

previously treated with fluconazole. A randomized trial comparing the efficacy of voriconazole with that of echinocandins for the treatment of candidemia is warranted.

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Dr. Carratalà reports receiving lecture fees from Pfizer.

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**THE AUTHOR REPLIES:** The recently published Swiss guidelines concur with the view of Garcia-Vidal and Carratalà that voriconazole should be considered as one of the second-line agents for treatment of candidemia in nonneutropenic pa-

tients with no prior exposure to an azole.<sup>1</sup> However, I see no clear indication for selecting voriconazole over fluconazole for such patients. *Candida* species with reduced susceptibility to fluconazole have proportionally reduced susceptibility to voriconazole. The major indication for the use of voriconazole is its clinical efficacy against invasive mold infections.<sup>2</sup> For candidemia, fluconazole is the preferred azole because of its superior safety profile, fewer known drug interactions, and lower cost, and because of the absence of restrictions on intravenous administration in patients with a creatinine clearance below 50 ml per minute.<sup>3</sup>

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## Effects of Dietary Nitrate on Blood Pressure in Healthy Volunteers

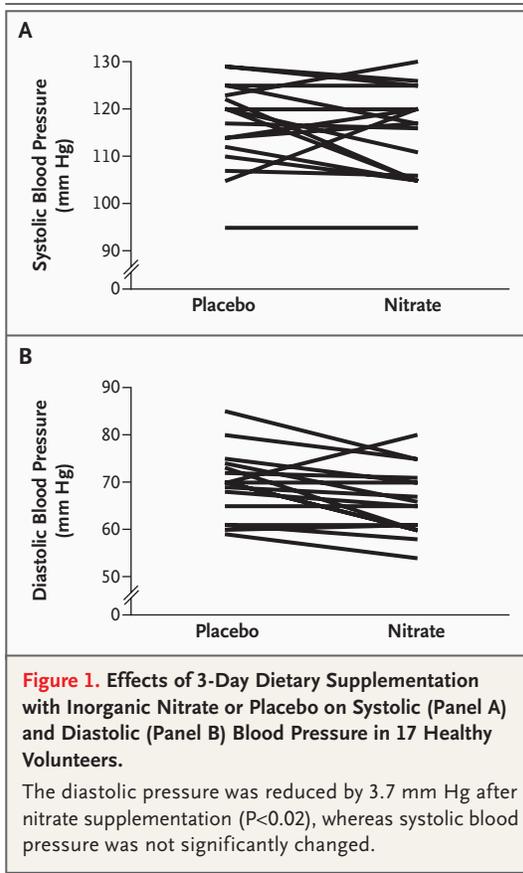
**TO THE EDITOR:** Nitric oxide, generated by nitric oxide synthase, is a key regulator of vascular integrity. This system is dysfunctional in many cardiovascular disorders, including hypertension. A fundamentally different pathway for the generation of nitric oxide was recently described in which the anions nitrate ( $\text{NO}_3^-$ ) and nitrite ( $\text{NO}_2^-$ ) are converted into nitric oxide and other bioactive nitrogen oxides.<sup>1-3</sup> Nitrate is abundant in our diet, and particularly high levels are found in many vegetables.<sup>3</sup>

We examined the effect of 3-day dietary supplementation with either sodium nitrate (at a dose of 0.1 mmol per kilogram of body weight per day) or placebo (sodium chloride, at a dose of 0.1 mmol per kilogram per day) on blood pressure in 17 physically active, healthy volunteers, none of whom smoked (15 men and 2 women; mean age, 24 years). The study had a randomized, double-blind, crossover design with two different treatment periods during which the subjects received either nitrate or placebo; the treatment periods were separated by a washout period of at least 10

days. The compounds were dissolved in water and could not be distinguished by taste or appearance. During the two treatment periods, the subjects were instructed to avoid all foods with a moderate or high nitrate content.<sup>3</sup>

Systolic blood pressure (Fig. 1A) and pulse rate did not change significantly after nitrate supplementation, as compared with placebo supplementation. However, the diastolic blood pressure was on average 3.7 mm Hg lower after nitrate supplementation than after placebo supplementation ( $P < 0.02$ ) (Fig. 1B), and the mean arterial pressure was 3.2 mm Hg lower ( $P < 0.03$ ). Plasma nitrate levels were higher after nitrate ingestion than after placebo ingestion (mean  $\pm$ SD),  $178 \pm 51$  and  $26 \pm 11 \mu\text{M}$ , respectively;  $P < 0.001$ ), as were plasma nitrite levels ( $219 \pm 105$  and  $138 \pm 38 \text{ nM}$ , respectively;  $P < 0.01$ ).

The daily nitrate dose used in the study corresponds to the amount normally found in 150 to 250 g of a nitrate-rich vegetable such as spinach, beetroot, or lettuce. It is clear from earlier studies, such as the Dietary Approaches to Stop Hyperten-



sion (DASH) trial, that a diet rich in fruits and vegetables can reduce blood pressure,<sup>4,5</sup> but attempts to modify single nutrients have been inconsistent. Therefore, it has been argued that the effect of any individual nutrient is too small to detect in trials. In our study, reduced blood pres-

sure was associated with nitrate supplementation alone; this effect was evident in young normotensive subjects. In fact, it was similar to that seen in the healthy control group in the DASH study.<sup>4</sup> The exact mechanism behind the blood-pressure-lowering effect of nitrate needs to be clarified in future studies.

We conclude that short-term dietary supplementation with inorganic nitrate reduces diastolic blood pressure in healthy young volunteers.

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