Correspondence

Sustained-Release Bupropion for Smoking Cessation

To the Editor: In their report on the results of a dose–response trial of sustained-release bupropion for smoking cessation, Hurt et al. (Oct. 23 issue)[1] "recommend using the 300-mg dose (150 mg twice a day) as the target dose for most patients, given the favorable side-effect profile and the fact that there was less weight gain during the medication phase with this dose." We believe an initial dose of 150 mg a day may be more reasonable.

Safety is a concern because of dose-related risks of seizures (1 case per 1000), anaphylactoid reactions (1 to 3 cases per 1000), and insomnia (in 34.6 percent of cases). In addition, if a million people (2 percent of U.S. smokers) used bupropion, the difference in cost between 150 mg a day and 300 mg a day would be $45 million to $60 million a year (assuming a cost of $90 to $120 for seven weeks of therapy with the 300-mg dose).

At one year, the point-prevalence cessation rates for the 150-mg and 300-mg doses were 22.9 percent and 23.1 percent, respectively. At the end of treatment, the rates were 38.6 percent and 44.2 percent — not a significant difference. The suggestion that a higher dose should be used because it is associated with less weight gain is curious; at the end of treatment, the difference in the mean weight change between the 300-mg group and the 150-mg group was less than 2 lb (0.9 kg) and no effect on weight was seen for any dose after six months.

Another rationale given for routine use of the 300-mg dose is that it "was the only one to show a difference in the rates of continuous abstinence from the target quitting date through the end of treatment." However, there was no significant difference between the rates of continuous abstinence associated with the 300-mg and 150-mg doses at the end of treatment. The authors do not report continuous-abstinence rates at one year, although the data submitted to the Food and Drug Administration showed no significant differences between the continuous-abstinence rates associated with placebo and bupropion (10 percent for placebo, 15 percent for 150 mg, and 13 percent for 300 mg) (Karath BM, Glaxo Wellcome: personal communication). From the perspectives of public health and individual patients, what matters most is permanent cessation, for which the point prevalence at one year is a better measure than abstinence at the end of treatment.

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1. Hurt RD, Sachs DPL, Glover ED, et al. A comparison of sustained-release bupropion and placebo for smoking cessation. N Engl J Med 1997; 337:1195-202.

To the Editor: Was the study by Hurt et al. truly blinded? They state, "A dose of 50 mg twice a day was sufficient to

produce side effects." Could the study participants have recognized that they were receiving the smoking-cessation medication, and could they have been influenced to quit by that perception? Since the relapse rates among the quitters were essentially equivalent for all the groups, is it possible that quitting, whether due to an actual medication effect or to suggestion, was the key?

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The authors reply:

To the Editor: Drs. McAfee and France seem to miss the importance of the significant linear dose responses at all time points during the study, including the one-year follow-up. These data indicate that the dose of 300 mg per day resulted in the highest abstinence rate. Furthermore, the study was designed to assess a dose response and to make pairwise comparisons of the active doses versus placebo at the end of short-term treatment. It was not designed to have adequate statistical power for a comparison of the 150-mg and 300-mg doses.

Continuous abstinence and long-term abstinence are important issues. Continuous abstinence, however, is a very conservative estimate. Subjects who miss visits or have any interval of smoking (even a puff) are considered to be smoking. Furthermore, expecting a treatment effect to persist for 46 weeks beyond the end of treatment is demanding a lot of any medication for a chronic medical condition. We have observed in this study as well as others that once the medication is stopped, the relapse rate is similar regardless of the initial medication assignment. The relapse rate might be decreased were the medication used for a longer period of time. The optimal duration of treatment with sustained-release bupropion that might result in higher long-term abstinence rates has not been determined.

The importance of the attenuation of the weight gain should not be underestimated. Fear of weight gain keeps many smokers from even attempting to stop. At the end of treatment, there was a clear difference, with less weight gain in the continuously abstinent subjects assigned to 300 mg per day. Unfortunately, the difference was not present at the end of a year. This finding also speaks to the issue of the optimal duration of treatment.

Safety is always a concern, but some of the issues are misstated. Seizures can occur with doses lower than 300 mg per day, but most seizures occur with doses of 450 mg per day or higher. Anaphylactic reactions are not dose-related. Insomnia was more frequent among the subjects receiving 300 mg per day than among those receiving placebo, but this finding could have been confounded by insomnia caused by nicotine withdrawal.

We assure Dr. Pasternak that this was a true double-blind study. In general, adverse events were similar in all the treatment groups, including the placebo group, and all the participants received two tablets daily along with brief counseling.

On the basis of the available data, we believe that the 300-mg dose of sustained-release bupropion is the best dose. Questions remain about the optimal duration of therapy, though 7 to 12 weeks seems to be a reasonable starting point for most patients.

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A Quadrivalent Rotavirus Vaccine

To the Editor: The paper by Pérez-Schael et al. (Oct. 23 issue)[1] on the efficacy of rotavirus vaccine in Venezuela and the accompanying editorial by Drs. Keusch and Cash[2] deserve comment. The study included mostly children of low socioeconomic status, who are representative of much of the population of the developing world. The results are similar to those from three other trials in diverse settings and provide strong evidence of vaccine efficacy in comparable regions around the world (Finland, the United States, and an Indian reservation in the United States).[3-5] The lower vaccine efficacy in the Peruvian and Brazilian trials may be related to the use of a lower dose of vaccine.[6,7] In Peru there were few moderate-to-severe episodes of diarrhea after vaccination, probably because of active surveillance with frequent home visits and perhaps in part because placebo recipients had a high seroprevalence of IgA antibody, indicating that most infants in the study had been exposed to wild-type rotavirus before or during vaccine administration.

There is strong evidence to suggest that rotavirus and oral poliovirus vaccines do not interfere with each other.[8] Poor serotype-specific immune responses certainly reflect poor assay sensitivity, since assays that measure broad antigenic profiles detect responses. Longitudinal studies that are better able to confirm exposure to rotavirus than the vaccine trials have consistently demonstrated that certain serum and fecal antibody titers are predictive of protection against natural infections.[9,10] Testing of similar samples from vaccine trials should be standardized for the assays used in studies in which antibody correlates of protection have been identified; antibody titers should be assessed in addition to serologic responses.

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1. Pérez-Schael I, Guntiñas MJ, Pérez M, et al. Efficacy of the rhesus rotavirus–based quadrivalent vaccine in infants and young children in Venezuela. N Engl J Med 1997;337:1181-7.

2. Keusch GT, Cash RA. A vaccine against rotavirus — when is too much too much? N Engl J Med 1997;337:1228-9.
3. Bernstein DI, Glass RI, Rodgers G, Davidson BL, Sack DA. Evaluation of rhesus rotavirus monovalent and tetravalent reassortant vaccines in US children. JAMA 1995;273:1191-6.
4. Rennels MB, Glass RI, Dennehy PH, et al. Safety and efficacy of high-dose rhesus-human reassortant rotavirus vaccines — report of the National Multicenter Trial. Pediatrics 1996;97:7-13.
5. Vesikari T. Clinical experience with rotavirus vaccine in Finland. Presented at the 2nd Satellite Symposium of the 14th Annual Meeting of the European Society for Paediatric Infectious Diseases (ESPID), Elsinore, Denmark, 18–21 June 1996.
6. Lanata CF, Midthun K, Black RE, et al. Safety, immunogenicity, and protective efficacy of one and three doses of the tetravalent rhesus rotavirus vaccine in infants in Lima, Peru. J Infect Dis 1996;174:268-75.
7. Linhares AC, Gabbay YB, Mascarenhas JD, et al. Immunogenicity, safety and efficacy of tetravalent rhesus-human, reassortant rotavirus vaccine in Belem, Brazil. Bull World Health Organ 1996;74:491-500.
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9. O'Ryan ML, Matson DO, Estes MK, Pickering LK. Anti-rotavirus G type-specific and isotype-specific antibodies in children with natural rotavirus infections. J Infect Dis 1994;169:504-11.
10. Velázquez FR, Matson DO, Calva JJ, et al. Rotavirus infection in infants as protection against subsequent infections. N Engl J Med 1996;335:1022-8.

To the Editor: Drs. Keusch and Cash express unwarranted pessimism in recommending against rotavirus vaccination in developing countries. First, they attribute the lower efficacy of the rotavirus vaccine in Peru and Brazil to failure in a poorer, sicker population rather than to the considerably lower doses used in those studies.[1,2] With respect to vaccine immunogenicity and protection (e.g., for oral poliovirus[3] and rotavirus[4] vaccines), the dose is important. Poor poliovirus-vaccine immunogenicity in developing countries has led to the need for additional doses or an alternative vaccine, but never to the absence of vaccination.

They question the practicality of the vaccine if it cannot be given with oral poliovirus vaccine, noting that it has not been given in combination in trials in developing countries. The study protocols for those trials were last revised before the availability of data showing that the two vaccines do not interfere with each other. Keusch and Cash acknowledge that the immunogenicity of poliovirus vaccine is unaltered by rotavirus vaccine; the efficacy of rotavirus vaccine against severe disease was 64 to 80 percent when it was administered with oral poliovirus vaccine to over 600 infants in two U.S. trials.[5,6]

Keusch and Cash speculate whether a two-dose regimen might be sufficient and less expensive than a three-dose regimen. Determining how little vaccine might be enough, a legitimate subject for future research, will ultimately involve trade-offs and is not a reason to withhold an available, safe, and effective vaccine that might save so many lives.

Finally, they indicate that at $30 a dose, the vaccine is far too expensive for developing countries. That U.S. price was derived from models; a double-blind trial that actually measured costs arrived at a considerably lower figure.[7] Moreover, vaccines are sold on the basis of "tiered pricing." This explains why the price of an infant dose of recombinant hepatitis B vaccine is $24 in the U.S. private market but under $1.40 in the public market of certain developing countries. The United Nations Children's Fund (UNICEF) and the World Health Organization can provide vaccines at even lower cost where they are needed most.

Must the vaccine pass additional tests, despite its proven success among poor Venezuelan children and others? Drs. Keusch and Cash should reconsider their opposition and help make this successful vaccine available to the developing countries that need it most.

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1. Lanata CF, Midthun K, Black RE, et al. Safety, immunogenicity, and protective efficacy of one and three doses of the tetravalent rhesus rotavirus vaccine in infants in Lima, Peru. J Infect Dis 1996;174:268-75.
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3. Patriarca PA, Wright PF, John TJ. Factors affecting the immunogenicity of oral poliovirus vaccine in developing countries. Rev Infect Dis 1991;13:926-39.
4. Flores J, Perez-Schael I, Blanco M, et al. Reactogenicity and immunogenicity of a high-titer rhesus rotavirus-based quadrivalent rotavirus vaccine. J Clin Microbiol 1993;31:2439-45.
5. Santosham M, Moulton LH, Reid R, et al. Efficacy and safety of high-dose rhesus-human reassortant rotavirus vaccine in a high-risk population. J Pediatr (in press).
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7. Griffiths RI, Anderson GF, Powe NR, et al. Economic impact of immunization against rotavirus gastroenteritis: evidence from a clinical trial. Arch Pediatr Adolesc Med 1995;149:407-14.

The authors reply:

To the Editor: Drs. O'Ryan and Matson and Dr. Davidson question our interpretation of the trial of rotavirus reassortant vaccine in Venezuela. We reiterate that we are impressed with the scientific vision, technological achievement, and persistence of the vaccine's developers. Data on vaccine efficacy in industrialized countries, especially for severe episodes,[1] support the use of this vaccine for infants in countries able to pay for it, because the vaccine will reduce morbidity, save lives, and save money.

The question remains whether to promote this vaccine for use in developing countries now. Given the limited health budgets of poor countries and the realization that when something is added to these budgets something else must be deleted, we think it is mandatory to know the cost-effectiveness ratio of the new strategy first.

Unfortunately, two factors differ between prior studies in Brazil and Peru with poor results and the more successful Venezuelan trial — namely, the increased antigenic load of vaccine and the lower background rate of diarrhea in Venezuela. Whenever two factors differ between studies with divergent results it becomes impossible to ascribe the improved performance to just one of them. Thus, we said that we simply did not know whether the improved results in Venezuela were due to an increased vaccine load or reduced environmental contamination with potentially interfering enteroviral infections or, possibly, better nourished subjects.

Because no correlation between immune response and

protection was obvious, we also questioned whether it had been proved that three doses of vaccine were needed. This was not studied, however, and whatever price is set for this vaccine, two doses will cost only two thirds as much as three doses. We also are not convinced that the absence of immunologic incompatibility between rotavirus and poliovirus vaccines in the United States proves that the same is true in developing countries.

Finally, there is the issue of cost. Many factors affect vaccine pricing, including public scrutiny and the involvement of international organizations such as the World Health Organization, UNICEF, and others. We hope that the price of rotavirus vaccine will drop; however, we will still need to prioritize which vaccines to use, even if rotavirus vaccine becomes affordable. Current data on the effect of conjugate vaccines against *Haemophilus influenzae* type b in poor, developing countries are compelling[2] and strongly support the early introduction of this vaccine.[3] To prioritize the introduction of rotavirus vaccine, we must have similar data in populations representative of the poor countries and those at highest risk.

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1. Joensuu J, Koskenniemi E, Pang X-L, Vesikari T. Randomised placebo-controlled trial of rhesus-human reassortant rotavirus vaccine for prevention of severe rotavirus gastroenteritis. Lancet 1997;350:1205-9.
2. Mulholland K, Hilton S, Adegbola R, et al. Randomised trial of *Haemophilus influenzae* type-b tetanus protein conjugate for prevention of pneumonia and meningitis in Gambian infants. Lancet 1997;349:1191-7. [Erratum, Lancet 1997;350:524.]
3. It's "all systems go" for the Hib vaccine. Vaccine & Immunization News. Vol. 4. Geneva: World Health Organization, June 1997.

Cytotoxic-T-Cell Responses in Early HIV-1 Infection

To the Editor: Musey et al. (Oct. 30 issue)[1] suggest that their study shows that cytotoxic T lymphocytes have a modest effect of reducing the viral load, on the basis of the cross-sectional inverse correlation between human immunodeficiency virus type 1 (HIV-1) Env-specific cytotoxic T lymphocytes and plasma HIV RNA. This correlation may instead be due to the fact that the viral load is an inverse measure of the number of CD4+ lymphocytes, which help CD8+ cytotoxic T cells maintain responsiveness. This possibility could be investigated by adjusting for the CD4+ count when assessing the association between the cytotoxic-T-lymphocyte response and the viral load. The association between HIV-1 Env-specific cytotoxic T lymphocytes and plasma HIV RNA was weakest soon after seroconversion, when the association between HIV-1 Env-specific cytotoxic T lymphocytes and the CD4+ count was also weakest. The authors' conclusion that "the induction of memory cytotoxic T lymphocytes, particularly those specific for Env, helps control viral replication" seems unwarranted, since a higher level of Pol-specific cytotoxic T lymphocytes was associated with a higher viral load in peripheral-blood mononuclear cells (Table 2 in the article) and, when reduced to a binary variable, with higher plasma HIV RNA levels (Table 3 in the article).

A failure to adjust for the initial CD4+ lymphocyte count may also explain the relation between a higher level of HIV-1 Env-specific cytotoxic T lymphocytes and a longer time to a decrease in the CD4+ count to a level below 300 per cubic millimeter. It would also be helpful to know the relation between cytotoxic T lymphocytes with specificities other than Env and a fall in the CD4+ count to a level below 300 per cubic millimeter, again adjusted for the initial CD4+ lymphocyte count.

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1. Musey L, Hughes J, Schacker T, Shea T, Corey L, McElrath MJ. Cytotoxic-T-cell responses, viral load, and disease progression in early human immunodeficiency virus type 1 infection. N Engl J Med 1997;337:1267-74.

The authors reply:

To the Editor: Since absolute CD4+ lymphocyte counts do not determine helper function, and because T-helper–cell dysfunction occurs in persons with early infection and relatively normal CD4+ T-cell counts (unpublished data), we did not adjust for CD4+ counts when we examined the association between HIV-1–specific cytotoxicity and viral load in our study. Nonetheless, in response to Dr. Phillips's comments, we compared the univariate analysis with the multivariate analysis, adjusting for the CD4+ lymphocyte count (Table 1). Our findings are unchanged and indicate an inverse correlation between HIV-1 Env-specific cytotoxic T lymphocytes and plasma HIV-1 RNA. Indeed, the correlation was weakest just after infection, and this finding may be explained by the large fluctuation in the viral load during this period.[1] Higher levels of Gag-specific cytotoxic responses were also associated with a lower viral load in some analyses (Table 2 in our article), which, together with Env-specific responses, justifies

TABLE 1. ASSOCIATION OF CYTOTOXIC-T-LYMPHOCYTE RESPONSES WITH VIRAL LOAD AND CD4+ T-CELL COUNT IN EARLY HIV-1 INFECTION.

ANALYSIS	VARIABLE*	DIFFERENCE IN LOG RNA LEVELS	P VALUE
Univariate	Env-specific pCTL frequency >5	−0.39	0.006
	CD4+ count >200 cells/mm^3	−0.81	0.003
Multivariate	Env-specific pCTL frequency >5	−0.38	0.0003
	CD4+ count >200 cells/mm^3	−0.71	0.0005

*pCTL denotes precursor cytotoxic T lymphocytes.

our conclusion that the induction of memory cytotoxic T lymphocytes contributes to the control of viral replication.

The relation between the frequency of precursor cytotoxic T lymphocytes recognizing HIV-1 Env and the decline in CD4+ counts to a level of less than 300 per cubic millimeter, when adjusted for the initial CD4+ count, does not change (unadjusted relative risk, 0.18; adjusted relative risk, 0.22), although the standard error increases (95 percent confidence intervals: unadjusted, 0.03 to 0.98; adjusted, 0.04 to 1.39). The levels of Gag-specific or Pol-specific precursor frequencies have virtually no predictive value in determining declines in CD4+ counts to a level of less than 300 per cubic millimeter (relative risk adjusted for CD4+ counts: Gag, 0.74 [P=0.69]; Pol, 1.03 [P=0.97]). Thus, we again conclude that Env-specific responses may contribute to the delay in the progression of HIV-1 disease.

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1. Schacker T, Hughes J, Shea T, Coombs R, Corey L. Biological and virological characteristics of primary HIV infection. Ann Intern Med (in press).

Anaphylaxis from the Carboxymethylcellulose Component of Barium Sulfate Suspension

To the Editor: In their report of an anaphylactic reaction caused by the carboxymethylcellulose component of barium sulfate suspension (Oct. 30 issue),[1] Muroi and colleagues refer to another case report[2] of an anaphylactic reaction during barium administration. They appear to cite the reference as an example of exposure to latex, which has been implicated among the causes of allergic reactions to barium contrast medium. The case report[2] demonstrated that carrageenan, a sulfated polysaccharide that is also used as a suspending agent in barium preparations, was the cause of the anaphylactic reaction, on the basis of positive skin-puncture testing and the detection of specific IgE antibodies to carrageenan in serum. Muroi et al. did not test for immediate hypersensitivity to carrageenan. Were trace amounts of carrageenan used in the preparation of the carboxymethylcellulose component? If so, might they have affected the results of the skin test and the leukocyte histamine-release assay?

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1. Muroi N, Nishibori M, Fujii T, et al. Anaphylaxis from the carboxymethylcellulose component of barium sulfate suspension. N Engl J Med 1997;337:1275-7.
2. Tarlo SM, Dolovich J, Listgarten C. Anaphylaxis to carrageenan: a pseudo-latex allergy. J Allergy Clin Immunol 1995;95:933-6.

The authors reply:

To the Editor: Although Tarlo et al.[1] reported an anaphylactic reaction to carrageenan during a barium enema and 3 of 33 barium sulfate suspensions that are commercially available in Japan contain carrageenan, the barium sulfate suspension used in the double-contrast upper gastrointestinal examination of our patient did not contain carrageenan. The impurities of carboxymethylcellulose are inorganic salts such as sodium chloride, sodium sulfate, and sodium silicate. No organic substances were added to the carboxymethylcellulose during manufacturing. It is generally accepted that carboxymethylcellulose is neither digested nor absorbed by the gastrointestinal tract. Our patient received about 3 g of carboxymethylcellulose, and a minute amount could have entered the circulation and caused the anaphylactic reaction, since the patient was sensitized to carboxymethylcellulose. The use of an air–contrast technique[2] might affect the tight junction between absorptive epithelial cells, allowing the transit of carboxymethylcellulose into the subepithelial space.

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1. Tarlo SM, Dolovich J, Listgarten C. Anaphylaxis to carrageenan: a pseudo-latex allergy. J Allergy Clin Immunol 1995;95:933-6.
2. Janower ML. Reactions to contrast materials during gastrointestinal studies. Radiology 1990;177:287.

Prevention of Barium Impaction

To the Editor: We would like to comment on the Images in Clinical Medicine showing barium impaction in the sigmoid colon (Oct. 30 issue),[1] because this complication is rare if some precautions are taken.

For two days before the examination the patient should be given a low-residue diet and fluids to ensure adequate hydration. On the day of the examination the patient should drink plenty of clear fluids. Laxatives with various actions may be given, such as stimulants (bisacodyl), hyperosmolar agents (magnesium sulfate), and directly acting substances (anthraquinone derivatives). We use ricinus oil and a solution containing 400 mg of senna with 5 mg of dexpanthenol per 5 ml. Cleansing enemas are reserved for bedridden or constipated patients.

We perform small-bowel investigation by positioning a large-bore tube at the level of the ligament of Treitz. Barium suspension (300 ml) is instilled at a rate of 75 ml per minute, followed by methylcellulose solution (600 ml). The follow-through is continued until the first barium evacuation is seen, after which the patient is encouraged to empty his or her bowels into the toilet.

Before the colonic investigation, the radiologist will fluoroscopically check for fecal residue. A rectal examination

is routinely performed to look for a rectal mass and to ensure that the rectum is empty. A direct double-contrast investigation is also routinely performed with 300 ml of barium suspension. The barium is instilled in a retrograde fashion, and the patient is positioned to allow gravity to spread the barium to the cecum and terminal ileum. Air is insufflated to distend the colon. Approximately 75 percent of the instilled barium is evacuated from the rectum with the patient prone and semi-erect. A second method is reserved for patients who are in poor physical condition and those over 70 years of age, in whom the direct double-contrast technique is deemed too strenuous. In these patients, the barium solution is diluted to 1 liter and a single-contrast investigation is performed.

After the completion of either method of investigation, the cannula is left in place for 10 minutes to allow further drainage of the barium. After the cannula is removed, the patient is encouraged to evacuate his or her bowels into the toilet.

Using this approach, we have not encountered any patients with impacted barium fecaliths after small-bowel enteroclysis or colonic investigations in the past 10 years.

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1. McDonnell WM, Jung F. Barium impaction in the sigmoid colon. N Engl J Med 1997;337:1278.

The authors reply:

To the Editor: Although we used techniques that were similar to those described by Drs. van Beek and Reeders, barium impaction still developed in our patient. We believe that it was not the technique of the barium study that led to complications in this debilitated, postsurgical patient but what occurred after the procedure. Attention to hydration, cleansing the bowel if necessary, and seeking medical care promptly if patients fail to have bowel movements are important in preventing impaction.

We surveyed five gastrointestinal-radiology departments to determine their post-procedure instructions. Four had no written instructions for the patient but verbally instructed patients to take plenty of fluids; two also told patients that they could take a laxative such as milk of magnesia. Only one department gave written instructions stating that the patients should "take a mild laxative . . . and drink more fluids than normal to help rid the body of barium" and that "laxatives may be repeated a second day, if needed." Patients were instructed to "call the physician's office if [they did] not have a bowel movement within 48 hours."

Drs. van Beek and Reeders imply that there have been no complications from barium studies performed in their department, but unless the data were obtained prospectively with follow-up telephone calls, they may have missed some patients who did have complications. When patients present with barium impaction, the problem is usually dealt with by physicians other than radiologists.

We believe attention should be directed especially to the patient's underlying medical condition and to the care given after a barium study.

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Treatment of Cystoid Macular Edema with Octreotide

To the Editor: Idiopathic cystoid macular edema is an uncommon form of retinal edema that is refractory to treatment with drugs such as acetazolamide[1] that are used in patients with other types of macular edema.[2,3] We describe the beneficial effect of octreotide in a patient with this disorder.

A 21-year-old man was found to have moderate color-vision defects at routine examination. One year later, he noticed blurred vision. His visual acuity was 20/50 in the right eye and 20/40 in the left eye (Snellen chart). Because he had bilateral cystoid macular edema, he was treated with diclofenac eye drops, peribulbar injections of betamethasone, acetazolamide, and enalapril without beneficial effect on the edema or visual acuity. His visual acuity slowly deteriorated in the subsequent years. When we examined the patient three years after he first noted blurring of his vision, his visual acuity was 20/100 in each eye, the macular regions showed large cystoid lesions (Fig. 1A), and there was no intraocular inflammation (anterior chamber flare or cells, vitreous cells, vascular sheathing, exudates, or pars planitis). He had no family history of macular edema. Fluorescein angiography showed accumulation of dye in the cystoid lesions (Fig. 1B and 1C). Because the previous therapy had failed to correct the problem, the patient was treated with octreotide, 100 μg subcutaneously three times daily, after he gave informed consent. He noted visual improvement after six weeks, and when tested after eight weeks his visual acuity was 20/40 in the right eye and 20/50 in the left eye. Ophthalmoscopically, the cysts had dried. The injections were stopped four weeks later, because there was no further improvement.

Within two weeks the patient noticed increased reading difficulty, his visual acuity was 20/50 in each eye, and some fluid was observed ophthalmoscopically. Treatment with 100 μg of octreotide subcutaneously once daily was resumed. Three months later the patient's visual acuity was 20/40 in each eye; fluorescein angiography showed some foveal fluorescein leakage (Fig. 1D, 1E, and 1F). He stopped treatment a second time; after four weeks his visual acuity was 20/70 in the right eye and 20/50 in the left eye. Octreotide therapy was resumed, and four weeks later his visual acuity was 20/40 in each eye. The patient had no side effects from the treatment. The decreased macular edema during treatment with octreotide, the recurrence after stopping treatment, and the response after restarting it suggest that the changes were due to octreotide.

The mechanism of inhibition of macular edema by oc-

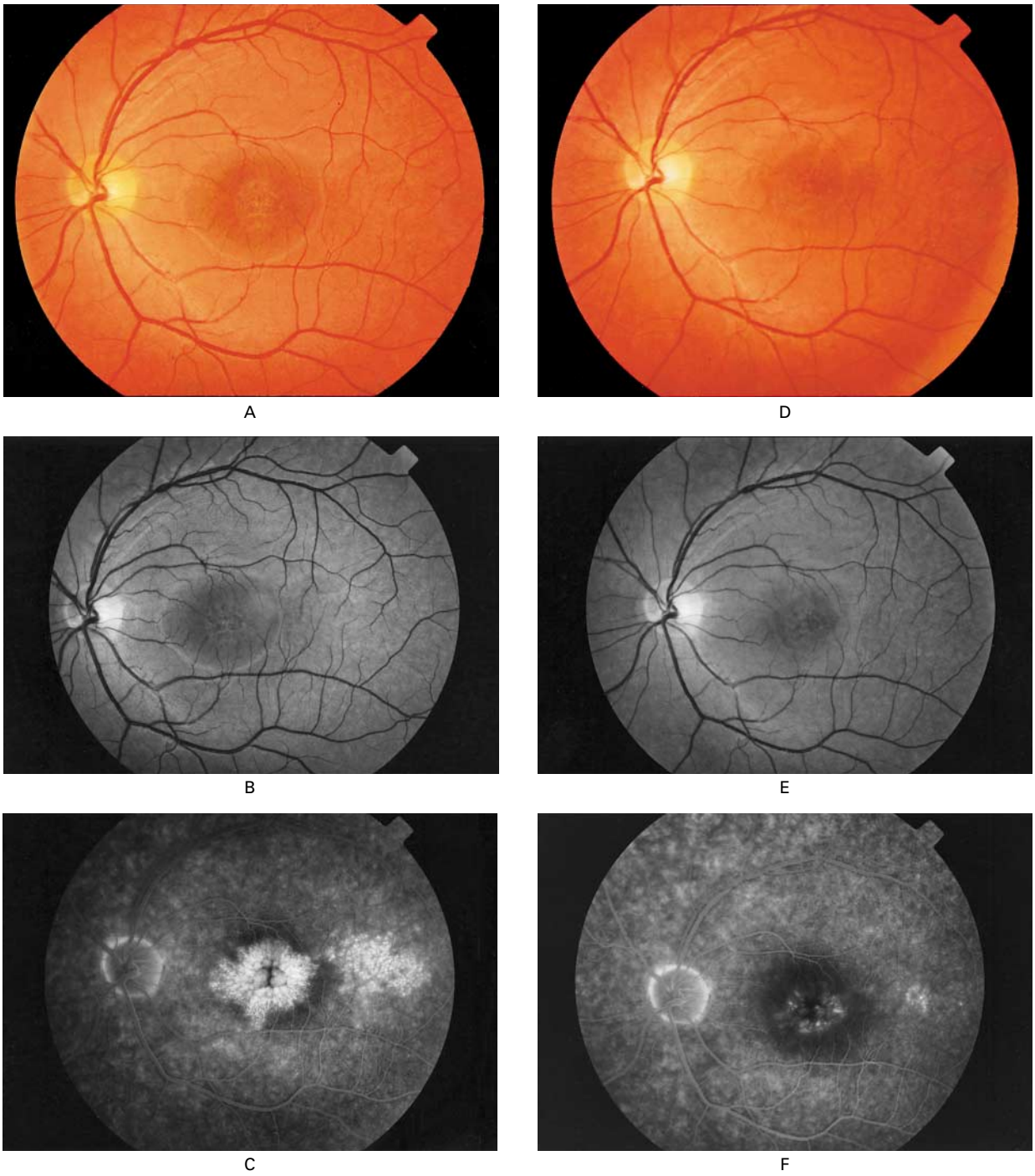

Figure 1. Photographs and Angiograms of the Left Retina before and after Treatment with Octreotide.

A pretreatment photograph of the retina (Panel A) and fluorescein angiograms of the left eye before (Panel B) and nine minutes after (Panel C) injection of the dye are shown. Panel C shows intense hyperfluorescence due to pooling of the dye in the cystoid lesions. Panels D, E, and F show a comparable photograph and angiograms of the left eye three months after the start of the second course of octreotide. The photograph in Panel F, taken 11 minutes after injection of the dye, shows some focal hyperfluorescence due to persisting intraretinal fluid.

treotide is not known. It may act directly on the capillary endothelial cells or through inhibition of growth hormone and production of insulin-like growth factor I.[4,5] On the basis of our results, we suggest that octreotide be evaluated in patients with other types of macular edema.

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National HIV Case Reporting

To the Editor: Although it is true that Maryland's surveillance system for human immunodeficiency virus (HIV), which has been in effect since 1994, is still being refined and improved, we have found that it has allowed us to perform all the public health functions described in the article by Gostin et al. (Oct. 16 issue).[1] Maryland's system of HIV surveillance by means of unique identifiers has allowed linkage of HIV case reports to death records, has assisted in investigations of unusual strains of HIV,[2] and has been used to inform decisions about allocating funds for service delivery. Our experience suggests that important epidemiologic information can be obtained through a non–name-based surveillance system.

Given the traditional American concern about the privacy of medical records and the very real potential for discrimination against people infected with HIV, we believe that our system provides the benefits of epidemiologic monitoring of the epidemic and averts the creation of barriers to HIV testing and treatment among those concerned about confidentiality. We suggest that states considering HIV surveillance investigate non–name-based HIV-surveillance systems as an important option.

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To the Editor: The information already available has not been used to prevent HIV transmission among injection-drug users, and widespread HIV case reporting, however meritorious, will not improve that situation.

AIDS-surveillance reports present sufficiently clear and reliable information on the prevalence, incidence, and direction of the epidemic. They indicate a shift in primary risk behavior to injection-drug users, in whom approximately 50 percent of new infections are estimated to occur.[1] The disproportionate impact of the twin epidemics of drug use and AIDS on minority groups, particularly minority women, and among neonates is well documented.[2] On the basis of evidence that HIV is transmitted among injection-drug users through shared use of contaminated needles — which, particularly in the United States, is necessitated by legal restrictions on drug paraphernalia — European countries have liberalized paraphernalia policies as a specific HIV-prevention strategy for this group. However, driven by a war-on-drugs ideology rather than by public health and epidemiologic imperatives, the United States has not taken this simple step and thus has unleashed the epidemic among injection-drug users.[3]

This burgeoning pool of infected injection-drug users is concentrated in poor, urban, and predominantly minority neighborhoods, where the epidemic continues to worsen. Relatively small declines in the numbers of deaths from AIDS among members of minority groups (decreases of 2 percent among non-Hispanic blacks and 10 percent among Hispanics as compared with 21 percent among non-Hispanic whites) are a sad commentary on those left behind[4] despite general "advances." Unless rational policy changes allowing drug users to buy and carry their own injection equipment are enacted, HIV case reporting will have no effect on this population.

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To the Editor: In June of 1988, the Presidential Commission on the Human Immunodeficiency Virus Epidemic, established by President Ronald Reagan, issued its final report. Its first point states:

> The term "AIDS" is obsolete. "HIV infection" more correctly defines the problem. The medical, public health, political, and community leadership must focus

> on the full course of HIV infection rather than concentrating on later stages of the disease. Continual focus on AIDS rather than the entire spectrum of HIV disease has left our nation unable to deal adequately with the epidemic. Federal and state data collection efforts must now be focused on early HIV reports, while still collecting data on symptomatic disease.[1]

Unfortunately, this sound recommendation was not acted on.

It is encouraging that many in the activist community and in academia are now supporting sound HIV policies. However, we should remember it was these same activists and academics who helped establish a very flawed policy in the first place. To continue to go to them for direction seems ill advised in the light of the admissions they now make regarding the sound HIV policy they fought against for so long.

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1. Report of the Presidential Commission on the Human Immunodeficiency Virus Epidemic, June 24, 1988. Washington, D.C.: Government Printing Office, 1988:87-9. (GPO publication no. 0-214-701:QL3.)

The authors reply:

To the Editor: The three letters in response to our article are representative of a growing consensus that a national system of HIV surveillance is essential for effective monitoring of and public health response to the HIV/AIDS epidemic. Our proposal for national HIV reporting will, of course, not solve all the perplexing public health and human-rights problems presented by the epidemic. HIV reporting is likely to demonstrate an increasingly disproportionate burden of infection among injection-drug users. In previously published research, we have strongly supported greater access to sterile injection equipment, as aptly suggested by Dr. Fernando.[1]

Drs. Solomon and Benjamin raise perhaps the most important intellectual challenge to a national system of named HIV reporting. Given the understandable concern about privacy, names should not be collected by the government unless it is necessary to achieve important public health purposes. Unfortunately, the data from Maryland do not demonstrate that a system of unique identifiers can provide accurate and reliable data. A recent evaluation of the Maryland system supported by the Centers for Disease Control and Prevention found substantial limitations.[2] Of 9971 laboratory reports entered in the Maryland system from July 1994 through December 1996, 29 percent of the reports were missing a portion of the unique identifier, including 22 percent that were missing the social security number (the most specific component of the unique identifier). The Maryland system is also limited by a low rate of completeness of reporting (50 percent), an inordinate number of duplicate reports, and a lack of HIV-risk information. Finally, a unique-identifier system may create additional risks to privacy by increasing the number of surveillance registries. In order to collect follow-up epidemiologic information, private physicians have to maintain logs that link the unique identifier to a name-based medical record. These multiple registries in the private sector may defeat the privacy purposes behind unique-identifier systems.

Congressman Coburn and Mr. Smith support named HIV reporting but suggest that public health officials, community-based organizations, and scholars have lost any legitimate claim to leadership. This is an unfortunate implication coming from two leaders in American politics. Our positions on HIV policies are not formed by political or ideological beliefs. Rather, they are based on objective assessments of the science and of the public health, which necessarily must take account of the medical benefits to and the human rights of people with HIV infection or AIDS. It is not we who have changed, but the epidemic. Given the remarkable progress in medical treatment and a more humane social and legal response to AIDS, new ways of thinking about the epidemic become critically important. We need to create a national HIV-surveillance system that is scientifically sound and supported by the public it serves.

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