TO THE EDITOR: Barrett and colleagues (1) reported a placebo-controlled trial of echinacea for the common cold. The Food and Drug Administration defines a placebo control as "an identical-appearing treatment that does not contain the test drug . . . the placebo control design, by allowing randomization and including a group that receives an inert treatment, controls for all potential influences on the actual or apparent course of the disease other than those arising from the pharmacologic action of the test drug" (2). Alfalfa does not meet these requirements because it is a potential influence on the course of the disease and therefore must be considered an active control.

Alfalfa is biochemically complex, containing large amounts of vitamins, minerals, phytoestrogens, and saponins. The saponin constituents alone (molecules with a triterpene or steroid moiety) have shown a wide range of biological activity. Alfalfa saponins are fungicidal, bactericidal, and insecticidal and have cholesterol-lowering properties (3). Alfalfa has also been found to contain an abundance of thyrotropin-releasing hormone-like material (4), which may be the basis of its traditional use in thyroid disease (5). Alfalfa tablets, seeds, and sprouts have also been associated with rare instances of the reactivation of systemic lupus erythematosus and the onset of other autoimmune disorders. As with echinacea, alfalfa is part of the herbal pharmacopoeia and has significant known and no doubt unknown biological effects.

Barrett and colleagues’ study informed us of the equivalent effect of alfalfa and echinacea on the outcomes measured. However, the results cannot be interpreted because neither herb is considered a standard treatment for the common cold.

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References

IN RESPONSE: Randomized, controlled trials are designed to test specific hypotheses. While bias can be reduced, generalizability and interpretation are limited. In our trial, a specific echinacea preparation was tested against a specific control as a treatment for the common cold. The choice of echinacea was influenced by the literature and by popular practice. Several trials of Echinacea purpurea and E. angustifolia preparations had been positively reported (1, 2). Products containing either or both species were in wide use. We chose a capsuleized whole plant preparation for its simplicity and ease of manufacture. We avoided a liquid preparation because the taste and tingling sensation of echinacea are notoriously difficult to disguise. We were intent on demonstrating intact blinding, since this had not previously been accomplished. This guided our choice of placebo. Because we used clear gelatin capsules containing the whole plant product, and because some of the herbal taste could leak from the capsules (and was available to participants who opened them), we needed a plant-based product that would be indistinguishable to participants and to research personnel. We settled on whole dried alfalfa because the color and consistency mimicked the echinacea product and no research had reported any effects of alfalfa on the severity or duration of the common cold. However, taste was still distinguishable, so technicians at Shaklee Technica experimented with various flavoring agents, eventually finding that a very small amount of thyme and peppermint successfully disguised echinacea’s flavor.

We agree that these choices could affect results. Although a bit far-fetched, it is possible that tiny amounts of peppermint or thyme could block a positive effect of echinacea. It is also possible, although unlikely, that a few grams of alfalfa could be an effective treatment for the common cold. If so, the multimillion-dollar cold remedy industry should shudder, as a few grams of alfalfa costs only a few pennies. Perhaps an alfalfa trial will be carried out, and perhaps some benefit will be found. In the meantime, we stand by the results of our trial: The echinacea preparation we used provided no measurable benefit to college students experiencing cold symptoms. Perhaps it would have worked in an older sample. Perhaps a refined extract or liquid preparation would have worked. Perhaps dosing should occur within 12 hours rather than 36 hours of first symptoms. Our results cannot address these important questions, nor can our trial by itself negate the results of the several positively reported trials. More and better research is warranted.

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References
2. Melchart D, Linde K, Fischer P, Kaesmayr J. Echinacea for preventing and treating the common cold. The echinacea preparation we used provided no measurable benefit to college students experiencing cold symptoms. Perhaps it would have worked in an older sample. Perhaps a refined extract or liquid preparation would have worked. Perhaps dosing should occur within 12 hours rather than 36 hours of first symptoms. Our results cannot address these important questions, nor can our trial by itself negate the results of the several positively reported trials. More and better research is warranted.

Alcohol, Postmenopausal Hormones, and Breast Cancer

TO THE EDITOR: In the Nurses’ Health Study cohort, Chen and colleagues (1) found an approximately 2-fold excess risk for breast cancer in women who currently used postmenopausal hormones and drank alcohol. However, the researchers were unable to consider high alcohol consumption. To address this issue, we analyzed data from 2 Italian case–control studies. The first was conducted between 1983 and 1991 in greater Milan (2), and the second was conducted between 1991 and 1994 in 6 centers in various regions of Italy (3). The studies involved 3573 postmenopausal women (median age, 61 years [range, 31 to 74 years]) with a histologically confirmed diag-

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Table. Odds Ratios for Breast Cancer in Postmenopausal Women, by Alcohol Intake and Postmenopausal Hormone Use

<table>
<thead>
<tr>
<th>Alcohol Intake</th>
<th>Postmenopausal Hormone Use</th>
<th>All Postmenopausal Women</th>
<th>Women Who Reported Natural Menopause</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Women with Breast Cancer</td>
<td>Controls</td>
<td>Odds Ratio (95% CI)*</td>
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<tr>
<td>None (abstainers)</td>
<td>Never</td>
<td>970</td>
<td>1152</td>
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<tr>
<td></td>
<td>Ever</td>
<td>97</td>
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<tr>
<td>1 drink per day</td>
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<td>Ever</td>
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<tr>
<td></td>
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<td>36</td>
<td>20</td>
</tr>
</tbody>
</table>

* Derived from multiple logistic regression models including terms for age, study center, calendar year of interview, education, smoking habit, body mass index, age at menarche, type of menopause, parity age at first birth, oral contraceptive use, history of benign breast diseases, and family history of breast cancer in first-degree relatives.

References

Update in Hospital Medicine

TO THE EDITOR: Regarding the section on avoiding femoral line placement in Flansbaum and Huddleston’s Update in hospital medicine (1), am I the only one who sees the folly of leaving a femoral line in place for more than 4 days? In the study reviewed (2), femoral lines were used for an average of 9.3 days!

I argue that in the short run a femoral line is far safer than a subclavian line. The complications associated with femoral lines all occur after 72 hours. Line infections are rare in this time window. If short-term access is needed, it makes more sense to use the femoral vein. If access may be needed for more than 72 hours, a subclavian line should be used. I use femoral lines for all of my patients with diabetic ketoacidosis. They don’t need the line longer than 72 hours, and they don’t get pneumothorax.

I would love to see a study that compares complication rates between subclavian lines left in longer than 5 days and femoral lines pulled in less than 72 hours. We all know that the infection rate and thrombotic rate will both be lower with the femoral line. If central access will be needed for less than 72 hours, I argue that the femoral vein is better.

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References