Letters

Early "Fast Track"

Modern technology may well be a driving force behind the current trend to rapid publication of scientific papers, as Leslie Roberts describes in her News & Comment article (18 Jan., p. 260). Yet more than three centuries ago, when the scientific journal was a new invention, mail was carried by horse, and printing was done by hand, it was possible to publish a scientific paper in a few weeks.

Isaac Newton's discovery of the compound nature of sunlight, published in *Philosophical Transactions*, no. 80 (19 February 1672), was the first major scientific discovery to be announced in a journal rather than a book (*1*). Just 7 years earlier, Henry Oldenburg (the "obscure secretary of the Royal Society of London" mentioned by Roberts) had founded *Philosophical Transactions*, the first periodical devoted solely to scientific matters. Newton's paper was dated "Cambridge/ Feb: 6th" and was received by Oldenburg in London on 8 February. The paper was therefore published in a near record 11 days after receipt. If in a skeptical spirit we choose to doubt that that issue actually appeared on its publication date, the paper was still published—at the outmost—in an impressive 32 days, for on 11 March, Oldenburg sent a copy of that issue to Christiaan Huygens in Paris.

The "fast track" also appears to have been established at this time. Although Newton was a young, unpublished professor, he was a rising star of English science. Shortly before Christmas 1671, his reflecting telescope (the first ever constructed) was greeted with great acclaim by the Royal Society, and Newton was immediately elected a Fellow. On 18 January, Newton advised Oldenburg that he was preparing another contribution that he considered "the oddest if not the most considerable detection which hath hithertoo beene made in the operation of Nature" (*1*, pp. 82–83). The week before the paper arrived, he promised Oldenburg he would soon dispatch his paper.

The refereeing process, however, was rather different then. The negative report of Robert Hooke, at the time England's leading authority on optics, neither halted nor even delayed publication. After Hooke delivered his critical report to the Society on 15 February, it nonetheless decided that "the printing of Mr. Newton's discourse . . . might go on" (*1*, p. 115). The matter did not end there, for the two carried out a notorious, rancorous dispute over the course of many years.

ALAN E. SHAPIRO
Program in History of Science and Technology, University of Minnesota, Minneapolis, MN 55455

NOTES

1. The chronology recounted here may be readily established from *The Correspondence of Isaac Newton, Vol. 1, 1661–1675* [H. W. Turnbull, Ed. (Cambridge Univ. Press, New York, 1959)].

Drug Abuse Policy

A. Goldstein and H. Kalant ("Drug policy: Striking the right balance," 28 Sept., p. 1513) discuss the ethical options facing policy-makers and argue for reducing both the supply and demand of illegal drugs. However, abuse of legal, presciption drugs accounts for the majority of drug-related emergency room visits, 70% of all drug-related deaths, and more injuries and deaths than all illegal drugs combined (*1*). More than 300 million doses of drugs that are regulated by the Controlled Substances Act are abused each year, 80 to 90% of which are obtained from physicians, pharmacies, and hospitals (*2*).

Efforts to control prescription drug abuse have received neither the attention nor the funds that illegal drug programs have. Individual states have successfully employed triple prescription programs (*3*) or developed new techniques for data analysis (*4*) to reduce the availability of prescription drugs, but there is little federal emphasis in this area. Some 0.3 to 0.4% of physicians overprescribe drugs with abuse potential (*4*), as can be identified by records of the Drug Enforcement Administration, prescription audits, Medicaid audits, and triple prescription programs. Because prescription drugs represent the majority of abused drugs and information is readily available regarding the manufacture and distribution of these agents, interventions to reduce the abuse of prescription drugs have a greater potential for reducing overall drug abuse than efforts directed at the abuse of illegal drugs.

ALAN S. HOLLISTER
Division of Clinical Pharmacology, University of Colorado Health Sciences Center, Denver, CO 80262

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1. "Project DAWN Annual Report, 1983" (National Institute on Drug Abuse, Rockville, MD, 1984); *Comprehensive Approach Needed to Help Control Prescription Drug Abuse. Report by the Comptroller General to the Congress of the United States* (Government Printing Office, Washington, DC, 1982).
2. *Retail Diversion of Legal Drugs—A Major Problem with No Easy Solution. Report by the Comptroller General to the Congress of the United States* (Government Printing Office, Washington, DC, 1978); G. R. Haislip, *Subst. Abuse* **4**, 4 (1982).
3. Drug Enforcement Administration, Department of Justice, *Multiple Copy Prescription Programs Resource Guide* (Government Printing Office, Washington, DC, 1987).
4. A. S. Hollister, *Subst. Abuse* **11**, 69 (1990).

Goldstein and Kalant provide an excellent review of the complex nature of forming a balanced policy on substance abuse both for an individual user and for the nation as a whole. There are, however, two areas that could have been clarified. The first relates to the use of operationally undefined terms such as "addiction" and "addictive drugs." The World Health Organization (WHO) (*1*) suggests that the term "neuroadaptation" be substituted for "dependence" and that the term "abuse" not be used because it is judgmental. WHO further recommends that "drug dependence syndrome" be used to encompass all of the phenomena previously described by the terms "dependence" and "abuse." The advantage of this new terminology is that it distinguishes between primary processes such as drug self-administration and the secondary consequences resulting from chronic drug intake (such as neuroadaptation). Finally, the terms proposed by WHO are more conducive to operational analyses and are devoid of value judgments, such as in the phase "dangerous addicting drugs. . . ."

The above is not merely a semantic argument, as the choice of terminology leads to a second point. The data in Goldstein and Kalant's table 1 include a ranking system for the relative risk of addiction. There is no citation for this rank order or description of the methods used to determine these values. From the perspective of drug testing, pharmacologic assessments can be most effectively demarcated by the events before or after repeated drug-taking behavior (*2*). Such distinctions provide the foundation for separating drugs on the basis of their liability for abuse or their dependence potential, two properties that may or may not coexist (*2*). With respect to the former, there are a number of well-validated techniques for determining a drug's liability for abuse, both within and between pharmacologic classes (*3*). Similarly, a drug's dependence potential can be determined by using procedures that quantify the signs and symptoms that appear upon termination of chronic administration (*2, 4*). In fact, the original (and erroneous) idea that cocaine was a nonaddicting drug was based on early observations that it failed to produce marked physical dependence—in spite of its pronounced liability for abuse. Under the ominous term "addiction," the

origins of the rank orderings in Goldstein and Kalant's table 1 are unclear and may represent a mixture of scientific, social, and economic factors. However, once the latter two are included, the table no longer serves to predict risk, but rather conveys the element of consequence. It would have been more helpful had the authors included two columns: one that ranked the relative degrees of liability for abuse and dependence potential by using scientific criteria and the other showing measures of economic and social consequences.

SCOTT E. LUKAS
Alcohol and Drug Abuse Research Center, McLean Hospital, Harvard Medical School, Belmont, MA 02178

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2. J. V. Brady and S. E. Lukas, Eds., *NIDA Research Monograph 52* (ADM 84-1332, Department of Health and Human Services, Washington, DC, 1984).
3. R. R. Griffiths, L. D. Bradford, J. V. Brady, *Psychopharmacology* **65**, 125 (1979); N. K. Mello, S. E. Lukas, M. P. Bree, J. H. Menderson, *Drug Alcohol. Depend.* **21**, 81 (1988); J. L. Katz, *Behav. Pharmacol.* **1**, 283 (1990).
4. C. K. Himmelsbach, *J. Pharmacol. Exp. Ther.* **67**, 239 (1939); H. F. Fraser and D. R. Jasinski, in *Drug Addiction I*, W. R. Martin, Ed. (Springer-Verlag, Berlin, 1977), pp. 589–612.

Goldstein and Kalant recognize the hypocrisy of the present differential prohibitions of psychoactive compounds. The authors are brave to call for decriminalizing the possession of small amounts of drugs, needle exchange programs, and treatments that begin by making the individual's drug of choice available. Unfortunately, the intensity of the "war on drugs" makes it difficult for even these authors to fairly estimate the hazards of revising the regulations for psychoactive compounds.

Goldstein and Kalant argue against drug legalization, fearing that the removal of explicit legal sanctions and subsequent increases in availability will lead to increased drug abuse. Data that are admittedly weakened by "the absence of sound national surveys" are cited to support the assertion that legalization would lead to an "increase in use [that] would be very large." However, the careful reader will find buried in reference 58 a more stringent evaluation; Goldstein and Kalant discredit similarly anecdotal reports that reducing penalties for possession of marijuana did not lead to substantially increased use of the drug in Holland or in many U.S. states. The authors note that "drug use has been declining . . . for all psychoactive drugs whether licit or illicit." Does not reduced consumption of cheap and legal drugs such as caffeine and nicotine imply that a well-educated, free citizenry can make healthful decisions about drugs in the absence of punitive legal sanctions?

Goldstein and Kalant lament that a rational drug policy may be impractical since scientific evidence does not compete well with "long-established values and practices." The authors themselves prove this point, as their proposed changes in drug policy perpetuate a bias in favor of legal drugs and in opposition to illegal drugs. Implementing their suggestions would leave a vast discrepancy between the relative legal status and relative harm of drugs such as marijuana and alcohol. A society that holds freedom to be a basic value should be able to implement a drug policy based on science and should be able to develop means of discouraging drug abuse without recourse to hypocritical prohibitions.

ARTHUR P. LECCESE
Department of Psychology, Kenyon College, Gambier, OH 43022–9623

Response: Hollister is quite right in emphasizing the relatively much greater damage to health from licit substances, including prescription drugs, than from illicit ones. We agree completely, and did point this out in several places in our article. Moreover, we also cited the triple prescription program as a measure that had proven effective in reducing the abuse of benzodiazepines. We differ from Hollister only in the relative emphasis placed on different types of licit substance. Hollister cites statistics demonstrating that prescription drugs account for the great preponderance of emergency room visits and acute drug-related deaths. We have put more emphasis on the much greater total damage, including chronic illness and death, attributable to abuse of other licit substances, specifically alcohol and tobacco. The point on which we obviously agree is that it is essential to retain proper perspective in viewing the problems of drug abuse and to recognize that these are most definitely not confined to illicit "street" drugs.

Lukas' criticisms are well taken, and we must plead guilty to using terms that are not satisfactorily defined operationally. We were aware of this when we wrote our article. Indeed, one of us (H.K.) was a member of the World Health Organization working group (*1*) that proposed the term "neuroadaptation" and that rejected the term "drug abuse" because of its lack of definition and its obvious value-judgmental character. However, we chose to use the terms "addiction" and "drug abuse" for a practical and significant reason. The article was meant to be read, as we believe it has been, by people

from a broad range of backgrounds, many of whom are not acquainted with the specific scientific concepts to which Lukas refers. We felt it better to write in terms that a general public knows and uses, so that attention would be directed to the major social policy issues surrounding the drug-related problems, rather than to the scientific analysis of the nature of dependence itself.

This is illustrated by our relative ranking of "risk of addiction" for different classes of drugs in our table 1. Lukas is correct in surmising that our rankings reflect "a mixture of scientific, social, and economic factors." Again, this was a deliberate choice. We acknowledge the scientific validity of Lukas' terminology; indeed, one of us (H.K.) was a contributor to the manual by Brady and Lukas (*2*) on scientific testing of drugs for their dependence potential and abuse liability. However, virtually every investigator in this field recognizes that the prevalence of problems attributable to any particular drug reflects not only the intrinsic pharmacological reinforcing effects of the drugs themselves, but also the influence of availability, fashion, social norms and current attitudes and beliefs. Our ranking was an (admittedly somewhat arbitrary) attempt to take these all into consideration. For example, if we had used only the results of test models such as those described by Brady and Lukas (*2*), we would not have included the hallucinogens at all, because they have proven to be aversive rather than reinforcing in animal models. Nevertheless, a few humans who use the drugs become sufficiently devoted to them to incur harmful consequences that justify inclusion of these drugs at the lowest level in our table.

Leccese appears to be suggesting that we supported our argument about the influence of easy availability on extent of drug use by referring to data that we ourselves recognized as faulty. This is not true. We noted the absence of sound national survey data about opiate use before the passage of the Harrison Act, but pointed out that Terry's work provided at least a valuable set of data for a circumscribed jurisdiction.

If Leccese's main contention is that "a well-educated, free citizenry can make healthful decisions about drugs in the absence of punitive legal sanctions," we agree with him completely. We stated, with respect to marijuana, "If preventive education achieves its goals, and public attitudes and other nonlegal controls over cannabis use become strong enough, it might eventually be possible to loosen the regulatory controls without risk of a major increase in use and the likely attendant problems." This would indeed be the ideal goal with respect to all drug use in a well-educated, free democratic

society. But merely wishing it to be so does not automatically make it so. Our point is that it takes time and major effort to reach that desirable state of educated individual decision. In the interim, restrictive regulations can complement educational efforts in changing social consensus. In moving toward the ultimate goal, it is necessary to proceed cautiously and pragmatically, to avoid making things worse than they now are.

AVRAM GOLDSTEIN
Department of Pharmacology, Stanford University School of Medicine, Stanford, CA 94305
HAROLD KALANT
Department of Pharmacology, University of Toronto, Toronto, Ontario, Canada M55 1A8

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Alzheimer's Disease Cell Bank

The News briefing "Cell bank for mental illnesses" (11 Jan., p. 159) may have led some readers to mistakenly conclude that the National Institute of Mental Health's National Cell Repository is "the first nationally coordinated initiative to aid researchers in defining the genetic basis for Alzheimer's disease. . . ."

In fact, the National Institute on Aging–supported Alzheimer's Disease Research Center National Cell Bank has been in operation since September 1989 at Indiana University, in collaboration with Duke University. It is devoted to providing lymphoblast cultures from patients and family members with clinically diagnosed and pathologically confirmed Alzheimer's disease to investigators nationwide in an effort to speed the determination of the genetic defect that is associated with Alzheimer's disease.

ALLEN D. ROSES
Duke University Medical Center, Durham, NC 27710
P. MICHAEL CONNEALLY
Department of Medical Genetics, Indiana University, Indianapolis, IN 46223

Erratum: The seventh sentence of the first paragraph of the letter from P. W. Anderson, E. Abrahams, and R. Laughlin that appeared in the issue of 1 March (pp. 1005–1006) was printed incorrectly. It should have read, "Others, such as the 'anyon' proponents, a group at Bell laboratories and Rutgers, and another at Princeton, are sure that this system is not a Fermi liquid."