Endocrine Society Urges Caution With Androgen

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Contributing Writer

The Endocrine Society is sounding a strong word of caution on the topic of androgen therapy with a new clinical practice guideline that recommends against diagnosing and treating androgen deficiency in women.

The guideline, published in the October issue of the Journal of Clinical Endocrinology and Metabolism, cites the "lack of a well-defined clinical syndrome" and the "lack of normative data on total or free testosterone levels across the life span" as reasons why a diagnosis should not be made.

On the issue of treatment, the document acknowledges "evidence for short-term efficacy of testosterone in selected populations, such as surgically menopausal women," but says that inadequate indications and insufficient evidence of long-term safety means that the "generalized use of testosterone in women" cannot be recommended.

"Based on [our literature review], we felt that at this time, we could not, as a committee and a society, recommend either for making the diagnosis or for treatment," said Dr. Margaret E. Wierman, the endocrinologist who chaired the seven-member task force that developed the guidelines.

"The quality of the literature was just not up to a standard [needed] to make a global recommendation," said Dr. Wierman, who serves as chief of endocrinology at the Veterans Affairs Medical Center in Denver and professor of medicine, physiology, and biophysics at the University of Colorado, Denver. "The sort of hype that testosterone has been given is not yet based on a lot of scientific fact."

The guideline, which also details basic research that must be done and calls for the development of more sensitive and specific assays for testosterone and free testosterone in women, has a tone and reach that differs from the less conservative "androgen deficiency" section in the American Association of Clinical Endocrinologists' recently updated menopause guidelines.

As observers—and even Dr. Wierman—see it, the guideline is bound to intensify debate about an already controversial issue. And if Dr. André Guay is any indication, it is endocrinologists who specialize in sexual dysfunction who may take issue with the guidelines most passionately.

"This isn't a guideline at all," said Dr. Guay, director of the Center for Sexual Function at the Lahey Clinic in Peabody, Mass. "I was hoping they would say, 'we don't have all the answers, but here are the answers we do have, and here is the best we can do,' just as we say with men—that I'll buy.

"But there's nothing in here that shows you how to deal with the problem given the knowledge we currently have. … It's a disservice," said Dr. Guay, who has argued for years in articles and at meetings that evidence supports off-label androgen therapy in women.

Not so, said Dr. Neil Goodman, professor of medicine at the University of Miami. The guideline is "excellently done" by "leading people in the field," he said. "They went through the literature systematically and documented levels of evidence … and they do point out the one area where there is good positive data—in the surgically menopausal group.

"I see it as a request for action," said Dr. Goodman, also a private-practice endocrinologist specializing in reproductive medicine. "It's a plea for better work to be done."

The guideline recommends that researchers use particular "human model systems" to study the benefits and risks of androgen therapy (for instance, it says that women with hypopituitarism can be used to study the physiological replacement of ovarian and adrenal androgen precursors).

It also recommends that particular end points—from appearance of or change in hirsutism to effects in the breast and alterations in the endometrium with and without estrogen coadministration—be considered in safety and risk assessments of androgen administration (J. Clin. Endocrinol. Metab. 2006;91;3697-710).

Dr. Wierman said she also hopes that the new guideline—as well as a document to be released by the Endocrine Society in the next 18-24 months on problems with sex steroid assays for both men and women—will drive development of more sensitive and specific assays. "I think the assay issue will soon be improved," she said.

Physicians also must appreciate the fact that the findings on estrogen from the Women's Health Initiative had some impact on the task force, Dr. Wierman said.

"At this point, we felt that the Endocrine Society needs to act as the word of caution so we're not coming back 5 years from now and saying, 'Why weren't we cautious? Why didn't we push our colleagues across academia to do the studies to better understand [androgens], so that patients will benefit and won't be harmed?' " she said.

Dr. Steven Petak, president of the American Association of Clinical Endocrinologists (AACE), said his organization took a different approach last year as they addressed the issue of androgen therapy when updating their menopause guidelines.

"We also were quite cautious, and we agree that long-term safety issues need to be clarified," he said. "But we still went on and stated that there are some criteria for diagnosis, and we gave some recommendations [for use of androgen]."

The Endocrine Society's guidelines "don't do much for patients whose therapies are being considered now," said Dr. Petak of the Texas Institute for Reproduction and Endocrinology. "The Endocrine Society's recommendations for further basic and clinical research in the field are of prime importance and we agree wholeheartedly."

Dr. Goodman cautioned against comparing the guidelines of the two organizations. "The Endocrine Society is looking at the entire, broader issue. They take a more universal kind of approach," he said. ■