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NEWS

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*****Postmenopausal women produce a different kind of estrogen, says Dr. Paul MacDonald.

DALLAS--"One-third of a woman's life is spent after menopause," says Dr. Paul MacDonald. Since there are now more than 40 million women in the U.S. who are more than 50 years old, changes that affect older women are of great importance to a large segment of the population.

"We need to understand the physiological changes that accompany menopause so that we can address the health problems that women experience during this time of their lives," says MacDonald, director of the Cecil H. and Ida Green Center for Reproductive Biology Sciences and holder of the Green Chair in Reproductive Biology Sciences at The University of Texas Health Science Center at Dallas.

Recognized internationally for their work on estrogen production in women after menopause, MacDonald and his co-workers were first to show that postmenopausal events are not due to total estrogen deprivation but to a different type of estrogen produced.

MacDonald relates that he got into research on postmenopausal women "by accident." He had found that in pregnant women, male-type hormones were converted to estrogen in the placenta. He recruited men, young women and postmenopausal women for a control group to show that androgens (male hormones) were not converted into estrogen in them. He was wrong. The hormone conversion took place in all groups. And in postmenopausal women, it was even higher than in men and in young women who were not pregnant.

He went on to describe the changes in estrogen production that occur after menopause.

It was already known that the ovaries stop making estrogen after menopause. MacDonald found that even though the ovaries stop making estradiol, the potent form of estrogen, the body becomes more efficient in producing a weaker form--estrone--in the tissues.

In fact, after about age 50 the efficiency of conversion of plasma androstenedione to estrone increases with age in both men and women. The conversion takes place in many tissues including bone, brain, hair follicles and skin. But most estrone is produced in fat tissue.

As both men and women become obese, more estrone is produced. In morbidly obese postmenopausal women, those who weigh 50 percent more than their normal weight, there may be enough estrone made to prevent hot flashes, says MacDonald.

It has puzzled researchers for a long time why obese people should be able to make more estrogen than normal weight people. Some thought that the answer was simply larger tissue mass. Fat cells (adipocytes) increase in size by storing lipids (fats), but they don't increase in number. At least this was the thought until recent work done at the health science center by Dr. Evan Simpson, associate professor of Obstetrics-Gynecology and Biochemistry, and Dr. Carole Mendelson, assistant professor of Biochemistry.

Building on MacDonald's clinical research, the biochemists found in working with adipose (fat) tissue removed surgically from obese patients that estrone is made in the stromal cells, the supporting cells of fat tissue. These stromal cells, they found, do increase in number with obesity, and they may possibly develop into fat cells.

This probably explains why when obese people lose weight, the efficiency in estrone production doesn't decrease--there is no decrease in the number of stromal cells.

Glucocorticosteroids, hormones that protect against stress and affect protein and carbohydrate metabolism, are found in obese people in higher levels than in normal weight people. Simpson and Mendelson found that glucocorticosteroids stimulate a conversion of androstenedione to estrone 60 times that found in fat tissue untreated with any hormone.

At first glance, it would seem highly desirable to produce estrone efficiently. Perhaps a woman could get through menopause with no hot flashes. But MacDonald has also found that an increase in estrone production is linked to endometrial cancer (cancer of the uterus lining).

Women at high risk for endometrial cancer are aging women, obese women and women with liver disease, ovarian tumors or polycystic ovarian disease. Also in all these groups, estrone production is above normal. And aging and obesity act synergistically on estrone production. An aging, morbidly obese woman may produce 10 times the estrone that a young normal woman produces.

Even low-dose estrogen therapy for postmenopausal women is linked with an increased risk of endometrial cancer. Recent work at other institutions has been done on cyclic administration of progestin to counteract the effects of estrogen on the endometrium.

However, MacDonald advocates caution in the use of progestin. Estrogen and progestin used in cycle are similar to "the pill," which, used for contraception, has been linked to heart disease and stroke. He calls for more studies of the risks and benefits before advocating the use of progestin in postmenopausal women because the risk of using progestin may not outweigh the risk of low-dose estrogen therapy.

"The risk of endometrial cancer is low and the cure rate of early diagnosed appropriately treated endometrial cancer is high," says MacDonald.

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