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Effects of Famciclovir in Acute Herpes Zoster

To the Editor: Tyring and colleagues' study of famciclovir in patients with acute herpes zoster (1) was placebo-controlled. I believe it is unethical to give placebo to such patients when a safe and effective drug such as acyclovir is available. Although one of the study's exclusion criterion was complications of herpes zoster, such as ocular or visceral involvement or disseminated herpes zoster, I question whether ethical committees consistently and properly evaluate studies sponsored by pharmaceutical companies. In addition, the authors did not state the start and end dates of the study. Although the authors stated in the Results section that "no benefit was seen for patients younger than 50 years" for famciclovir compared with placebo for the treatment of postherpetic neuralgia, they did not stress this important aspect in the Discussion section.

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Reference

1. **Tyring S, Barbarash RA, Nahlik JE, Cunningham A, Marley J, Heng M, et al.** Famciclovir for the treatment of acute herpes zoster: effects on acute disease and postherpetic neuralgia. A randomized, double-blind, placebo-controlled trial. Ann Intern Med. 1995;123:89-96.

In response: The investigators and the institutional review boards of the 36 participating centers in the United States, Canada, and Australia considered the study design to be both ethical and acceptable. Our first patient received study medication in November 1990, shortly after acyclovir had been approved for the short-term treatment of herpes zoster without documented effect on postherpetic neuralgia (April 1990). In contrast, as stated in our report, famciclovir significantly reduced the time to resolution of postherpetic neuralgia (a prospectively defined end point) in the overall sample, as well as in patients 50 years of age or older, who are at greatest risk for developing postherpetic neuralgia. Finally, as Dr. Tirelli acknowledges, we clearly stated the lack of benefit from famciclovir for patients younger than 50 years of age. We felt no need to further stress a result that was neither particularly surprising nor in conflict with existing thinking about treating herpes zoster in persons younger than 50 years of age.

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Renal Impairment Associated with Losartan

To the Editor: Losartan, the first angiotensin II receptor antagonist, is used to treat hypertension. We report a case of renal impairment associated with this drug.

A 77-year-old woman began receiving losartan, 50 mg/d, for hypertension. Concomitant medications included long-term use of allopurinol for gout. The patient's serum creatinine level at that time was 132.6 μmol/L (1.5 mg/dL). Six weeks later, the patient was hospitalized with a 1- to 2-week history of diarrhea and anorexia. On admission, her serum creatinine level was 327.1 μmol/L (3.7 mg/dL), and her blood urea nitrogen level was 36.1 mmol/L (101 mg/dL). The patient was oliguric for the following 3 days, and serum creatinine and blood urea nitrogen levels increased to 424.3 μmol/L (4.8 mg/dL) and 43.6 mmol/L (122 mg/dL), respectively. Results of renal ultrasonography showed no significant changes compared with results from 2 years earlier. After the patient began receiving diuretics and after losartan and allopurinol therapies were discontinued, renal function returned to levels near baseline.

Pharmacologic blockade of angiotensin II can lead to deterioration of renal function in patients at risk (those with preexisting renal impairment, concomitant use of diuretics, or congestive heart failure). Our patient had a history of type II diabetes and known diffuse vascular disease and thus was at risk for this event. A small right kidney suggested renal vascular disease. In one study (1), renal function deteriorated with angiotensin-converting enzyme inhibitors. Because losartan has a similar pharmacologic result—blockade of the renin–angiotensin–aldosterone system—it may be expected to produce a similar renal effect. A search of the MEDLINE database for reports published from 1980 to 1995 showed no case reports of renal impairment associated with losartan. When prescribing losartan for patients at risk for renal failure, clinicians should be aware of the possibility of renal impairment.

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Reference

1. **Hricik DE, Dunn MJ.** Angiotensin-converting enzyme inhibitor-induced renal failure: causes, consequences, and diagnostic uses. J Am Soc Nephrol. 1990;1:845-58.

Drug Legalization, Harm Reduction, and Drug Policy

To the Editor: The drug legalization debate, addressed by DuPont and Voth (1) diverts attention from the need to fix prohibition's worst (but fixable) fault—its drug and crime subsidy. The

latter is the difference between the real economic value of drugs and the scarcity-inflated market price.

By official estimates, U.S. drug sales in 1993 totaled $49 billion. Black-market drug prices are estimated to range from 70 to 140 times the true economic value (2). If the real worth of drugs sold was one seventieth of the market price, then current policy caused U.S. drug users to pay $49 billion for drugs worth only $700 million. The difference between the price paid and the real value is $48.3 billion. Prohibition's drug and crime subsidy supports gangs and gangsterism, drug running, and corruption of the criminal justice system, and it motivates the seduction of new drug users.

How can this situation be fixed? Because addicts are estimated to consume 80% of illegal drugs, we could eliminate 80% of the drug and crime subsidy by treating addiction as a disease rather than as a crime and by providing treatment that is acceptable to addicts. Instead, prohibitionist policies exclude most addicts from treatment with long waiting lists, with arbitrarily high admission thresholds, by punishing relapse with expulsion from therapy, and with treatment regimens many addicts find worse than the disease. Prohibition leaves untreated addicts as captured clients of the drug merchants.

Sweden prohibits private commerce in alcohol but avoids criminogenic effects: A state monopoly supplies existing demand, thus preventing black-market sales and the creation of demand. Swedish indices of alcohol-related pathologies rank among the lowest (3).

The Swedish precedent suggests that we could eliminate the remaining 20% of the drug and crime subsidy with a state monopoly that would supply recreational drug users. Harm from adulterated black market drugs would be eliminated, the drug syndicates would be out of business, and the economic incentive to seduce new drug users would be curtailed (4).

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1. **DuPont RL, Voth EA.** Drug legalization, harm reduction, and drug policy. Ann Intern Med. 1995;123:461-5.
2. **Duke SB, Gross AC.** America's Longest War: Rethinking Our Tragic Crusade Against Drugs. New York: Putnum's; 1993:7.
3. The Bottom Line on Alcohol in Society. Lansing, MI. 1995;16:28.
4. **Smart DC.** Market Interposition: A Comprehensive Public Health Strategy for Control of the Drug/Crime Epidemic. Berkeley, CA; 1995.

To the Editor: DuPont and Voth's defense of the status quo in drug policy (1) begs for some response. The selective use of statistics, especially those derived from a private source, is unconvincing. The insinuation that persons who disagree with current policy do so because of a personal drug habit is pejorative, cannot be clearly evaluated, and sidesteps the issues. In fact, several large groups have strong incentives to assert a need to maintain the current system, including persons making a living on the government side of the current "war on drugs" and those who profit by supplying drugs in the current price-supported environment.

The decrease in the number of deaths from cirrhosis during prohibition is interesting, but, for many of us, the real question is "was it a better society in which to live?" Were people happier, more free to achieve their dreams? Medical facts may inform the discussion of sociopolitical problems, but the medical model seems inadequate to resolve fundamental issues of power, freedom, and benevolence.

The assertion of a "war on drugs" is a misrepresentation of reality. War is not waged against the inanimate. It is waged against people—people who disagree for whatever reasons.

The attitude that most human problems have political solutions has been deeply ingrained in U.S. society in this century's construction of a welfare state. Seldom has open discussion addressed the fact that politics is largely the consideration of how and where to use legalized violence in human society. Political solutions ultimately rely on force (violence) for their implementation, except in the uninteresting and irrelevant case of consensus.

Most illicit drugs are bad for most human bodies, and I would not use them myself even if they were legal and free; however, the question is larger than that. It seems that the illegal drug trade is the major source of the money that buys soldiers and guns on the street, corrupts law enforcement, and leads to a declining respect for government.

Because there are other ways of coping with these problems, I urge that equal space be given to other views. No human sociopolitical arrangement is ideal; all are compromises. We are mortals, not gods, and in our politics we should not risk that role.

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Reference

1. **DuPont RL, Voth EA.** Drug legalization, harm reduction, and drug policy. Ann Intern Med. 1995;123:461-5.

To the Editor: The article by Dupont and Voth (1) and the editorial by Dr. Musto (2) fail to address the question of crime related to the drug trade, that is, violent acts committed to obtain money for the purchase of drugs. If addicts were given drugs from the huge stores of seized cocaine and heroin and were given sterile syringes and needles, the profit motive would disappear, the crime rate would be reduced, and the rate of transmission of the human immunodeficiency virus and other pathogens by injection would be decreased. Legalization could be aided by appropriate education of younger persons to prevent initial use of drugs.

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1. **DuPont RL, Voth EA.** Drug legalization, harm reduction, and drug policy. Ann Intern Med. 1995;123:461-5.
2. **Musto DF.** Perception and regulation of drug use: the rise and fall of the tide [Editorial]. Ann Intern Med. 1995;123:468-9.

To the Editor: The article and editorial on the perception and regulation of drug use in the United States (1, 2) were illuminating but not convincing. One factor about legalization of drugs was not discussed; that is, nationalization of drugs and free distribution to all addicts, an approach that would eliminate the profit from drug use. The advantage of this approach would be twofold. First, the addict would not need to commit a crime to obtain money to buy drugs. The drug to which he or she is addicted would be given free. Second, because no profit would be associated with addiction, the impetus for the pusher to obtain new customers would be eradicated.

To make this system work, the manufacture of heroin and the fields where poppies, cannabis, and cocaine are grown would also have to be nationalized, either by the host country or by direct purchase of the fields by the United States. Otherwise, the producers will have an incentive to increase the use of their products to remain competitive in the drug market.

If the government provides production and free administration of the drugs to all addicts, then possibly, at the very least, the problem will be brought under statistical evaluation and other methods of control could be developed.

Along with the provision of drugs, of course, educational and detoxification programs should be provided. I believe that the expense to the taxpayer will not be any greater than that involved in chasing drug pushers, trying them, incarcerating them, and fighting the street crime that seems attendant to drug use.

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1. **DuPont RL, Voth EA.** Drug legalization, harm reduction, and drug policy. Ann Intern Med. 1995;123:461-5.
2. **Musto DF.** Perception and regulation of drug use: the rise and fall of the tide [Editorial]. Ann Intern Med. 1995;123:468-9.

To the Editor: In their recent article (1), Dupont and Voth characterize harm reduction as "a creative renaming" of the "dismantling of legal restrictions against the use and sale of drugs." This is a fundamental misconception of harm reduction as we understand it (2–4). Indeed, within the harm-reduction perspective, "civil and criminal laws are seen as potent tools" (4) for reducing drug-related harm.

DuPont and Voth apparently view drug policy as a dichotomous choice between "two opposing policy options": prohibition and legalization. In our understanding of harm reduction, the intellectual power of the concept comes precisely from its potential to transcend the old "legalization versus prohibition" debate (3). Consider the following prototypes of harm-reduction programs:

1) Providing many easily accessible treatment programs for persons dependent on psychoactive drugs (both legal and prohibited); 2) providing syringe-exchange programs for injection drug users at risk for infection with the human immunodeficiency virus and other blood-borne pathogens (note that syringe-exchange programs have not led to increased drug use and have been found to reduce transmission of blood-borne viruses [5]); 3) providing "designated driver" and "call a taxicab" programs to reduce drunken driving; and 4) restricting advertising for, and banning vending machine sales of, cigarettes. None of these programs should be considered as requiring either full legalization or full prohibition of the drugs in question.

We invite readers to take the following short test: Can you think of several new programs, new public policies, new laws, or new social customs that might reduce drug-related harms—without resorting to the old forced choice between legalization versus prohibition? If you can, then you can understand the fundamentals of harm reduction and of contributing constructively to this new paradigm.

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1. **DuPont RL, Voth EA.** Drug legalization, harm reduction, and drug policy. Ann Intern Med. 1995;123:461-5.
2. **Des Jarlais DC.** Harm reduction—a framework for incorporating science into drug policy. Am J Public Health. 1995;85:10-2.
3. **Des Jarlais DC, Friedman SR, Ward TP.** Harm reduction: a public health response to the AIDS epidemic among injecting drug users. Ann Rev Public Health. 1993;14:413-50.
4. **Heather N, Wodak A, Nadelmann E, O'Hare P, eds.** Psychoactive Drugs and Harm Reduction: From Faith to Science. London: Whurr; 1993.
5. **Normand J, Vlahov D, Moses LE, eds.** Preventing HIV Transmission: The Role of Sterile Needles and Bleach. Washington, DC: National Academy Pr; 1995.

In response: As we pointed out in our article on drug policy (1), the important question involves not so much the details of a particular policy but whether the policy would result in more or less drug use. We do not support any drug policy that would result in an increase in drug abuse. Legal drugs cost society far more than illegal drugs in terms of medical care, lost productivity, death, crime, and the acquired immunodeficiency syndrome (AIDS) ($66.9 billion compared with $170 billion). We have never seen anyone addicted to legal or illegal drugs who was "happier, more free to achieve their dreams," because of his or her drug use, as Dr. Wilbur suggests. As we also noted, some of the advocates of legalization support such policy to reduce the pressure on their own admitted drug use, and many of the supporters of legalization have no experience or understanding of addiction.

The negative responses to our article advance the notion that legalization or decriminalization of drugs would drive out the criminal element and thus would result in lower overall harm to society. Any action that increases availability of drugs risks increases in drug-associated crime. Fifty-six percent of violent crimes are committed under the influence of drugs (2). Crime has drastically increased in the Netherlands since the decriminalization of marijuana. In 1988, only 3 organized crime groups were listed in Holland; this number had increased to 93 in 1993 (3). Because of associated crime and drug dealing, actions have been taken in the Netherlands to tighten controls on marijuana coffee shops. It is naive to suggest that criminals would throw down their weapons and take up clean living simply because drugs were made available to addicts.

What substances would the government distribute if currently illegal drugs were legalized? All drugs, including tobacco and alcohol? Only certain strengths? Attempts to standardize or control the types or strengths of drugs would result in illegal drug markets.

Although the comments of Des Jarlais and colleagues are sophisticated, they miss our point. We do not simply support restrictive drug policy—we want to discourage drug use. We support greater treatment availability, but not among programs that cannot show clear reductions in drug use. Needle exchanges address only a tiny fragment of the overall drug-using community, have a questionable effect on the reduction of the incidence of AIDS, and do nothing to reduce the underlying problem of illicit intravenous drug use. Also, no evidence of crime reduction has been associated with needle exchanges. The Montreal experience (not yet published) may even show an increased number of cases of AIDS in association with needle exchanges.

Finally, no one has yet shown any system that reduces the legal use of alcohol or tobacco or their associated harms while simultaneously reducing constraints or controls on those substances. Because these agents cause the most harm to society, this would be a good place to begin true harm reduction.

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1. **DuPont RL, Voth EA.** Drug legalization, harm reduction, and drug policy. Ann Intern Med. 1995;123:461-5.
2. **U.S. Department of Justice, Bureau of Justice Statistics.** The costs of illegal drug use. In: Drugs, Crime, and the Criminal Justice System. NCJ-133652, 126-127. U.S. Department of Justice, Bureau of Justice Statistics; 1992.
3. Centrale Recherche Informatie 1993 report. Criminal Investigation Department. Rotterdam, the Netherlands; 1993.

Correction: Prevalence Ratio

In Table 3 of a recent article on the battering syndrome (1), the crude prevalence ratio for the column "Abused as a Child" should be 3.7, not 13.7.

Reference

1. **McCauley J, Kern DE, Kolodner K, Dill L, Schroeder AF, DeChant HK, et al.** The "battering syndrome": prevalence and clinical characteristics of domestic violence in primary care internal medicine practices. Ann Intern Med. 1995;123:737-46.