EDITORIALS

Vivek Murthy for Surgeon General

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Surgeons general of the United States have often championed important causes that improve the nation's health. Leroy Burney and Luther Terry took on the issue of smoking and health. C. Everett Koop championed the treatment of HIV-AIDS as a medical condition. With the nomination of Dr. Vivek Murthy, who aims to take on the epidemic of obesity, President Barack Obama is striving to continue this tradition.

Murthy, whose parents immigrated to the United States from India, has lived the American dream. He was educated at two of our nation's most prestigious universities, earning his undergraduate degree at Harvard and both an M.D. and an M.B.A. degree at Yale. He currently practices medicine at Boston's Brigham and Women's Hospital and is a member of the faculty of Harvard Medical School.

Murthy was one of the founders and is currently the president of Doctors for America, an organization focused on broadening access to high-quality health care. In his impressive career, he has been strongly committed to disease prevention and health promotion, having served on the Presidential Advisory Group on Prevention, Health Promotion, and Integrative and Public Health. He cofounded Visions Worldwide, a nonprofit organization working on HIV prevention and education. He is the chair of TrialNetworks, an initiative that assists drug developers with clinical trials.

On February 27, a bipartisan group of senators on the Health, Education, Labor, and Pensions (HELP) Committee approved Murthy's nomination for surgeon general and forwarded it for a vote by the full Senate. But now, astonishingly, the nomination appears to be in jeopardy and may be delayed or withdrawn altogether. How could this have happened to such a distinguished and highly qualified nominee?

The answer lies with the National Rifle Association (NRA). It is of great concern to us and to many other members of the health care community that Murthy's nomination is in jeopardy because of NRA opposition. The NRA opposes Murthy solely on the grounds that he has advocated reasonable and mainstream forms of gun regulation, including an assault-weapons ban, a limit on ammunition sales, and required safety training. Given that there are more than 30,000 firearm deaths in the United States each year, Murthy's views on potential safeguards are unsurprising.

This is the first time that the NRA has flexed its political muscle over the appointment of a surgeon general. The NRA has taken this action even though the surgeon general has no authority over firearm regulation and even though Murthy made it clear in his testimony before the Senate HELP Committee that if he is confirmed, his principal focus will be on the important national problem of obesity prevention, not firearm policy. Still, 10 Senate Democrats are apparently prepared to vote against Murthy's confirmation because of his personal views on firearms — a demonstration of just how much political power our legislators have ceded to the NRA.

The critical question is this: Should a special-interest organization like the NRA have veto power over the appointment of the nation's top doctor? The very idea is unacceptable.

Despite the continuing American tragedy of mass shootings — Newtown, Aurora, Fort Hood, Virginia Tech — the NRA has redoubled its ef-

forts to prevent enactment of stricter firearm regulations. Lawmakers who run afoul of the NRA face political retribution. By obstructing the President's nomination of Vivek Murthy as surgeon general, the NRA is taking its single-issue political blackmail to a new level. With the record of past surgeons general as their guide, senators should do what is right for the health of our country by confronting the NRA and voting their own conscience. Dr. Murthy is an accomplished physician, policymaker, leader, and entrepreneur. He deserves the President's continued backing and should be confirmed.

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Taming the Transplantation Troll by Targeting Terminase

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The immunosuppressive drugs required after stem-cell transplantation render patients susceptible to opportunistic infections. The most important of these infections, in terms of both abundance and severity, is cytomegalovirus (CMV), which has been dubbed the "troll of transplantation."[1] Fortunately, the clinical effects of CMV infection have been reduced by preemptive therapy. Levels of CMV DNA in the blood (viremia) are monitored with the use of polymerase-chain-reaction (PCR) assays and, if viremia is detected, patients receive ganciclovir (or its prodrug valganciclovir) until viral DNA is no longer detectable.[2] In addition to controlling overt CMV end-organ disease, since these agents are used only if viremia is detected, this strategy minimizes the bone marrow toxicity of ganciclovir and valganciclovir, which is clinically highly important after stem-cell transplantation.[2] After solid-organ transplantation, these agents can be administered prophylactically with efficacy and safety that are similar to those of preemptive therapy.[3,4] For patients who have undergone transplantation, drugs with reduced toxicity, improved potency, or both, as compared with ganciclovir and valganciclovir, are highly desirable. An appropriate study design[2] in a placebo-controlled trial is to administer the experimental drug prophylactically and determine whether selected doses, as compared with placebo (the standard of care), can reduce the need for preemptive therapy.

In this issue of the *Journal*, Chemaly et al.[5] describe the phase 2 evaluation of a new anti-CMV drug. In this study, the incidence of virologic failure decreased in a dose-dependent fashion: 36% in the placebo group, 21% in the group that received 60 mg per day, 19% in the group that received 120 mg per day, and 6% in the group that received 240 mg per day. The new drug in question is an inhibitor of a key enzymatic component of the "terminase complex." Viral DNA is synthesized by means of rolling circle replication to produce long concatemers of DNA. As shown in Figure 1, these concatemers are analogous to individual coaches in a train. The unit-length DNA (like an individual coach) is actively packaged into a newly formed capsid until a defined sequence (analogous to a coupling between two coaches) is recognized, the DNA is cut, and the capsid is sealed.[6,7] This cleavage is effected by terminase, which thus is a novel target both in the context of the virus (most other drugs in clinical use have targeted the viral DNA replication machinery) and in the context of the human host, because no such equivalent process is known to occur in human cells.[8] Following successful phase 1 studies, this drug, letermovir, has passed its phase 2 evaluation with impressive results.[5]

One of the problems with performing CMV prophylaxis studies in a population of patients who have undergone stem-cell transplantation is deciding when to start therapy.[2] Whereas prophylaxis in patients who have received solid-organ transplants can be initiated almost immediately after transplantation, in patients who have undergone stem-cell transplantation, prophylaxis has usually been initiated after engraftment (after the neutrophil count reaches a minimum threshold, usually ≥500 cells per cubic millimeter) because of the bone marrow toxicity of ganciclovir and valganciclovir.[2] A new drug without such an adverse side-effect profile could be used much earlier after stem-cell transplantation; this was