As public interest in bioidentical hormones has grown, so has the need to examine the regulation and use of bioidentical hormone (BH) therapy closely and to include uniform patient safety information in all hormone products. The following position statement on the use and regulation of BH is one in a series of statements that The Endocrine Society is developing to communicate to policymakers and the media its official position on a range of existing and emerging issues. The American Medical Association adopted the Society’s position statement at its recent House of Delegates meeting (see page 17).
Introduction

“Bioidentical hormones,” particularly estrogen and progesterone, have been promoted as safer and more effective alternatives to more traditional hormone therapies, often by people outside of the medical community. In fact, little or no scientific and medical evidence exists to support such claims about “bioidentical hormones.” Additionally, many “bioidentical hormone” formulations are not subject to FDA oversight and can be inconsistent in dose and purity. As a result of unfounded but highly publicized claims, patients have received incomplete or incorrect information regarding the relative safety and efficacy of hormone preparations that are referred to as “bioidentical.”

“Bioidentical hormones” are defined as compounds that have exactly the same chemical and molecular structure as hormones that are produced in the human body. Though any hormone can be made to be “bioidentical,” the term is often used to describe formulations containing estrogens, progesterone, and androgens. Replacement of estrogen and progesterone is a common and effective treatment for symptoms associated with menopause, but may carry some risk of potentially serious side effects. As women seek safer treatments, they often request “bioidentical hormones” from their physicians.

Background

The Women’s Health Initiative (WHI), a long-term study of a large number of women taking traditional hormone therapy or placebo, has raised concerns about hormone therapy. This has created an environment for the propagation in the lay media of the scientifically unproven idea that “bioidentical hormones” are safer and more effective than traditional hormone therapy. No such comprehensive study has been done to examine the effects of “bioidentical hormones.” In fact, very few long-term scientific studies assessing clinical outcomes have been completed on “bioidentical hormones.”

The WHI measured a number of criteria, including the incidence of cardiovascular disease, cancers, and bone fractures. The study was cut short due to the observations of increased risks of cardiovascular disease and breast cancer in women taking combination hormone therapy. There were positive effects such as a decreased risk of colorectal cancer and bone fracture, but it was concluded that the adverse events outweighed the benefits of hormone therapy of the type and dosage used in the WHI. Nonetheless, many physicians felt that the results of the WHI did not warrant a total discontinuation of hormone therapy. Rather, the scientific and medical community currently recommends that a menopausal or post-menopausal woman discuss her individual risks and benefits of hormone therapy with her physician. If they decide that hormone therapy would be overall beneficial, then the physician should prescribe a regimen and closely monitor her.

Considerations

The hormones used in the WHI are commercially available, and their chemical and molecular structures closely resemble, but do not exactly replicate, those of hormones produced in the human body. The dosage of each hormone used in the WHI was constant among those women receiving hormone treatment.

No medical or scientific evidence exists to support the idea that the adverse and/or beneficial effects found in the WHI resulted from the molecular structure of the hormone in question. The result of this advice has been confusion about the definition of “bioidentical hormones.” Here the terms associated with hormone therapy are clarified.

- **Bioidentical:** Having the same chemical and molecular structure as a substance produced in the human body.
- **Compounded:** Manipulated by a compounding pharmacist so that the dose or formulation of an FDA-approved substance is changed to a different dose or formulation without FDA oversight.

Public confusion about the terms being used could cause miscommunication between doctors and their patients and make the difficult task of identifying appropriate hormone therapy even more complicated. Physicians who are aware of public misconception on the definition of “bioidentical” can better communicate with their patients and help them understand the risks and benefits of all hormone therapies.
of the synthesized hormones, nor is there any sound scientific evidence to show that a different or “customized” dose of hormones would have changed the outcome. If dosage and purity were equal, then all estrogen-containing hormone therapies, “bioidentical” or “traditional,” would be expected to carry essentially the same risks and benefits. Therefore, regardless of the source or structure of the hormone administered therapeutically, all hormone therapy regimens—even those that are so-called “customized”—must be carefully controlled.

Hormone customization is very difficult to achieve, because blood hormone levels are difficult to measure and regulate accurately due to normal physiologic variations. Nonetheless, proponents of “bioidentical hormones” assert that simple tests of saliva can provide the information necessary to customize hormone doses. They also allege that customized “bioidentical hormones” are safer and more effective than modified hormones synthesized under close FDA supervision—again those that are so-called “customized”—must be carefully controlled.

The controversies surrounding the safety and efficacy of “bioidentical hormones” illustrate the need for further scientific and medical scrutiny of these substances. Until such studies are completed, physicians should exercise caution when prescribing “bioidentical hormones” and counsel their patients about the controversy over the use of these preparations. Additionally, patients should educate themselves about hormone therapies and engage in candid discussions with their doctors. Much consideration should be given to the decision to undergo any hormone therapy, and “bioidentical hormones” present unique and additional concerns because of the process by which many of them are made.

## Positions

The Endocrine Society is concerned that patients are receiving potentially misleading or false information about the benefits and risks of “bioidentical hormones.” Therefore, the Society supports FDA regulation and oversight of all hormones—“bioidentical” and traditional—regardless of chemical structure or method of manufacture. This should include, but not be limited to, the following:

- Surveys for purity and dosage accuracy.
- Mandatory reporting by drug manufacturers of adverse events.
- A registry of adverse events related to the use of hormone preparations.
- Inclusion of uniform information for patients, such as warnings and precautions, in packaging of hormone products.

### Comparing traditional hormone therapy with “bioidentical hormone” therapy.

<table>
<thead>
<tr>
<th></th>
<th>Traditional Hormones</th>
<th>Many “Bioidentical Hormones”</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Molecular structure</strong></td>
<td>Similar or identical(^1) to human</td>
<td>Identical to human</td>
</tr>
<tr>
<td><strong>FDA oversight</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>Monitored; accurate and consistent</td>
<td>Not monitored; may be inaccurate or inconsistent</td>
</tr>
<tr>
<td><strong>Purity</strong></td>
<td>Monitored; pure</td>
<td>Not monitored; may be impure</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>Tested; risks known</td>
<td>Not FDA tested; risks unproven</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td>Tested and proven</td>
<td>Not FDA tested; unproven</td>
</tr>
<tr>
<td><strong>Scientific evidence</strong></td>
<td>Existent; conclusive</td>
<td>Insufficient</td>
</tr>
</tbody>
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\(^1\) A few “bioidentical hormones”—those available from retail pharmacies, such as estradiol and progesterone—are produced under FDA supervision and are monitored for dosage and purity as are preparations of traditional hormones. However, even FDA-monitored “bioidentical hormones” have not been examined in long-term studies such as the WHI and, therefore, have unproven safety and efficacy.
American Medical Association Adopts The Endocrine Society’s Position

At its semi-annual meeting on November 13, 2006, the American Medical Association’s (AMA) House of Delegates unanimously and enthusiastically passed a resolution introduced by The Endocrine Society and other concerned organizations urging the U.S. Food and Drug Administration (FDA) to increase its oversight and regulation of so-called bioidentical hormones. The resolution was based on the Society’s position statement on bioidentical hormones (see page 15).

Public interest in bioidentical hormones has been fueled recently by articles and books in the popular press touting them as safer and more effective alternatives to traditional hormone therapies, though little or no scientific and medical evidence exists to support these claims. “No comprehensive study has ever been done to establish that bioidentical hormones are safer or more effective than traditional hormone therapies,” said Society president Leonard Wartofsky, M.D. “The decision to undergo any hormone therapy should be carefully weighed, and the dearth of accurate information on bioidentical hormones makes that decision even more complicated as patients and doctors work together to find the best treatment.”

Technically, bioidentical hormones are compounds that are the same chemically as hormones produced naturally in the body. The term, however, is commonly used by those outside the medical community to describe hormone treatments custom made by compounding pharmacies, individually tailored based on saliva tests. The accuracy and usefulness of such tests, however, are highly questionable.

Patients can obtain bioidentical hormones either as FDA-approved drugs, formulated with strict oversight and dispensed by retail pharmacies, or as non-FDA-approved dosages and formulations (such as topical creams) from compounding pharmacies.

Because the final hormone formulations of compounding pharmacies are not subject to FDA monitoring for dose, purity, safety, or efficacy, there could be additional, and at this point unknown, risks associated with them. Post-market surveys of such hormone preparations have uncovered inconsistencies in dose and quality.

“The inconsistencies and unknown risks of bioidentical hormones are of great concern,” said Dr. Wartofsky. “Without proper oversight and control, the public has no way of knowing precisely what they’re getting or what effect it will have on an individual’s body.”

Several physicians representing a range of specialties rose on the floor of the House of Delegates to speak in support of The Endocrine Society’s resolution, including representatives of the American College of Obstetricians and Gynecologists and the American Academy of Family Practitioners. AMA Board Member Ardis Hoven, M.D., also raised concern for patient safety under the current regulatory system. “Confidence in the safety and effectiveness of the therapies patients take is absolutely essential for both patients and physicians,” said Dr. Hoven. “New FDA policies that would require manufacturers and compounding pharmacies to provide adverse event information on compounded bioidentical hormones—and share the warnings and precautions with patients on the drug label—will help patients and doctors make better informed decisions on the course of treatment.”

The statement, introduced by The Endocrine Society, the American Association of Clinical Endocrinologists, and the American Society of Reproductive Medicine, resolves that the:

• AMA urge the Food and Drug Administration to conduct surveys for purity and dosage accuracy of all compounded bioidentical hormone formulations.
• AMA urge the Food and Drug Administration to require mandatory reporting by drug manufacturers, including compounding pharmacies, of adverse events related to the use of bioidentical hormones.
• AMA urge the Food and Drug Administration to create a registry of adverse events related to the use of compounded bioidentical hormone preparations.
• AMA request that the Food and Drug Administration require the inclusion of uniform patient information, such as warnings and precautions, in packaging of compounded bioidentical hormone products.
• AMA urge the Food and Drug Administration to prohibit the use of the term “bioidentical hormones” unless the preparation has been approved by the FDA.

“With this vote, it is clear that organized medicine recognizes that FDA oversight of bioidentical hormones is critical to ensure patient safety,” said Dr. Wartofsky. “The Endocrine Society looks forward to working with the AMA to advocate strongly for a meaningful policy change.”

The Endocrine Society Seeks Media Experts on Bioidentical Hormones

The Society relies on expert members to provide informed and accurate responses to media requests on bioidentical hormones and other salient or emerging topics. This effort is coordinated through the Society’s Government & Public Affairs office, and requires ongoing revision and update of an existing expert database. Society volunteers willing to serve as media experts on bioidentical hormones and other topics should contact Chuck Blue, director of communications, at cblue@endo-society.org. For more information about being a media expert and the coordination of activities, see the story in the Society Update pages of this issue of Endocrine News (page 27).