infections, such as those affecting the gastrointestinal tract, that fuel HIV replication.

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THE AUTHORS REPLY: Our study was a proof-of-concept trial and so did not allow prediction of the effect of HSV suppressive therapy as a public health intervention to prevent the transmission of HIV. Available data regarding resistance to acyclovir are reassuring. The occurrence of acyclovir-resistant HSV-2 strains in HIV-infected patients (4 to 7%) has not increased during the past two decades in Western countries, despite the frequent use of acyclovir and valacyclovir. Instead, resistance to acyclovir could be declining, since the use of highly active antiretroviral therapy has become widespread. When such resistance occurs, it is not predictive of clinical failure. In addition, the occurrence of genital ulceration during the course of HSV suppressive therapy does not necessarily mean that the causative strain is resistant to acyclovir. We agree that in the absence of second-line therapy in resource-constrained countries (and considering the paucity of data available to date), the importance of resistance to acyclovir should be investigated further. However, even if such resistance is confirmed, it is unlikely to counterbalance the potential positive effect of HSV suppressive therapy on HIV-1 disease progression and transmission.

The HIV-1 plasma viral load in the placebo group increased slightly during our study, but we doubt this rise was due to HIV-unrelated gastrointestinal diseases. Several women reported having more than one symptom, so the P value calculated by Dr. Eisenhut needs modification. In fact, the proportion of women who reported at least one gastrointestinal symptom tended to be higher in the placebo group (38.2%) than in the valacyclovir group (25.0%) but without reaching statistical significance (P = 0.10). Valacyclovir and acyclovir have been used for decades with a safety profile similar to that of placebo. The hypothesis by Brenchley et al. that a sustained systemic immune activation is fueled by intestinal bacteria through a translocation mechanism is based on the commensal enteric flora and not on pathogens. It is unlikely that this mechanism could be altered or enhanced by the intake of valacyclovir. It should also be noted that our primary outcome was genital HIV viral load, and there was little difference in this outcome in the placebo group before randomization and after randomization (mean number of log_{10} copies per milliliter, 2.97 and 3.02, respectively).

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Coronary Microvascular Dysfunction

TO THE EDITOR: Camici and Crea (Feb. 22 issue) review the different causes and mechanisms of coronary microvascular dysfunction. However, coronary microvascular dysfunction due to aging deserves further comment. Age is a recognized risk factor for cardiovascular disease, and senescence is associated with morphologic and functional changes in the coronary microvasculature. Studies in animals have shown that coronary flow reserve and the endothelium-dependent dilatation

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of the resistance arteries decrease with age. It has been suggested that endothelium-dependent dilatation of the resistance coronary arteries evoked by acetylcholine may decrease with age in humans.

The mechanisms underlying the age-associated reduction in the ability of the coronary microvasculature to dilate in response to acetylcholine are controversial. With advancing age, nitrous oxide–dependent mechanical and agonist-mediated endothelial vasodilatation is reduced in humans and animals. Coronary microvascular dysfunction due to aging should not be underestimated. Although pharmacologic treatment has been shown to restore coronary blood reserve in endothelial dysfunction due to aging, its effect on the clinical outcome remains to be determined.

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THE AUTHORS REPLY: We agree with Duran and Taffet that coronary microvascular function changes significantly with aging. Indeed, we stated, “In healthy persons, however, coronary flow reserve varies according to age and sex. Therefore, it is essential to compare data on coronary flow reserve in patients with data obtained in age-matched and sex-matched control subjects.” Using positron-emission tomography, Uren et al., and Chareonthaitawee et al.2 have shown that resting and hyperemic myocardial blood flow remain unchanged in persons up to 60 years of age. After 60 years of age, there is a significant increase in resting myocardial blood flow, associated with an increase in systolic blood pressure. After 70 years of age, there is a significant reduction in hyperemic myocardial blood flow and in coronary flow reserve. There are probably multiple causes of these age-related changes, and they remain incompletely understood.

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Perioperative Stroke

TO THE EDITOR: In his review of perioperative stroke, Selim (Feb. 15 issue) states that regional anesthesia may pose less risk of perioperative complications than general anesthesia and that “isoflurane and thiopentone may provide neuroprotection.” However, the references that he cites do not provide support for these contentions. Breen and Park’s review of the literature showed that no conclusions could be drawn about the risk of stroke associated with general as compared with regional anesthesia for carotid endarterectomy. In fact, the results of the randomized trials reviewed indicated that postoperative hypotension was more likely after regional anesthesia. The differences that have been identified may not have a great clinical impact and require further study.

Turner et al. reviewed the literature on agents for induction of general anesthesia and conclude that thiopental, propofol, and etomidate have similar effects on intracranial pressure, cerebral blood flow, and cerebral oxygen consumption, so the selection of an agent should be based on other considerations. They did not discuss isoflurane. The most one can conclude from the extant literature is that there are a number of hypotheses