

would not prevent further spread, but it might reduce the shedding of the virus and would, in any event, be required for ethical reasons. All these actions rely on early recognition through good surveillance and the ability to deliver the antiviral drug at a time when transmission might still be inefficient.

The logistic hurdles are formidable. A mobile stockpile of the drug would have to exist and be made available in the affected country. Oseltamivir is now being stockpiled by a number of developed countries for use once a pandemic virus becomes established and begins to spread rapidly around the globe. Developing a stockpile in an attempt to restrict the spread of the new virus at its source might mean diverting drugs from other national stockpiles. However, this diversion must happen. The notion of trying to control a pandemic at its source would have been considered laughable just a few years ago — but that was before SARS transmission was controlled by public health measures. We have no idea whether a type A (H5N1) virus that

was fully adapted to humans would continue to be highly lethal, but it is nevertheless incumbent on the global community to try to contain it.

The avian origin of previous pandemic viruses was recognized only after the fact; this time, we have been given a warning. We really are not sure when, or whether, the type A (H5N1) virus will start to spread among humans, but we must be ready to stop it if we can — and, if we cannot, at least to mitigate its effects through the use of stockpiled antiviral drugs and, eventually, strain-specific vaccine.

Dr. Monto reports having received consultation fees and grant support from Roche.

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To Inform or Persuade? Direct-to-Consumer Advertising of Prescription Drugs

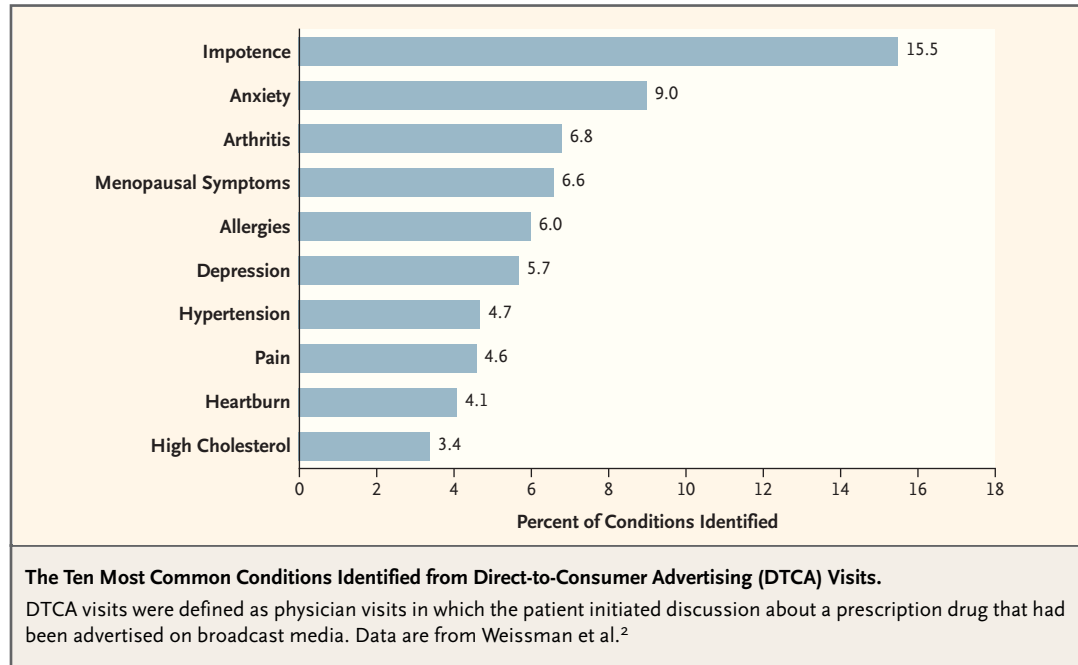
Ernst R. Berndt, Ph.D.

Merck's withdrawal of rofecoxib from the market last September and Pfizer's announcement in December of possible cardiac risks associated with high doses of celecoxib reignited long-simmering controversies regarding drug promotion, in part because both cyclooxygenase-2 inhibitors have been heavily marketed directly to consumers. Indeed, after discussion with the Food and Drug Administration (FDA), Pfizer suspended all direct-to-consumer advertising of celecoxib. Adding fuel to the fire is class-action litigation filed against AstraZeneca alleging that its direct-to-consumer advertising misrepresents the superiority of its proton-pump inhibitor esomeprazole over less expensive alternatives.

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Although the information made public in these cases is probably incomplete, these events offer an opportunity to step back and consider the appropriate role of drug promotion in general and direct-to-consumer advertising of prescription drugs in particular. What are its effects on physician-patient relationships? How might FDA oversight of such advertising of prescription drugs (and now also of prescribed medical devices) and the content of industry advertising be improved through evidence-based policy changes?

Advertising has long been controversial. Although Thomas Jefferson once claimed that "advertisements contain the only truth to be relied on in a newspaper," F. Scott Fitzgerald voiced a more common view when he opined that "advertising is a racket . . . its constructive contribution to humanity is exactly minus zero." In the context of pre-



scription-drug advertising, new research, some of it sponsored by the FDA, has shown that physicians' overall evaluations of direct-to-consumer advertising are decidedly mixed: 40 percent of physicians believe that it has had a positive effect on their patients and practice, 30 percent say it has had a negative effect, and 30 percent see no effect at all.^{1,2}

Some critics of the pharmaceutical industry and the FDA have sought to ban direct-to-consumer advertising of drugs entirely. Such drastic action is unlikely to be taken, however, for two primary reasons. First, particularly during the tenure of the outgoing chief counsel of the FDA, Daniel Troy, the courts and the FDA have affirmed the applicability of First Amendment rights to commercial free speech, affecting not only direct-to-consumer advertising, but also the FDA's approach to regulating the promotion of off-label uses of drugs.³ Second, a substantial body of research¹ indicates that there is strong (albeit qualified) consumer support for direct-to-consumer advertising. This support reflects a demand for information on the part of patients who have been affected by recent changes in insurance benefits that increase the amount consumers pay for drugs: typically, prescription drugs are subject to higher copayments than any other medical service except visits to the emergency room. As patients take on an increasing portion of the financial

responsibility for their use of medications, they can be expected to demand more information about them, and drug manufacturers have strong incentives to supply it. Thus, I think that direct-to-consumer advertising is here to stay, and I expect its use to continue to grow.

Of course, not all such advertising is equally reliable, valuable, or effective. Economists' evaluations of the effects of marketing efforts typically focus on two types of advertising content that are not necessarily mutually consistent and the proportions of which vary considerably: information and persuasion. In the health care context, marketing that informs by discussing a disease or health condition or that advocates screening but does not mention or make any claim or suggestion concerning a specific drug or device is seen as encouraging consumers to seek, and health care practitioners to provide, appropriate treatment, thereby supporting the public health. These beneficial types of advertisements, known as help-seeking and disease-awareness communications, are not even subject to regulation by the FDA.

Consumer-directed advertising that mentions a specific drug or device, on the other hand, is subject to FDA regulation, including requirements for a balanced disclosure of risks and benefits. Many of these advertisements do more than simply in-

form consumers about the availability of a drug; they also attempt to persuade consumers to use it. Although the boundary between informative and persuasive advertising is porous, it is the latter type that has generated much controversy.

Patients and physicians have mixed reactions to both types of content, but part of the problem with the persuasive content lies in the frequent inadequacy of the information: there is a perceived imbalance between the information about risks and the information about benefits that most advertisements convey. For example, in surveys conducted in 1999 and 2002, nearly 60 percent of patients agreed with the statements that “Advertisements for prescription drugs do not give enough information about the possible risks and negative effects of using the drug” and that “Advertisements for prescription drugs make the drugs seem better than they really are.” In 1999, about half of consumer-respondents agreed that “Advertisements for prescription drugs help me make better decisions about my health,” but by 2002, the share had fallen to a third.¹

When physicians were asked about recent office visits in which a patient initiated discussion about a prescription drug that had been advertised on broadcast media, they reported that in 88 percent of such cases, the patient did in fact have the condition that the drug was meant to treat — but that the majority of patients understood the benefits of the drug much better than they did its risks.¹ In another recent study, more than two thirds of responding physicians indicated that direct-to-consumer advertising helped to educate patients about available treatments, and a slightly smaller proportion reported that it helped them have better discussions with patients. However, four of five physicians believed that such advertising did not provide information about risks in a balanced manner, and a similar proportion thought that it encouraged some patients to seek unnecessary treatments. Slightly less than half agreed that direct-to-consumer advertising “increases patients’ compliance with doctor recommendations, tests, or prescriptions.”²

Physicians reported that about 25 percent of visits in which a patient asked about an advertised prescription drug resulted in the identification of a new condition; the 10 most common conditions are listed in the graph. They include both some that are likely to be identified and treated effectively

thanks to informative advertising (depression, anxiety, hypertension, and hyperlipidemia) and some that have allegedly been targeted by persuasive advertising of certain prescription drugs even though less expensive alternative treatments are available (heartburn, allergies, and arthritis).²

Currently, print direct-to-consumer advertising materials typically contain, in fine print, the complete section on risks from the FDA-approved product labeling. Although the inclusion of this section satisfies the applicable requirements of the FDA for a brief summary, the highly technical medical terminology in such labeling is not patient-friendly. Indeed, the proportion of people who saw a print advertisement but read the summary “not at all” or “a little” reportedly increased from 56 percent in 1999 to 73 percent in 2002.¹

In February 2004, the FDA announced that it is considering adopting a “less is more” policy, whereby information about the most important and common risks is presented in a less cluttered format and in language that can be easily understood by the average consumer. One such option would be a “risk-information window” in the main body of the advertisement that featured a concise, clear, bulleted summary.⁴

The proposed labeling for patients would include information on all the contraindications and warnings that are listed in the professional labeling; major precautions, including any that describe serious adverse events related to the use of the drug; and the three to five most common nonserious adverse reactions that are the most likely to affect the patient’s quality of life or compliance with drug therapy. The proposed changes are currently under review by the FDA.

Although these changes in FDA policy are promising, industry must also address the imbalance between risk information and benefit information in its direct-to-consumer advertising. The acting FDA commissioner, Lester Crawford, has argued that such advertising “is supposed to get patients who need the medication to know about the drug so they can ask their physician about it. . . . Direct-to-consumer advertising correctly done is a great public health tool.”³ But “correctly done” is the operative term; too often, says Crawford, such advertising fails to achieve its highest aim. “We now have ads on television that show people walking through meadows as the name is subliminally flashed, and there are birds singing and bees

copulating. . . . We've got to cut that out, because that is not what direct-to-consumer advertising is supposed to be."

As an instrument promoting public health, direct-to-consumer advertising has considerable potential. But industry needs to respond to consumers and physicians, who seek more balanced communication of risks and benefits.

Dr. Berndt reports having served as a consultant to and having received grant support from pharmaceutical companies. A list is available with the full text of this article at www.nejm.org.

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MEDICAL ETHICS

Consent or Obedience? Power and Authority in Medicine

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A recent biography of the social psychologist Stanley Milgram (*The Man Who Shocked the World*, by Thomas Blass) details the "obedience experiments" that made Milgram famous. These studies demonstrated that ordinary people could be induced by an authority to deliver to a victim what they believed were increasingly harmful electric shocks. Milgram's contribution was not in showing that human beings obey authority, but in demonstrating how powerful and potentially dangerous that predisposition is. It doesn't take evil or deranged people to do awful things to others; normal people will act that way if commanded by a legitimate authority. Sadly, although these were laboratory experiments, the results are substantiated by daily experience.

Milgram's work taught us something profoundly revealing about human nature: how prone we are to obey the commands of an authority even when they conflict with our expressed desires or moral principles. Here was a common, perhaps universal, human characteristic that came as much as a surprise to psychologists and physicians as it did to others. Indeed, the real surprise may be how little research-confirmed knowledge there is about everyday human behavior.

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Milgram's research carries implications for at least two important issues in the hierarchical world of medicine: the role of inappropriate obedience as a source of abuse in the teaching hospital and the effect of obedience on patients' autonomy and consent. In the hospital, faculty members have jurisdiction over house staff, house staff have authority over students, and all these people are seen as authorities by patients. There is probably no physician or medical student who has not seen or participated in callousness (or worse) in the treatment of patients in response to an order of a resident or an attending physician.

We might simply feel bad, and let it go at that, when patients are mistreated because of undue obedience on the part of health care personnel, if it weren't for other findings of Milgram's research. For not everybody obeyed. Some research subjects who thought they were hurting someone refused to continue. In general, more subjects refused to obey when the victim was brought physically closer to them, with the greatest disobedience occurring when the subjects could touch the victims. Perhaps we should expect episodes of bad treatment of patients by people following the orders of remote authorities. Accepting this fact is necessary in order to prevent ill treatment. To some degree, obedience is a requirement of training, but abuses of authority do not have to happen in medical institutions;