Statement on Bio-identical Hormones

December 05, 2006

After a literature review and discussions with physicians from all over the world who are well versed in treating patients with endocrine abnormalities, we, the members of the International Hormone Society, think the time is right to release a statement on the use and delivery of bio-identical hormones.

A "bio-identical hormone" has exactly the same chemical structure as a hormone produced by the human body. The term "bio-identical" is generally used for preparations containing sex hormones such as estradiol, estrone, estriol, progesterone and testosterone. The alternatives are non-bio-identical hormone preparations such as those widely commercialized in most birth-control pills and in post-menopausal hormone treatments. The prevailing concept is that bio-identical hormones may be safer to use than non-bio-identical hormones because they fit the body, in particular when a safer route of administration is used such as transdermal delivery.

The members of the International Hormone Society were concerned about product safety long before the publication of studies such as Women's Health Initiative [WHI] in 2002 and the British One Million Women study in 2003 that found an increase in the incidence of breast cancer in postmenopausal women using non-bio-identical hormones as compared to placebo or nonusers. In the WHI study, the use of non-bio-identical female hormones was also associated with an increased risk of cardiovascular and cerebrovascular diseases.

In accordance with the recommendations of a growing number of medical societies, the International Hormone Society, in a consensus on **"Estrogen and Progesterone Treatment of Pre- and Postmenopausal Women**" issued on December 11, 2005, **did not and still does not recommend the use of non-bio-identical estrogens and progestogens for the treatment of ovarian deficiencies**. However, the use of synthetically modified female hormones used for birth control may be considered for a limited time if no other contraceptive alternative exists. The consensus is based on an extensive review of the literature on the use of bio-identical and non-bio-identical estrogens and progestogens. Greater potential toxicity and risks were found in the non-bio-identical compounds.

On the other hand, the **International Hormone Society did and still does recommend in the consensus the use of bio-identical estrogens, in particular estradiol and estriol, and also bio-identical progesterone**, for the correction of ovarian deficiencies. In contrast with the recent Endocrine Society's position (October 2006) and the American Medical Association's resolution (November 2006) that state that little or no scientific and medical evidence exists to support the claims that bio-identical hormones may be safer, a review of the literature contradicts this statement**. There currently is sufficient evidence confirming the**

greater safety of bio-identical sex hormones compared to the non-bio-identical ones, in particular when the transdermal, nasal or intramuscular routes are used instead of the oral route.

Critics object to bio-identical hormones sold by compounding pharmacies due to the lack of oversight by the Food and Drug Administration (FDA), and assume that there is no guarantee of dosage, purity, efficacy and safety. We share with the American Medical Association, the Endocrine Society, the American College of Obstetricians and Gynecologists, and the American Academy of Family Practitioners the concern that patients should be offered the best products at all times, and that all products must be as consistent as possible in dosage, and as pure, efficient and safe as possible.

The physicians of the International Hormone Society think they can provide a valuable, decisive opinion in this debate for two reasons. First, many of them have broad experience in the use of bio-identical hormones compounded by compounding pharmacies, experience which does not seem to be shared by the writers of the various positions and resolutions of the aforementioned societies. Second, the opinion of the International Hormone Society members is independent of any pressure from advertisers, sponsoring pharmaceutical firms, or compounding pharmacies.

The physicians of the International Hormone Society wish to stress the following points:

1. **Control of compounding pharmacies:** The production of bio-identical hormone preparations by compounding pharmacies is under control of the pharmacy state board in each state. This control has sufficiently warranted high quality products, in dosage, purity, efficacy and safety, to satisfy physicians. Better control may be acceptable as long as it does not restrict physicians from exercising their therapeutic freedom to prescribe compounded preparations for the full benefit of patients.
2. **Major advantage of compounded preparations**: Compounded preparations of bio-identical hormones offer a major, indispensable advantage over standardized preparations, namely that the dosage and formulation of the product can be tailored to each patient. Concentration and composition, including solvents or fillers, can be individualized to what the patient needs or is able to tolerate. We think personalized treatments such as those offered by compounding pharmacies offer the best prospect for optimal health care.
3. **Production and distribution of bio-identical hormones is not limited to compounding pharmacies**: The FDA approval of "bio-identical" hormones already exists in the form of patches and mass-produced estrogen gel and cream. Compounding pharmacies are merely making a cream or gel that better suits the individual patient.
4. **Conjugated estrogens, an example of widely sold non-bio-identical hormones**: The form of estrogen, conjugated estrogen, which initiated this

entire debate, is actually an estrogen waste product found in the urine of pregnant mares. Many of the estrogens in horse urine cannot be considered "bio-identical" to the human body because they are structured differently than human estrogens. Although some of the estrogens are equivalent to human estrogen, they have been altered biochemically by conjugation. Conjugation takes place in the liver of horses and humans in order to excrete unwanted estrogen. Therefore, conjugated estrogen medications are not bio-identical because they are waste product forms of estrogen marked for removal by a horse liver.

5. **Use of the term "bio-identical" hormones**. The AMA's request to the Food and Drug Administration to prohibit use of the commonly employed term "bio-identical hormones", unless the preparation has been approved by the FDA, contradicts the first amendment rights of the Constitution of the United States, denying the freedom of speech ensured by the amendment, and unacceptably interferes with the rights of medical doctors currently prescribing compounded preparations of bio-identical hormones. Section 503A of the FDA Modernization Act of 1997 attempted to restrict the first amendment rights of compounding pharmacies, stipulating "that they refrain from advertising or promoting particular compounded drugs". However, the Supreme Court, in a 2002 decision, found that restriction unconstitutional. In the words of the FDA itself: "The Supreme Court affirmed the 9th Circuit Court of Appeals decision that found section 503A of the Act invalid in its entirety because it contained unconstitutional restrictions on commercial speech". This Supreme Court decision should firmly establish for all parties that first amendment speech applies to compounding pharmacies as to all Americans, and that first amendment speech does not require approval from anyone, including the FDA.

6. **Testing**: Most physicians who work with bio-identical hormones from compounding pharmacies use traditional blood tests, not saliva tests, as incorrectly stated by the American Medical Association (resolution of November 2006) and the Endocrine Society (position statement of October 2006).

7. **Safety**: As previously stated, there is currently sufficient evidence confirming the greater safety of bio-identical sex hormones as compared to non-bio-identical ones, particularly when administered transdermally, nasally or intramuscularly instead of orally.

8. **Research**: We recommend future research in this area, and, in particular, we support independent research on the potential risks and benefits of bio-identical and non-bio-identical hormones.

In conclusion, we urgently advise the American Medical Association to revise its position and the Food and Drug Administration to take all points of the International Hormone Society's statement into consideration and to preserve physician's rights to prescribe the best possible products for their patients, including compounded preparations of bio-identical hormones.