Ronald M. Epstein, MD
University of Rochester
Rochester, NY 14620

Tom R. Freeman, MD
Byron Family Medical Centre
London, Ontario N6K 1C7, Canada

References

1. **Smith GR, Rost K, Kashner TM.** A trial of the effect of a standardized psychiatric consultation on health outcomes and costs of somatising patients. Arch Gen Psychiatry. 1995;52:238-43.
2. **Stewart M, Brown JB, Donner A.** The Impact of Patient-Centred Care on Patient Outcomes in Family Practice. Final Report to the Ministry of Health of Ontario. London, Canada: Thames Valley Family Practice Research Unit; 1996.
3. **James W.** The Varieties of Religious Experience: A Study in Human Nature. New York: New American Library; 1958.

Medicinal Uses of Marijuana

To the Editor: Voth and Schwartz (1) sound like patriarchal moralists, not scientists. They conveniently ignore scientific studies, patient anecdotes, court decisions, and voters who disagree with them when discussing a 5000-year-old herbal medicine. Many physicians and organizations—including Dr. Kassirer, Editor of *The New England Journal of Medicine* (2); the National Institutes of Health (3); the American Public Health Association; the San Francisco Medical Society; the California Academy of Family Physicians; Harvard professor Dr. Grinspoon; the Federation of American Scientists; and the National Academy of Sciences (4)—believe that cannabis may be beneficial and that further research should be done. Users of medical cannabis are not criminals. If this issue is controversial, then suffering patients deserve the benefit of the doubt so that they can have access to medical cannabis while more research is being done. The National Institute on Drug Abuse has even impeded medical research on medical cannabis (5).

Voth and Schwartz also seem to encourage the use of Marinol, an oral product produced by a large pharmaceutical firm (Unimed, Inc., Buffalo Grove, Illinois) and containing only the psychoactive cannabinoid (delta-5-tetrahydrocannabinol) instead of the cannabis plant. Is it possible that they have a conflict of interest? What is the International Drug Strategy Institute? Do they directly or indirectly get any pharmaceutical money? The *Annals* Editors may have been negligent by failing to disclose to their readers information about financial incentives to promote the agenda of the large pharmaceutical companies over the agenda of suffering patients.

The "War on Drugs" is a political war on compassionate U.S. physicians and their patients. The "War" spills into our examination rooms and influences how we prescribe. Even when clinical practice guidelines on pain management have been followed (U.S. Department of Health and Human Services publication AHCPR-0032), I have found that appropriate narcotic prescriptions can trigger an investigation by the state Board of Medical Examiners. Calling off the "War on Drugs" will be good for science, physicians, and patients. Accurate (not DARE propaganda) methods for prevention and harm reduction need to be instigated.

Voth and Schwartz do not present a compelling reason to oppose the desires of our patients, the scientists who disagree with the authors, and the democratic process of voter initiatives.

Richard Bayer, MD
Portland, OR 97225

References

1. **Voth EA, Schwartz RH.** Medicinal applications of delta-9-tetrahydrocannabinol and marijuana. Ann Intern Med. 1997;126:791-8.
2. **Kassirer JP.** Federal foolishness and marijuana [Editorial]. N Engl J Med. 1997;336:366-7.
3. **Voelker R.** NIH panel says more study is needed to assess marijuana's medicinal use. JAMA. 1997;277:867-8.
4. NORML Medical Marijuana Documents ONLINE. http://www.natlnorml.org/medical/medmj.shtml.
5. MAPS Newsletter on Marijuana and AIDS Wasting Syndrome Study. http://www.maps.org/news-letters/v06n2/06207mmj.html.

To the Editor: Voth and Schwartz's perspective on medicinal use of marijuana (1) is significant for several reasons. Most disturbing to me is that it represents a departure from principle by a medical journal.

The federal government responded to "medical marijuana" by threatening physicians. Unlike Jerome Kassirer, in his straightforward editorial objection in *The New England Journal of Medicine* (2), you've chosen to obliquely endorse marijuana prohibition by publishing a slanted review article by two of marijuana's most infamous doctrinaire opponents.

Anyone unaware that the politics of this issue have overshadowed science for six decades is not in touch with reality. This purported review of the literature clearly supports continued listing of "crude" marijuana on schedule 1, while allowing its synthetic analogue, Marinol, to be legally prescribed on schedule 2.

This is logical sleight of hand: Schedule 1 cites three criteria: (lack of) safety, potential for addiction, and (lack of) medical utility. Because the two agents are nearly identical, neither efficacy nor potential for addiction can justify their separate listing. Furthermore, because acute toxicity of marijuana is nonexistent, the major justification for continued listing on schedule 1 while leaving Marinol on schedule 2 would have to be fear of chronic harm from a delivery system requiring smoking. This argument loses all validity when used by a government that allows tobacco use.

The selective nature of Voth and Schwartz's perspective can be inferred from their choice of 92 references claiming to examine "relevant research published between 1975 and 1996" but that ignores Hollister's exhaustive 1986 review article (3). The latter cited twice as many references as did Voth and Schwartz and reached quite different conclusions. Voth and Schwartz submitted their modern "scientific" version of a 1930s "reefer madness" article, and you published it. For shame.

Thomas J. O'Connell, MD
Daly City, CA 94015

References

1. **Voth EA, Schwartz RH.** Medicinal applications of delta-9-tetrahydrocannabinol and marijuana. Ann Intern Med. 1997;126:791-8.
2. **Kassirer JP.** Federal foolishness and marijuana [Editorial]. N Engl J Med. 1997;336:366-7.
3. **Hollister LE.** Health aspects of cannabis. Pharmacol Rev. 1986;38:1-20.

To the Editor: The well-documented review of medicinal potential of delta-9-tetrahydrocannabinol and marijuana by Voth and Schwartz (1) is timely because the well-funded drug legalization lobby, which includes physicians, is actively trying to duplicate the California and Arizona marijuana initiatives in many other states. Voth and Schwartz's surveys show that only a small percentage of oncologists would recommend marijuana as medicine. Moreover, no evidence suggests that even this small number of physicians have the necessary information on which to base their opinion. The U.S. Food and Drug Administration's approval of drugs as medicine is based on well-controlled scientific studies, not on surveys, polls, anecdotes, or popular vote. Furthermore, with the current heavy advertising of prescription drugs on television and radio and in the print media, physicians are under unprecedented pressure to prescribe drugs that their patients demand. Indeed, it was the multimillion-dollar television blitz fraudulently advertising marijuana as medicine that deceived the voters in California and Arizona. It is not compassionate for physicians to recommend an unsafe, unproven substance that may worsen their patients' condition, especially when better, safer drugs are available.

Janet D. Lapey, MD
Concerned Citizens for Drug Safety
Hanover, MA 02339

Reference

1. **Voth EA, Schwartz RH.** Medicinal applications of delta-9-tetrahydrocannabinol and marijuana. Ann Intern Med. 1997;126:791-8.

In response: The attitudes of Drs. Bayer and O'Connell are precisely why we undertook the project of sorting out emotion and passion from science and fact as they relate to the use of crude marijuana as a medicine. We found no compelling reason to abandon the Food and Drug Administration process of proving safety and efficacy and stepping back to the days of unproven and potentially toxic potions and tonics. That is the net effect of views represented by Drs. Bayer and O'Connell. Unlike the anecdotal diatribes that pervade support for the medicinal use of marijuana, our review was extensive and covered existing science.

O'Connell's comments are consistent with those that he voices on pro-legalization or "drug policy reform" World Wide Web sites. He overlooks the fact that crude marijuana is a toxic, impure herb containing more than 480 substances. Marinol has side effects (as does marijuana) but at least is a single, pure substance.

Bayer mixes fact with fiction in his criticism. In fact, many of the positions to which he refers are based on uncontrolled anecdotes, not controlled studies. Contrary to Bayer's assertions, the National Institutes of Health have previously stated that marijuana adds nothing to the currently available regimens for such conditions as nausea, glaucoma, and spasticity (Lee PR. Personal communication to Congressman Dan Hamburg).

Bayer raises questions about the International Drug Strategy Institute. We are a group of more than 40 physicians, attorneys, and drug policy specialists, including some of the most respected authorities on drug policy in the world. We receive no "pharmaceutical" funding and have no vested interest in anything except the health and well-being of patients. In contrast, the medicinal marijuana movement was fathered by the National Organization for the Reform of Marijuana Laws. The stated goal of this organization is to use the medical marijuana issue to gain public support and the ultimate legalization of marijuana (1). Bayer even cites the NORML Web site as a resource. That site also outlines the medical marijuana and hemp legislative strategy for the United States.

Dr. Lapey draws attention to the organized and well-funded ballot initiatives in Arizona and California, in which millions of dollars from wealthy supporters of legalization essentially bought drug policy. Dr. Lapey makes a calm and sane plea to base medical decisions on the Food and Drug Administration process of proving safety and efficacy—something that the supporters of medicinal marijuana are quick to abandon.

We continue to maintain that research should continue into alternative delivery systems for pure delta-9-tetrahydrocannabinol and its analogues. Patients should be provided with predictable, safe, and effective medicines, not unproven herbal potions.

Eric A. Voth, MD
Richard H. Schwartz, MD
International Drug Strategy Institute
Topeka, KS 66606

Reference

1. **Cowan R.** Building a new NORML: strategies for the legalization of marijuana by 1997. High Times. 1993;January:63.

Intractable Hiccups and Gastroesophageal Reflux Disease

To the Editor: I read with interest the brief communication by Brzana and Koch (1) describing 10 patients with intractable nausea who were found to have gastroesophageal reflux. One of my patients presented with intractable hiccups that did respond to traditional medical therapy. Results of physical examinations, laboratory evaluation, and abdominal radiography were all normal. Upper gastroendoscopy revealed severe reflux and esophagitis. The hiccups responded well to omeprazole. Schreiber and colleagues (2) described a similar case, in which gastroesophageal reflux caused intractable hiccups. An interesting fact is that hiccups in infants are strongly associated with reflux (3).

I agree with the authors that atypical symptoms of gastroesophageal reflux disease may present a diagnostic challenge. Thus, it should be kept in the differential diagnosis and be worked up if symptoms cannot be explained otherwise.

M. Ammar Hatahet, MD
Wayne State University
Detroit, MI 48201

References

1. **Brazana RJ, Koch KL.** Gastroesophageal reflux disease presenting with intractable nausea. Ann Intern Med. 1997;126:704-7.
2. **Schreiber LR, Bowen MR, Mino FA, Craig TJ.** Hiccups due to gastroesophageal reflux. South Med J. 1995;88:217-9.
3. **Feranchak AP, Orenstein SR, Cohn JF.** Behaviors associated with onset of gastroesophageal reflux episodes in infants. Clin Pediatr. 1994;33:654-62.

In response: Nausea is a common symptom that can range in intensity from irritating and bothersome to incapacitating. Dr. Hatahet reminds us of another common symptom, hiccups, which can also range from irritating to disabling. Dr. Hatahet's observation underscores the point that gastroesophageal reflux disease is a great masquerader in its own right and that the possibility of reflux should be entertained when clinicians evaluate a variety of symptoms that can be related to the stomach or esophagus. Nausea or hiccups are not trivial symptoms. Establishment of a specific diagnosis and a successful therapeutic outcome are appreciated by the patient and gratifying for the physician.

Ronald J. Brzana, MD
Kenneth L. Koch, MD
Milton S. Hershey Medical Center
Hershey, PA 17033

Recurrent Severe Acute Hepatitis and Omeprazole

To the Editor: Omeprazole is widely used to treat acid-related disorders. The overall incidence of adverse events is low; most events, including diarrhea, flatulence, constipation, and abdominal pain, involve the gastrointestinal tract (1, 2). Isolated reports have described other adverse effects, including fulminant hepatic failure (3). We report a case of recurrent severe acute hepatitis induced by omeprazole.

A 30-year-old man with advanced renal failure secondary to diabetic nephropathy was admitted to our hospital in September 1995 because of epigastric pain, nausea, and darkened stools. He had been taking ranitidine, calcium carbonate, furosemide, and nifedipine for the previous 4 months. On admission, physical examination findings were irrelevant, and results of liver function tests and abdominal ultrasonography were normal. Endoscopy showed erosive gastritis and a duodenal ulcer. Ranitidine therapy was stopped and omeprazole, 20 mg once daily, was prescribed. Nine days later, the patient reported abdominal pain. Physical examination showed diffuse tenderness and hepatomegaly. Serum chemistry showed acute liver injury (aspartate aminotransferase level, 1788 U/L; alanine aminotransferase level, 1294 U/L). Prothrombin time was normal. Results of hepatitis serologic testing for hepatitis A, B, and C virus; Epstein–Barr virus; herpes simplex virus; and cytomegalovirus were negative. Immunologic studies, including measurement of immunoglobulins; rheumatoid factor; complement (C3 and C4); and antinuclear, antineutrophilic, antimitochondrial, and anti–smooth-muscle antibodies, had normal or negative results. Ferritin, ceruloplasmin, and α_1-antitrypsin levels were also normal.

Omeprazole therapy was discontinued, and the liver function test results returned to normal within 4 weeks. Six months later, the patient presented with symptoms suggestive of esophagitis. Findings on liver function tests were normal. Omeprazole therapy was then started. Blood chemistry done 1 week later indicated acute liver injury (aspartate aminotransferase level, 954 U/L; alanine aminotransferase level, 762 U/L). Results of hepa-