

## Waiting for Plan B — The FDA and Nonprescription Use of Emergency Contraception

Robert Steinbrook, M.D.

The proposal to switch levonorgestrel emergency contraception (sold under the brand name Plan B) to over-the-counter status in the United States is in limbo. In May, the Food and Drug Administration (FDA) rejected the application of Barr Pharmaceuticals for nonprescription sales of Plan B. Dr. Steven Galson, the acting director of the FDA's Center for Drug Evaluation and Research, wrote that the company had "not provided adequate data to support a conclusion that Plan B can be used safely by young adolescent women for emergency contraception without the professional supervision of a practitioner licensed by law to administer the drug." Although Galson said that the FDA was "not shutting the door" on an eventual status change for Plan B, it is uncertain whether — or when — a revised application might be approved.

Approved for prescription use in 1999, Plan B consists of two 0.75-mg pills of levonorgestrel; it should be taken as soon as possible and within 72 hours after an episode of unprotected intercourse. The rate of pregnancy is 0.4 percent when treatment is initiated within 24 hours and 2.7 percent when treatment starts 48 to 72 hours after intercourse. In 2003, the FDA received an application for nonprescription status for the product.

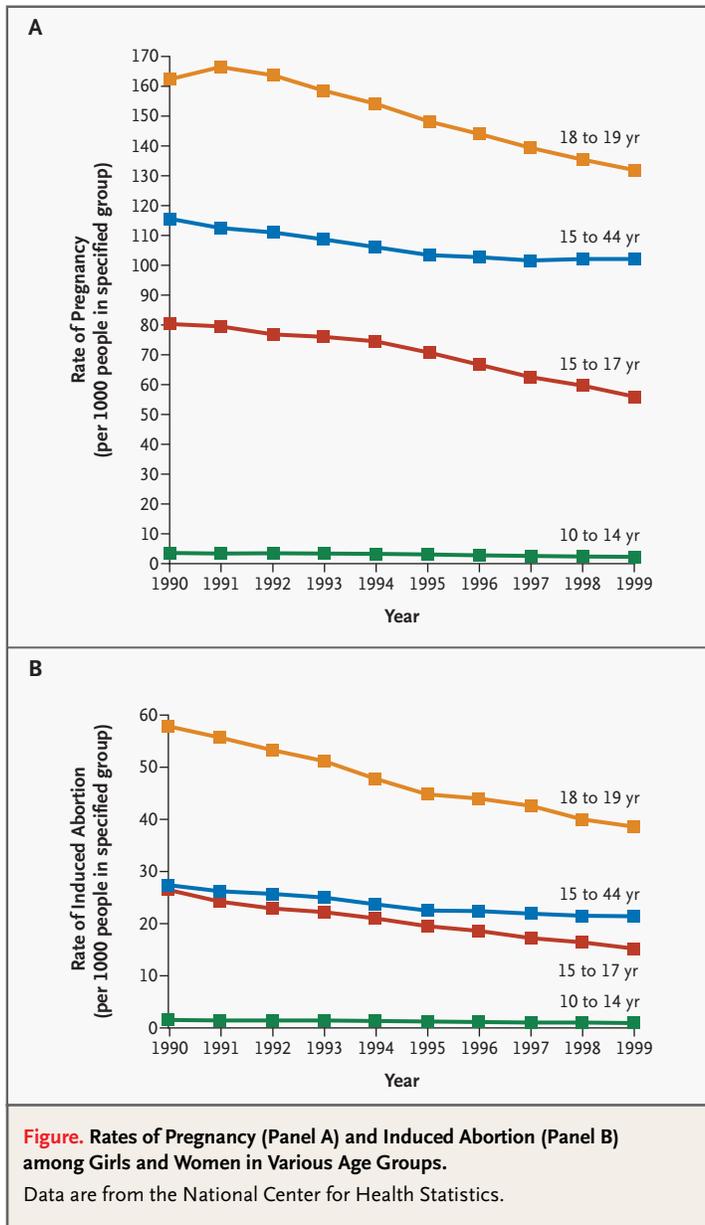
Rates of pregnancies and induced abortions have decreased in the United States, particularly among adolescents (see Figure) — primarily because contraceptive use has improved and because girls have been starting to have intercourse at older ages, according to James Trussell, director of the Office of Population Research at Princeton University. Nonetheless, unwanted pregnancy remains a major personal and public health issue. Commonly cited estimates are that half of all pregnancies are unintended, that one of every two girls or women between 15 and 44 years of age has had at least one unintended pregnancy, and that in 2000, as many as 51,000 abortions were averted with the use of emergency contraceptive pills.<sup>1,2</sup> Nonprescription

use of emergency contraception would not eliminate unwanted pregnancies or induced abortions, nor would it end the social debate about them. But it would, as Galson said, "dramatically increase access to oral contraceptives and will represent an important incremental step forward in availability of these products."

There are extensive data about the safety and effectiveness of Plan B, and there have been only isolated findings of increased rates of intercourse, unprotected intercourse, or intercourse without appropriate contraceptive methods in association with its availability. In rejecting the applications, the FDA also rejected the advice of its advisory committees and its medical-review staff. In December 2003, the Nonprescription Drugs Advisory Committee and the Advisory Committee for Reproductive Health Drugs, meeting in a joint session, recommended that Plan B be switched from prescription to over-the-counter status; the vote was 23 to 4. Committee members voted unanimously that "the data demonstrate that Plan B is safe for use in the non-prescription setting" and that there is no evidence that over-the-counter "availability of Plan B leads to substitution of emergency contraception for the regular use of other methods of contraception." Concerns about young teenagers were discussed, but these were not the focus of the deliberations; committee members were not asked to vote on whether girls younger than 16 years could use nonprescription Plan B safely.

FDA staff members also recommended the approval of the application. As a result of the difference of opinion within the Center for Drug Evaluation and Research, Galson, the acting director, signed the "Not Approvable" letter, a very unusual action. Galson said that although he "consulted with the Office of the Commissioner," he himself "made the decision," on the basis of the scientific data.

Political considerations — such as a desire to put the matter off until after the presidential elec-



American College of Obstetricians and Gynecologists (ACOG), said the FDA’s action was “morally repugnant.”

The FDA usually requires at least two types of studies before approving a switch to over-the-counter status for the first product in a class: a study of the comprehensibility of the label and an “actual use study” of the medication. Of the 585 subjects in the study of the actual use of Plan B, 29 were between 14 and 16 years of age, and none were younger than 14 years. Although Galson concluded that Barr Pharmaceuticals had not demonstrated that the use of Plan B was safe in girls younger than 16 years, he did not specify what data were lacking. When the application was being planned, the FDA could have requested the collection of more information about younger adolescents as part of the study.

Young teenagers account for only a tiny fraction of the potential users of emergency contraception (see Figure). Moreover, the anticipated cost of nonprescription Plan B — perhaps \$30 or \$40 — and its side effects, such as nausea and menstrual disruption with repeated use, would probably be powerful deterrents to frequent use. Of the 425,493 births to mothers 19 years of age or younger in 2002, only 18,703 (4.4 percent) involved mothers who were 15 years of age, and 7315 (1.7 percent) mothers younger than 15 years. During 29 months between 2001 and 2003, of 7774 callers to a telephone prescription service in North Carolina designed to increase access to emergency contraceptive pills, 40 percent were teenagers,<sup>4</sup> but only 2 percent of the callers were 15 years of age, and only 0.5 percent were younger than that, according to Dr. Elizabeth Raymond of Family Health International in Research Triangle Park, North Carolina. “The FDA’s fixation on young adolescents is simply unjustified,” Raymond said. “In addition to the small numbers who will likely buy emergency contraceptive pills over the counter, our research, and that of others, shows that they can use the pills correctly and safely.”

In March 2004, after Barr realized that the FDA was unlikely to approve the original application, it proposed to market Plan B as a prescription-only product for girls younger than 16 years of age and as a nonprescription product for older users. Although this approach offers an alternative to providing more data about the safe use of Plan B by young teenagers, it raises new difficulties. The proposal is “unprecedented,” according to Galson. The

tion in November — have been the spoken and unspoken subtext of this decision.<sup>3</sup> As part of a “questions and answers” document, the agency asked itself, “Did the FDA bow to political pressure in making this decision?” and answered “No.” Before the decision was made, conservative members of Congress and socially conservative groups lobbied for the application’s rejection. After the decision, other members of Congress called for it to be reviewed and overturned and for Galson and Lester Crawford, the acting commissioner of the FDA, to resign. Dr. Vivian Dickerson, the president of the

FDA has yet to determine whether dual status for the same medication in the same dose is permissible under its statutory authority. It is also not clear how this approach would work or whether most pharmacies would stock the product under this condition. For example, would Plan B be placed behind the front counter or the pharmacy counter or on open shelves? Who would verify the age of the purchaser? Would there be additional procedures or restrictions? Any such barriers to over-the-counter sales might dissuade any woman who requires access to emergency contraception, thus defeating the purpose of the switch.<sup>3</sup>

The FDA's decision may also have implications for medications that already have over-the-counter status or those for which a status change may be proposed in the future. For instance, children may purchase acetaminophen, aspirin, and nonsteroidal antiinflammatory medications without a prescription and without an age check. The FDA has never required specific data on the safe and correct use of these or other medications in children and adolescents, although their improper use is harmful and potentially lethal. When asked in a conference telephone call with reporters about the effect of the decision, Galson said that every review is different and "requires a separate kind of risk-benefit assessment." He added, "I wouldn't think it is accurate to predict what we are going to do with future products based on what we are doing now."

In the coming months, Barr hopes to submit a

revised application to the FDA for nonprescription sales of Plan B. After it does, the FDA will have six months to reach another decision. In the interim, the publicity may increase awareness of emergency contraception and thereby improve access.<sup>5</sup> According to Trussell, "not knowing about [emergency contraception] is the far bigger problem at the moment than not accessing it." In five states (Alaska, California, Hawaii, New Mexico, and Washington), emergency contraceptive pills are available without a prescription in some pharmacies under specified conditions. They will soon be similarly available in Maine. There are toll-free telephone hotlines and Web sites that help women get last-minute prescriptions, and ACOG urges all obstetrician-gynecologists to provide advance prescriptions for emergency contraception to all women of reproductive age at every office visit. Although over-the-counter status for Plan B will wait, the need for emergency contraception will not.

1. Henshaw SK. Unintended pregnancy in the United States. *Fam Plann Perspect* 1998;30:24-9, 46.
2. Jones RK, Darroch JE, Henshaw SK. Contraceptive use among U.S. women having abortions in 2000-2001. *Perspect Sex Reprod Health* 2002;34:294-303.
3. Drazen JM, Greene MF, Wood AJJ. The FDA, politics, and Plan B. *N Engl J Med* 2004;350:1561-2.
4. Raymond EG, Spruyt A, Bley K, Colm J, Gross S, Robbins LA. The North Carolina DIAL EC project: increasing access to emergency contraceptive pills by telephone. *Contraception* 2004;69:367-72.
5. Trussell J, Ellertson C, Stewart F, Raymond EG, Shochet T. The role of emergency contraception. *Am J Obstet Gynecol* 2004;190:Suppl 4:S30-S38.

## Health Care for Homeless Persons

Bruce D. Levy, M.D., and James J. O'Connell, M.D.

We met him in the winter of 1996, when he had severe frostbite in both feet. Forty-eight years old and homeless, he had been living in shelters and on the streets since his early 20s. Saddled with a severe anxiety disorder that could be quieted only by sufficient alcohol, he was known in every emergency department in the city, with frequent medical complications, more than 50 admissions to detoxification units, and only two extended periods of sobriety during the past decade. During the months after we met him, the first and second toes of his left foot autoamputated, horrifying both of us. We saw

him regularly on our outreach van, but he was too ashamed to accept offers of help. In 2000, he again suffered severe frostbite in both feet. Staying in our medical respite unit for several months, he battled chronic pain and lost several more toes. Ultimately, we won his trust and were able to help him secure sufficient government benefits to qualify for a rooming house and health insurance. Though still fragile, he now comes regularly to the clinic for treatment of hypertension and anxiety.

This patient's story illustrates the substantial challenges and hidden rewards that clinicians en-