Estrogen Use Linked to Breast Cancer

The long-term use of estrogen hormones for treating menopausal symptoms may increase a woman's risk of developing breast cancer, according to a new study by Swedish and U.S. researchers. The new findings come just when estrogen use has been escalating because of research indicating that the hormone can protect against osteoporosis and the heart and circulatory problems that may develop after menopause. They thus present women and their physicians with a painful dilemma.

The possible risk of developing breast cancer will have to be weighed against the benefits of estrogen use. And so far at least, the experts are coming down on the side of the benefits. For example, Malcolm Pike of the University of Southern California in Los Angeles estimates that for every woman who might lose her life to breast cancer because of long-term estrogen use, another seven or eight might be spared from premature death by heart attack or stroke.

And in an editorial that appeared with the study results in the 3 August issue of the New England Journal of Medicine, Elizabeth Barrett-Conner of the University of California at San Diego wrote: "In my opinion, the data are not conclusive enough to warrant any immediate change in the way we approach hormone replacement, but they do show the need for additional research."

The issue is also somewhat complicated for U.S. women because they generally do not take the same estrogen as the Swedish women do, and no one currently knows whether this makes any difference for their breast cancer risk.

The study that linked estrogen use and breast cancer was conducted by Leif Bergkvist, Hans-Olov Adami, and Ingemar Persson of University Hospital in Uppsala, Sweden, and Robert Hoover and Catherine Schairer of the National Cancer Institute in Bethesda, Maryland. They used prescription records to identify more than 23,000 women, living in and around Uppsala, who had been taking estrogens for menopausal symptoms. The researchers were then able to compare the estrogen users' names with those of the breast cancer patients who appeared in the Swedish Cancer Registry.

Overall, estrogen use increased the risk of breast cancer only slightly. Women who took the hormone developed about 10% more than the expected number of breast cancers. But Adami says, "The risk increased with increased duration of estrogen use and became statistically significant after 9 years." For that group, the relative risk almost

doubled, going up some 70%.

The new study is also the first to look at the effects of combining an estrogen with a progestin on breast cancer risk. Since the early 1980s, physicians have been prescribing the hormone combination for their menopausal patients with increasing frequency because estrogen alone had been linked to an increased risk of developing uterine cancer and adding a progestin was found to counteract that effect.

The hope was that progestin could also protect against breast cancer development, but the current study shows that that has not been the case. If anything, Adami says, the combination therapy increased the breast cancer risk more than estrogen alone did,

although he cautions that more work will be needed to confirm that possibility.

Not everyone was surprised that estrogenprogestin combinations might be worse for breast cancer development than estrogen alone. Estrogen apparently has a carcinogenic effect because its stimulates the growth of the cells of the breast and the uterine lining. According to Pike, progestin counteracts that effect on the uterine cells but acts with estrogen to stimulate breast cell growth. He had predicted that progestin might therefore potentiate estrogen's effects on breast cancer risk.

Earlier studies of estrogen's effects on breast cancer had given mixed results. The new study, by coming down firmly on the increased risk side, will make it harder for a woman to decide if she wants long-term estrogen therapy after menopause.

■ JEAN L. MARX

New Rules on Misconduct

Scientists anxiously awaiting new federal policies on misconduct in the laboratory should be relieved by the rules published by the Department of Health and Human Services in the 8 August Federal Register.

The rules confirm that "the awardee institutions will have the primary responsibility for preventing, detecting, investigating, reporting, and resolving allegations of scientific misconduct." But HHS "retains the ultimate responsibility and authority for monitoring such investigations and becoming involved in those investigations if appropriate or necessary." Institutions are required to complete investigations promptly—60 days for an initial inquiry unless circumstances clearly warrant more time. If a full-scale investigation is required, it should ordinarily be completed in 120 days.

Scientists will also welcome the HHS definition of scientific misconduct: "fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted.... It does not include honest error or honest differences in interpretations or judgments of data." The definition embraces the term "misconduct" rather than "fraud" to avoid "confusion with common law fraud," according to the Federal Register notice.

Institutions receiving Public Health Service money will have to provide "assurances"—like those already required for research involving animal or human subjects—that they have policies and procedures for dealing with misconduct.

The new rules outline procedures for maintaining order and confidentiality in misconduct investigations, including "diligent efforts" to restore reputations in cases where misconduct allegations are unproved. The rules also require protections for "persons who, in good faith, make allegations [of misconduct]" so that their positions and reputations will also be protected.

This clause may help assuage some of the concerns raised by Representative John D. Dingell (D–MI), who has been hammering away at what he perceives as an unwillingness within the scientific community to protect whistle-blowers.

This week's Federal Register notice is not the final word from HHS about scientific misconduct. HHS is planning to issue rules that will define specific steps institutions can take to foster scientific integrity. Other issues to be addressed in future rule-making include authorship practices, retention of lab data, and procedures for audits to prevent misconduct.

PHS has already set up two new offices on scientific misconduct—the NIH-level Office of Scientific Integrity and the Office of Scientific Integrity Review in the Office of the Assistant Secretary for Health.

Does this put Congressman Dingell out of business when it comes to fraud legislation? The chairman of the oversight and investigations subcommittee of the House Energy and Commerce Committee has been cooking up a wide-ranging bill on the prevention, detection, and investigation of scientific misconduct, the contents of which are yet to be disclosed. A staff member said that the congressman has no comment on the PHS rules and that no decision has yet been reached on whether to proceed with the legislation.

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