

proval of the Food and Drug Administration.” This statement is incorrect; throughout American history, vitamins and herbs have been sold without prior federal permission. The Dietary Supplement Health and Education Act of 1994, to which Drazen apparently refers, formalized the status of supplements in response to fears that those products could be banned.

Under this act, manufacturers must submit safety documentation for new ingredients, which the FDA may disallow at will. Existing products that prove to be hazardous can also be prohibited. These requirements strike a fair balance between laboratory science and human experience. The safety of common herbs is as well established by traditional knowledge as is the safety of many vegetables, spices, and beverages with presumed fitness for consumption that is unsupported by rigorous American studies in animal models or clinical studies. Indeed,

arguments against the act carry the bizarre implication that dual-use botanicals, such as ginger, may be safe when eaten as vegetables but hazardous when taken as supplements.

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DR. DRAZEN REPLIES: The letters from Drs. Applequist and de Lemos and Mr. Taylor all indicate that consumers in the United States are confused about the exact status of dietary supplements. Since, for all practical purposes, these materials are advertised as if they were medicines, they should, in my opinion, be regulated as such.

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Human Growth Hormone and Aging

TO THE EDITOR: Vance’s discussion of growth hormone (Feb. 27 issue)¹ omits important reports in the literature. The combination of growth hormone and exercise (unlike exercise alone) has been shown to increase type II muscle fibers in the elderly² — an important finding, since frailty and sarcopenia are predominantly related to the loss of type II fibers. There is no mention of the fact that decreased levels of insulin-like growth factor I have been reported to be associated with angina pectoris,³ myocardial infarction,⁴ and atherosclerosis,⁵ which are the leading causes of death in this country. The discussion also excludes a recent report that aging men with low levels of insulin-like growth factor I die earlier than those with high levels.⁶

Long-term prospective studies on the potential of growth hormone will take decades. In the meantime, the use of growth hormone should be based on a patient’s clinical status and on a candid patient–physician discussion of current information on the pros and cons of such therapy.

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diameter in moderately frail older people. *J Am Geriatr Soc* 2001;49:852-8.

3. Conti E, Andreotti F, Sestito A, et al. Reduced levels of insulin-like growth factor-1 in patients with angina pectoris, positive exercise stress test, and angiographically normal epicardial coronary arteries. *Am J Cardiol* 2002;89:973-5.

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DR. VANCE REPLIES: Dr. Mahmud correctly notes that the combination of growth hormone and exercise increases type II muscle fibers in the elderly. As stated in my Retrospective article, changes in body composition with growth hormone administration do not improve function in the elderly. Reduced levels of insulin-like growth factor I may be associated with other diseases, although such an association is not proof of cause and effect and may echo the effect of disease; for example, insulin-like growth factor I may be low in young women with anorexia nervosa.¹ That older men with low levels of insulin-like growth factor I may die earlier than those with high levels may reflect underlying diseases. Rudman et al. reported that elderly men living independently had

higher levels of insulin-like growth factor I than those living in a nursing home and had fewer medical problems.² Again, these associations are valid but do not demonstrate cause and effect.

“Long-term prospective studies on the potential of growth hormone will take decades”: I agree. Without such studies, anyone can easily fall prey to unproven claims. Recall laetrile for cancer: How many people “believed” that it was efficacious? How many did not receive appropriate therapies, in the quest for a “magic bullet”? Appropriate studies, not opinions, are the only way to determine whether a treatment is beneficial.

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Nephropathy Induced by Contrast Medium

TO THE EDITOR: The article by Aspelin et al. (Feb. 6 issue)¹ regarding the lower incidence of contrast-medium-induced nephropathy in patients with diabetes and a serum creatinine concentration of 1.5 to 3.5 mg per deciliter who were treated with iodixanol, as compared with those who received iohexol, is promising. The authors claim that a high ratio of urinary albumin to creatinine did not correlate with a high peak increase in the serum creatinine concentration. Although it is easier to use a single urinary albumin-to-creatinine ratio than a 24-hour urine collection to screen for proteinuria, this approach has its own limitations.² We would have liked to see more data regarding differences between the two groups in the degree of proteinuria and the presence or absence of retinopathy. Since more than twice as many patients in the iohexol group as in the iodixanol group had proteinuria, such differences might have confounded the results. In addition, we would have liked to see data on the concomitant use of angiotensin-converting-enzyme (ACE) inhibitors and angiotensin-receptor blockers in the two groups.

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2. Rodby RA, Rohde RD, Sharon Z, Pohl MA, Bain RP, Lewis EJ. The urine protein to creatinine ratio as a predictor of 24-hour urine protein excretion in type 1 diabetic patients with nephropathy. *Am J Kidney Dis* 1995;26:904-9.

TO THE EDITOR: The patients in the randomized trial of Aspelin et al. were probably not a truly high-risk population, since the base-line serum creatinine concentration (mean, 1.49 mg per deciliter) and the base-line creatinine clearance (mean, 50.1 ml per minute) did not indicate the presence of severely impaired renal function. In addition, it is likely that the protective effect of iodixanol was overestimated, since the patients did not receive vigorous hydration (mean volume, 977 ml in the iodixanol group and 934 ml in the iohexol group); vigorous hydration effectively decreases the incidence of contrast-medium-induced nephropathy.¹ Hydration regimens used in other randomized trials^{2,3} have included substantially larger volumes of intravenous saline (mean volumes, 3311 ml and 2022 ml). Finally, rather than prevent a (reversible) increase in the serum creatinine concentration, measures aimed at reducing contrast-medium nephrotoxicity should decrease the incidence of clinically important adverse events. Given these concerns, we would suggest that the study of Aspelin et al. shows mainly a nonsignificant reduction in the rate of adverse events related to the use of contrast medium (2 of 67 patients vs. 8 of 67 patients, $P=0.09$ with a two-sided Fisher’s exact test, according to our calculations).

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