended researchers at the University of Wisconsin who isolated stem cells from embryos and created embryonic stem cell lines in the laboratory.

"The good news is that Thompson, with the blessing of the president, has set up a study commission to try to see what the lay of the land is, and see what [the administration's] position would be," said Mary Woolley, president of Research!America, a Washington, DC–based education and advocacy organization.

CROSSING PARTY LINES

Woolley said biomedical research leaders generally feel that the longer the study commission works on the issue, the less quick the administration would be to reverse current rules that allow embryonic stem cell research. She described the issue as "enmeshed inappropriately in abortion politics," but said implications for treatment of such devastating conditions as Alzheimer disease and spinal cord injury are so great that they cross party lines. She mentioned Sen Strom Thurmond (R, SC) as an abortion foe who still may support embryonic stem cell research because his family is affected by diabetes.

"We have our fingers crossed that this won't become a partisan issue," she said.

Antitobacco forces, on the other hand, are wary that new Attorney General John Ashcroft may dismiss a pending Department of Justice lawsuit against the tobacco industry. Carter Headrick, a manager with the privately funded Campaign for Tobacco-Free Kids, said the former Missouri senator's votes on tobacco-related issues rarely agreed with positions of antitobacco groups.

Ashcroft has said he is not predisposed to dismissing the lawsuit. But in a letter to a Missouri state organizer for the Campaign for Tobacco-Free Kids, Ashcroft said he had reservations about the federal government suing a legal industry. Headrick said his organization's concern is heightened because as Texas governor, Bush took no position on the lawsuit and said decisions concerning it should be up to the US attorney general.

Headrick said that while Bush apparently doesn't consider tobacco "as an issue of the presidential level," antitobacco groups plan to lobby the president and Congress to allow the Food and Drug Administration to regulate tobacco products.

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Parents "Letting Rip" at British Pediatricians

Michael Fitzpatrick

DUBLIN—A recent study suggests that as many as two of three pediatricians in the United Kingdom experience violent behavior by patients' relatives each year.

A recent report by Gerry Mackin, MD, of the Little Acorns Pediatric Unit, Derry, Northern Ireland (*Arch Dis Child.* 2001;84:106-108), online at http://www.archdischild.com, reports the results of a survey of 75 pediatricians in three UK regions: Northern Ireland, South Thames, and North West England. The study showed that more than 90% of respondents had experienced at least one violent incident. Nearly two thirds of the incidents had occurred during the previous 12 months.

Surprisingly, said Mackin, aggression came not just from patients' fathers, and various factors were the source of provocation. "Abuse could come from both mothers and fathers, and I found a lot of attacks were the result of parents' drug- or alcohol-associated problems. With a sick child you often have parents who are incredibly stressed, and, of course, some people release their stress by becoming angry or aggressive. The feeling from a lot of the study respondents was that the aggression came from parents just 'letting rip.'"

He also pointed out that because pediatricians often work in trauma and emergency departments and are involved in child protection matters, emotions can run high and tempers can easily be lost.

ABUSE AND THREATS

Mackin studied a population of middle-grade pediatricians (specialist registrars, senior registrars, and experienced senior house officers). Of the 75 physicians questioned, 42 (56%) were women. Threats were reported by 31 (41%) of the recipients and included one death threat and one particularly menacing warning that a paramilitary group in Northern Ireland would be called on to deal with one child's case.

Verbal abuse was the most common type of hostility reported, and four in 10 had been threatened at least once. Although only 5% of the physicians had been physically assaulted, more than one in 10 had been in a situation in which a patient's relative had attempted assault. More than half of the assaulted physicians—both men and women—said that they continued to worry about the incident afterward. Only one person was offered counseling after a violent incident.

Almost none of those who experienced a violent episode had made any formal report to a hospital or outside authorities following such attacks. In the past, said Mackin, medical staff have been reluctant to bring charges after attacks, but that must change. "The only way we can make any change is to formally report any incidents and ensure that hospitals back us up. If it was a violent episode, I feel such cases should be reported to the police and left to them to decide on prosecution." He also called for more training for pediatricians in how to manage aggressive patients and their relatives.

NATIONAL PROBLEM

Although comparable data on violence involving physicians in other medical specialties are not available, a 1999 report from the National Health Service (NHS) in the United Kingdom said that based on information from 364 NHS trusts (health care facilities), there were, on average, 13 violent incidents per trust recorded each month. A total of 96% of NIH trusts had some sort of violence reduction plan in place.

The problem of aggression against health care professionals by British patients was the subject of a book, *Violence in Health Care: A Practical Guide to Coping With Violence and Caring for Victims* (Shepherd J, ed. New York, NY: Oxford University Press; 1994), that has been reviewed in this journal (*JAMA.* 1995;273:1796-1797).

MISCELLANEA MEDICA

• **John J. Regan,** MD, an orthopedic surgeon, has been appointed Director of Research and Education at the new Cedars-Sinai Institute for Spinal Disorders in Los Angeles, Calif. He was previously at the Texas Back Institute in Plano.

• **Gerald L. Mandell,** MD, professor of medicine and Owen R. Cheatham Professor of the Sciences at the University of Virginia School of Medicine, Charlottesville, and **Fred Jones, Jr,** PhD, dean emeritus of the Graduate School at Meharry Medical College in Nashville, Tenn, have been appointed to the National Advisory Allergy and Infectious Diseases Council, the principal advisory body of the National Institute of Allergy and Infectious Diseases, a component of the National Institutes of Health in Bethesda, Md.

• **R. Nathan Link,** MD, has been appointed Chief of Medical Service at Bellevue Hospital in New York City. While retaining his post as assistant professor of clinical medicine in the Division of Primary Care in the Department of Medicine at New York University, Link will be responsible in his new role for the administrative, clinical, educational, and research activities on the Medical Service at Bellevue.

Editor's Note: Miscellanea Medica appears in the Medical News & Perspectives section occasionally. Items submitted for consideration should be directed to the attention of Marsha F. Goldsmith, Editor, Medical News & Perspectives.

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