

# Hormones: Is age the key?

*Replacement therapy affects younger women differently than older women. Exaggerated perception of risks persists.*

By Shari Roan

Los Angeles Times, July 23, 2007



HORMONES seemed like the answer for Nancy Adams when hot flashes began disrupting her sleep seven years ago. The little pill that she got from her doctor solved the night sweat problem and she slept like a baby once again.

All went well -- "until," the L.A. resident says, "the study came out."

"The" study 58-year-old Adams is talking about was part of the landmark Women's Health Initiative that tracked 16,608 women and rocked doctors and patients alike in 2002 with the news that women taking estrogen and progestin had a higher risk of heart attacks, strokes and breast cancer than women who didn't take hormones.

"It terrified me and everybody else," Adams says.

An estimated 15 million U.S. women were taking hormones at the time, and within a year more than 40% of them, Adams included, quit cold turkey. In Adams' case, it was only for a while. Her hot flashes faded, but other bothersome symptoms -- vaginal dryness and the frequent urge to urinate -- cropped up. After dealing with this duo for some months, she opted for the hormones once again.

"I still have concerns about using hormone replacement therapy -- the increased risk of heart attacks, stroke, breast cancer, all those things," she says. "The doctors are still learning about what the effects are, and we are helping them learn. And that is frustrating."

But for women like Adams -- those younger than 60 who have troublesome menopausal symptoms -- hormone therapy has recently been given something of a reprieve. A new analysis of the Women's Health Initiative data suggests that the hormone story is actually two stories -- one for women near the age of menopause and one for women age 60 and older who are a decade past that life change.

For older women, the story appears to be written: Hormones aren't for you.

For younger women who are bothered by menopausal symptoms, the story is more encouraging. Hormones may be a lot kinder to the heart than scientists said back in 2002 when directors of the Women's Health Initiative announced that the risk of heart attack, stroke and breast cancer was increased in women "irrespective of age."

Stroke risk is slightly increased for all women on hormones, and breast cancer risk is slightly elevated in women taking estrogen plus progestin. But the risk of heart attack does not, after all, appear raised in younger women -- and may even be lower.

Especially in light of these new data, many doctors and scientists think the wide-scale tossing away of hormone pills five years ago was an overreaction and that many who could have been helped suffered needlessly.

Some things haven't changed. Very few doctors today would suggest women take hormones for anything other than moderate to severe menopausal symptoms -- and only for a few years, at that. And there are nuances to the hormone decision based on a woman's health, family history and personal lifestyle.

## **No fountain of youth**

Despite the uproar and confusion it caused, the Women's Health Initiative revealed important facts, experts say. It reversed a popular theory permeating women's health in the late 1990s that hormones benefited every woman. This so-called "forever young" hypothesis suggested that hormones would stave off heart disease, osteoporosis and dementia and keep women looking and feeling young well into old age.

Instead, the study showed that, except for controlling menopausal symptoms and helping prevent osteoporosis, hormones appear to have few preventive benefits for the average woman in the study.

But that average woman was 63 -- far past the age when most women go through menopause.

Because of the age of the women in the group, many scientists and doctors have maintained that the 2002 WHI announcement may have done younger menopausal women -- particularly those who suffer severe menopausal symptoms, such as hot flashes, night sweats and vaginal dryness -- a disservice. Two recent studies analyzing data of younger women in the Women's Health Initiative, with an average age of 55, suggests a different risk-benefit profile.

One study, published in April in the Journal of the American Medical Assn., reported that although the risk of heart attacks is increased in those who initiate therapy more than 10 years after menopause, the risk is not increased in women who start hormones less than 10 years after. This analysis of more than 27,000 women combined data from the women in the study who took only estrogen with those who took both estrogen and progestin. It found the risk of stroke was higher for all ages but the risk of death from any cause was lower in women who were 50 to 59 when they started taking hormones, either estrogen alone or estrogen with progestin.

And last month, an analysis published in the New England Journal of Medicine reported that among younger women who'd gone through menopause after having hysterectomies, those who took estrogen alone had much less buildup of calcium plaque in their coronary arteries compared with women who hadn't taken estrogen. Calcium plaque is a risk factor for heart disease.

The study looked at 1,064 women who were ages 50 to 59 when they started taking estrogen and who took the hormones for an average of five years. Although the study examined only estrogen, some experts say women ages 50 to 59 taking estrogen plus progestin might also see similar benefits. That's because it is the estrogen that is thought to slow the early stages of plaque buildup in coronary arteries.

But no one knows for sure if younger menopausal women taking estrogen plus progestin might experience this benefit, says Marcia Stefanick, a professor of medicine at Stanford University's Prevention Research Center who chaired the WHI steering committee.

Women who still have a uterus must take progestins to protect themselves from a raised risk of uterine cancer that comes from taking estrogen. "The data don't apply to that group," Stefanick says. "They apply to women who specifically had a hysterectomy and had their ovaries removed. These weren't women who started hormones at the time of menopause. I think it would be a mistake to extrapolate that."

Nonetheless, the additional data are still evidence that cardiovascular effects of hormones differ in women depending on age, says Dr. Jacques Rossouw, chief of the Women's Health Initiative Branch at the National Heart, Lung and Blood Institute. "Taking those studies together, we can say there doesn't appear to be any increased risk for cardiovascular disease in younger women," he says. "And that is reassuring for women who want to use it for four or five years."

## **Benefit for arteries**

Although scientists don't know for sure why the effects of hormones on the heart would be different for younger and older women, they do have theories based on animal and human experiments. Lab studies show that estrogen increases levels of nitric oxide in blood vessels, which protects the heart, and limits free radicals, which can damage blood vessels. Estrogen also improves blood cholesterol profiles (although progestins seem to blunt this effect).

For these reasons, many doctors now think hormones may have beneficial effects in women whose arteries are still healthy. Age may be key here, says Dr. C. Noel Bairey Merz, medical director of the Preventive and Rehabilitative Cardiac Center at Cedars-Sinai Medical Center.

By the time women reach the average age of those in the WHI, many will have begun to develop heart disease, such as the accumulation of atherosclerotic plaque. Once that has happened, other actions of the hormones, such as the ability to promote blood clots, may contribute to the increase of heart attacks and stroke.

What this means is that age is a strong guide to whether taking hormones will be harmful or not, although not an absolute one, Bairey Merz says. "It's possible there may be 70-year-olds with pristine arteries -- no plaque -- and they would be able to use hormones with no risk," she says. "Vice versa, there are a few 45-year-olds who have plaque. It's the degree of heart disease that may matter. Maybe we can refine our recommendations if this turns out to be true."

In hindsight, much confusion could have been avoided had the 2002 findings been presented as applicable only to women around the age of 63, some experts say.

And many women still have an exaggerated view of the risks involved in taking hormones, says Dr. Wulf H. Utian, executive director of the North American Menopause Society. In a 2004 University of Florida survey of mostly menopausal women, almost one-third said they thought that their risk of heart disease was increased 10% to 30% a

year by taking hormones. In fact, the risk is elevated less than one-tenth of 1% a year.

Utian says that breast cancer risk is increased by 26% among women taking estrogen and progestin compared with those taking nothing. Although that sounds like a big risk, the actual number of new cases of breast cancer attributed to hormone use -- what is known as the "absolute risk" -- is eight cases per 10,000 women per year.

"They made this huge fuss about risk, and women were terrified," Utian says. "And what happened was a lot of women who probably should have been on hormones came off of them."

Now experts appear to be uniting on one point: Hormones are still a reasonable option for younger menopausal women with severe symptoms. But evidence suggests consumers haven't gotten that message yet.

Data from IMS Health, a national healthcare information company, show that even after the huge plunge in the last half of 2002, hormone sales have continued to decline each year through 2006.

Confusion has been rife, says Karen Giblin, founder of Red Hot Mamas, a national menopause education group. "I do believe women are concerned about the conflicting data and the barrage of media reports that leave our heads spinning," she says. "A lot of women are tortured by symptoms. But they are unable to come up with an equation for themselves on whether hormone therapy is worth the risks for the benefits."

Sharon Glaser, 71, wonders if she is doing the right thing by taking vaginal progesterone. Her mother was on hormone replacement therapy from age 55 until 90 and died at age 94.

"It's absolutely confusing," says Glaser, who lives in Los Angeles. "But I decided I wasn't going to put anything in my mouth that wasn't tried and true."

Nancy Cohen Kram, now 62, says menopause descended on her at age 51 like a thunderbolt.

"I didn't just have a hot flash," says the Los Angeles woman. "I would have hot flashes that would crescendo. It was like an out-of-body experience. I couldn't concentrate. I felt sick. I felt off-base all of the time. It caused a lot of problems."

Kram began taking hormone replacement therapy. "I was great until the study came out," she says. "But I stopped, and was good for three months, and then all of the symptoms came back." She resumed taking hormones. She tried -- unsuccessfully -- to go off the medication earlier this year, and still takes them.

"I worry about the risks," she says. "But my quality of life is totally diminished without them. You are left between a rock and a hard place with hormone replacement therapy."

## **Reasons to reconsider**

About 2 million American women go through menopause each year, and as many as three-quarters experience some menopausal symptoms. In about 20%, the symptoms are

severe, causing such problems as disrupted sleep, daytime fatigue, decreased sexual function and strained personal relationships. Those are the women -- those new to menopause or who are in their 50s and suffering -- who may want to reconsider hormones, experts say.

One reason: Despite much research since 2002, alternatives to hormones for treating hot flashes and other symptoms have come up short, experts say. Herbal and other alternative remedies, such as mind-body techniques, have little to no effect for moderate to severe symptoms, according to a study published last year in the Archives of Internal Medicine.

Selective serotonin reuptake inhibitor (SSRI) antidepressants, such as Prozac, and some medications used to treat seizures may help some women. But those medications have potential risks too, Bairey Merz says.

"They are really untested with regard to safety concerns," she says. "I would rather take something like hormones that have been tested in over 50,000 women and found to have no overall increased mortality effect. And they are the most effective."

Bioidentical hormones have also been highly touted by some pharmacists and health practitioners as a safer alternative to traditional hormone therapy. But there is no scientific evidence to support that, according to both the Endocrine Society and the American College of Obstetricians and Gynecologists. Moreover, bioidentical hormones are not subject to government oversight and can be impure and inconsistent.

Government health officials still say the main advice from the Women's Health Initiative hasn't changed: Women who need hormones for symptom relief should take the lowest effective dose for the shortest amount of time needed.

Many new lower-dose products, including skin patches and gels, have come on the market since 2002. The new products allow many women to take lower doses of hormones for specific symptoms, such as topical creams for vaginal dryness. However, there are no studies yet on whether these new formulations or lower doses may alter the risks related to hormone therapy that were revealed in the Women's Health Initiative.

Women taking hormones should also have regular mammograms and blood pressure checks because their risk of breast cancer and stroke is slightly elevated. And, Rossouw says, after a few years, women should stop taking the medications to assess their condition. In about 25% of women, the symptoms will come back, but they may be less severe.

"Give it six months to be sure that symptoms will persist. I know that is tough," he says.

Still, in about 5% to 10% of women (both women who have had hysterectomies and those who haven't), menopausal symptoms will persist into their 70s. But hormones are simply not recommended today for women who are 10 or more years past the onset of menopause.

"It's not OK to use hormones for symptom relief at older ages," Rossouw says. Adds Stefanick: "The biggest problem is, if you start, when do you stop? I think the whole physiology of hot flashes needs more research. We have this very uncomfortable change of life, and we don't know very much about it."

There are some women who should avoid taking hormones or consult with a doctor about the advisability of taking them, experts say. These include women with a recent history of breast or uterine cancer, a strong family history of breast cancer or a history of atypical hyperplastic changes in breast tissue; women with clotting disorders, such as phlebitis or deep vein thrombosis; and women with unexplained vaginal bleeding.

And for those who don't have problems with menopause, there is no good reason to take hormone therapy. Women at risk for osteoporosis have a choice among several medications to prevent thinning bones. Even younger menopausal women with risk factors for heart disease, such as high blood pressure, can use other medications to treat those problems.

Yet a key question about hormone use in younger women remains, and it's a question women will hear experts debate for years to come: Do hormones confer any long-lasting benefit to the heart that extend far past the years that women take them?

This theory is sometimes called the timing theory or window-of-opportunity theory. If true, it would suggest that even women who do not need hormones for hot flashes might help the health of their hearts into old age by taking hormones beginning at menopause. "It's a minority view," Rossouw says. "We don't support it because we know starting hormones at an older age is bad." Doctors can't assume that any possible short-term cardiovascular benefit would extend into older ages if women were to continue using hormones, he says.

Two studies currently underway in the United States will look for evidence of long-term cardiovascular benefits among women taking hormones. But for now there is insufficient evidence to say hormones offer such protection to younger menopausal women, most experts say.

"I wouldn't say *carte blanche* that everyone take hormones," Utian says. "I would say if there is a good reason to take it, meaning there are symptoms, women need not have the fear that was generated by the WHI reports."

shari.r [oan@latimes.com](mailto:shari.r_oan@latimes.com)

For complete article, go to: [http://www.latimes.com/features/health/la-la.1.he\\_coverjul23,1,2517067.story?page=1&ctrack=1&cset=true&coll=la-headlines-health](http://www.latimes.com/features/health/la-la.1.he_coverjul23,1,2517067.story?page=1&ctrack=1&cset=true&coll=la-headlines-health)

