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S P E C I A L S E C T I O N

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## New Looks At Old Questions

By SUSAN LOVE, M.D.

E have just undergone a seismic shift in our understanding of the second half of women's lives and the aftershocks will continue for some time. So if vou're confused - it means vou've been listening.

These big changes come in medicine when new data show that we were on the wrong path. It can be upsetting to everyone who thought they had the answer, but it can also be refreshing. New information forces us to re-evaluate our preconceived notions no matter how we came to them.

For example, I was taught in medical school that at menopause the ovaries stop functioning, shrivel and dry up. (In fact, I was taught that that was what happened to postmenopausal women as well.)

The problem was that we did not low levels of hormones in the blood, so we thought postmenopausal women did not produce any of these hormones. Studies treated women who had undergone natural menopause and those who had had their ovaries removed as if they were the same.

Now we know that the ovaries do not stop producing hormones; they just shift to a much lower level, a level that is probably enough to prevent fractures and maintain libido in most women.

With that knowledge, we need to go back and carefully study which menopausal and postmenopausal problems are related to the surgical removal of ovaries and which are tied to the natural course of menopause itself. And we still need to develop blood tests that can more reliably measure a woman's hormone levels. That's the only way we will know what is normal for a postmenopausal woman.

Since the conclusions in 2002 of the Women's Health Initiative, which studied the effects of hormone replacement therapy using the popular formulations Premarin and Provera, several studies have examined the effects of other variations of estrogen and progestin that are more like the hormones a premenopausal woman would make naturally.

For example, the Million Women Study, a British study reported in 2003, showed that even estradiol and progesterone, which have been considered bioidentical hormones, increased the incidence of breast cancer; and Well-Hart, a national study reported in 2003, showed that estradihave tests sensitive enough to detect ol did not prevent the progression of atherosclerosis. These findings are supported by the fact that postmenopausal women with high levels of their own natural estrogen and/or testosterone are at higher risk of breast cancer than women with lower levels.

HE problem with hormone therapy does not lie in the "flavor" of hormones (bioidentical or synthetic), but the fact that women are programmed to have high levels of hormones for reproduction and then shift down to lower, safer levels postmenopausally. However, even this, my favorite hypothesis, needs to be tested.

We can no longer take for granted that we understand how postmenopausal women's bodies work. We need to pay more attention to individual organs. The breast duct and lobules, where breast cancer begins, contain fluid with estrogen levels many times higher than the levels in the blood. This would suggest that the breast makes its own estrogen. Is this true in everyone, or only in women with a high risk for breast can-

And the relationship of estrogen and progesterone to breast cancer is not straightforward. High doses of estrogen and progestin have been used to treat metastatic breast cancer with success. At the same time. current treatments, which reduce estrogen levels, are equally beneficial. How does this work? I wish I knew.

The one thing we know for sure is that it's time to get the elephant out of the middle of the room. Until these recent studies overturned the theory, we have blamed all the diseases of aging, from Alzheimer's to incontinence, on "estrogen deficiency."

The fact that hormone therapy has not been shown to prevent these problems but in many cases (for example, dementia, incontinence and stroke) to increase them means this theory was wrong. Now we must study the real causes for these problems and develop appropriate treatments. We need to know that our therapies are both effective and safe over the long term. With testosterone patches for women with low libido on the horizon, we should be asking how much we really know about their long-term safety.

For now, before any final answers are in, what should a postmenopausal woman do? Taking hormones short term (three to five years) if needed for symptom relief is probablv safe. But we need to realize that we are making decisions on the use of hormones based on inadequate information. This is not so unusual. We make decisions this way all day every day.

The difference is that this time around, we must acknowledge that that is what we are doing. And we must demand the research that is necessary to clarify the issues. Stay tuned, the results could be even more earth-shaking.

Susan Love is the medical director of the Susan Love, M.D., Breast Cancer Research Foundation.