

'Hormonal Vaccine' May Prevent Breast Cancer

BY BRUCE JANCIN

SAN ANTONIO — Truly large-scale prevention of breast cancer will require the development of a "hormonal vaccine" for young women that mimics the effects of repeated childbearing and breastfeeding, according to a prominent expert in cancer epidemiology.

"It's not research that many people are doing. It's not cutting edge. It won't get



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DR. BERAL

into [the journals] Nature or Science. But it will get a Nobel Prize in Medicine," Dr. Valerie Beral predicted at the San Antonio Breast Cancer Symposium.

More than 1 million new cases of breast cancer occur annually worldwide. It is known that relatively short-term exposure in early adulthood to the hormones of late pregnancy and lactation confers lifelong protection against the malignancy. No other preventive factor can approach the size of this protective effect. But it's utterly unrealistic to expect women in developed countries to revert to such childbearing patterns.

That's why a "hormonal vaccine"—something that could be given to young women for 9 months at a time, perhaps

repeatedly, in order to mimic the effects of childbearing on breast tissue—is a must in order to achieve great success in breast cancer prevention. It's badly needed not only in the developed world, but also in the major urban areas of the developing world, where the incidence of breast cancer is climbing rapidly, according to Dr. Beral, director of the cancer epidemiology unit and professor of epidemiology at the University of Oxford (England).

The notion that a major cause of breast cancer is small family size and a lack of prolonged breastfeeding is not new. It recapitulates an observation made by Dr. Bernardo Ramazzini, the Italian physician known as "the father of occupational medicine," who in the early 1700s described breast cancer as "an occupational disease of nuns."

"We're all like nuns now," Dr. Beral said. "Women in developed countries have had few or no children and haven't breastfed. If there were large numbers of women in the West who'd had many children and kept breastfeeding for a long time, we'd see the difference, but we're all like that now."

Other modifiable risk factors for breast cancer draw a lot of attention, but the best estimates are that even if no women drank alcohol, were obese, or used hormone therapy, the U.S. incidence of breast cancer would drop only moderately, from 180,000 cases annually to 140,000.

"That's a lot, but it's still only about a 20% decrease," she noted.

Dr. Beral cited World Health Organi-

zation data in support of her argument that drastically different childbearing and breastfeeding practices account for the great bulk of variation in breast cancer rates between the developed world, where the cumulative incidence to age 70 years is 6.3%, and rural areas of Asia and Africa, where the figure is just 1.0%.

Modeling studies indicate that if women in developed countries were to adopt the childbearing and breastfeeding practices that are the norm in rural Africa and Asia, their cumulative incidence of breast cancer to age 70 would plunge from 6.3% to 2.7%. Eliminating postmenopausal obesity, alcohol consumption, and hormone therapy would knock the rate down further to 1.6%, which is very close to the rate in the rural undeveloped world.

Genetic studies of breast cancer risk grab headlines. But when investigators at the University of Oxford-based Million Women Study (www.millionwomenstudy.org), for which Dr. Beral is the principal investigator, applied seven recently identified breast cancer risk alleles (N. Engl. J. Med. 2008;358:2796-803) to their massive study population, they found that in terms of risk conferred by the seven single nucleotide polymorphisms, the top quintile had a relative risk only about 1.5-fold greater than the lowest quintile.

"It's not a huge variation in risk. It's not as big as people perhaps might have wished to find," she continued.

And that observation led Dr. Beral to what she stressed was the most important point of her plenary lecture: Few

women in developed countries are at low risk of breast cancer.

"One in 10 women in developed countries will get breast cancer by age 80. The reason that 1 in 10 does and the other 9 don't is largely chance. The people who get it are just unlucky, and the ones that don't are lucky. There is, of course, some variation due to genes and other things, but the predominant factor is luck," she said.

The Oxford-based Collaborative Group on Hormonal Factors in Breast Cancer, which meets every 5 years to analyze pooled data from roughly 100 epidemiologic studies conducted worldwide, has shown that a woman's breast cancer risk drops by about 10% for each live birth. Only term births count: Miscarriages and induced abortions have no impact on risk. It takes about 10 years for the preventive effect to appear, and then it persists for life.

What is it about term pregnancies and lengthy breastfeeding that confers delayed but subsequently lifelong protection against breast cancer? It's not just the elevation in estrogen and progesterone. The Collaborative Group and others have shown that oral contraceptives and hormone therapy are associated with increased breast cancer risk during their use and soon after, but a few years later the increased risk is gone.

"It's not just estrogens and progesterone that change during pregnancy. We have to be looking for something beyond," Dr. Beral said.

Dr. Beral indicated that she has no relevant financial relationships. ■

Stellate Ganglion Block Effective for Severe Hot Flashes

BY BRUCE JANCIN

SAN ANTONIO — Stellate ganglion block may be an option for severe, treatment-refractory hot flashes and sleep disturbances in breast cancer patients.

In a prospective study, stellate ganglion block procedures led to significant improvements in 17 of 24 breast cancer patients with severe hot flashes despite pharmacotherapy with venlafaxine (Effexor) and/or clonidine, Dr. Patrick Neven reported at the San Antonio Breast Cancer Symposium.

The ganglion block is performed as an outpatient procedure and takes about 5 minutes. An anesthetist uses fluoroscopic guidance to inject 10 cc of anesthetic at the anterolateral aspect of the C-6 vertebra.

Benefits endured 12 or more weeks in 12 of the 17 responders. A single right-sided stellate ganglion block was effective in five patients. Following a second block placed on the opposite side, 5 of 10 patients had responses. Benefits also were seen in two of three patients who got a third block 2-3 months after the first, according to Dr. Neven of the University of Leuven (Belgium).

Stellate ganglion block was associated with no side effects other than the temporary Horner syndrome, which merely indicates the block has been successful. Horner syndrome involves pupillary changes, a droopy

eyelid, and a one-sided decrease in facial sweating, typically lasting for about 20 minutes. The syndrome is "scary," according to Dr. Neven, but patients are informed about it in advance.

Stellate ganglion blocks have been used for at least 6 decades to treat a variety of pain conditions, including chronic regional pain syndrome, migraine, and angina. The notion of using the procedure to treat severe hot flashes in postmenopausal women and in breast cancer patients is credited to Dr. Eugene G. Lipov, director of pain research at North-

west Community Hospital, Arlington Heights, Ill. In his 13-patient pilot study, the mean number of hot flashes per week plummeted from 79 at baseline to 7 at 42 weeks of follow-up. Ten patients needed additional blocks after a mean of 11 weeks (Lancet Oncology 2008;9:819-20).

Dr. Lipov demonstrated that the stellate ganglion has second-

and third-order neuronal connections to key areas of the brain involved in temperature regulation and other functions. His proposed mechanism of benefit is that stellate ganglion block causes a prolonged reduction in brain nerve growth factor levels, resulting

in decreased brain norepinephrine (Med. Hypotheses 2009;72:657-61).

Dr. Neven reported that sleep quality improved significantly in 14 of the 24 Belgian breast cancer patients, although the effect was temporary in 2 of them.

Stellate ganglion block improved symptoms in 17 of 24 breast cancer patients with severe hot flashes.

DR. NEVEN

Session chair Dr. Charles L. Loprinzi said he found the Belgian study particularly interesting because, after speaking with Dr. Lipov, he too has undertaken a prospective pilot study of stellate ganglion block for hot flashes, with data available on eight breast cancer patients.

"Let me just say that similar results are being observed. We gave only one block, and we've seen a drastic decrease in hot flashes in the first 1-3 weeks. With follow-up out to 6 weeks, some women have their hot flashes come back, others don't," commented Dr. Loprinzi, professor of oncology at the Mayo Clinic, Rochester, Minn.

A parallel improvement in sleep disturbances was seen. "Sleep problems in patients with hot flashes are often due to night sweats. Get rid of the hot flashes and the patients often sleep better," he said.

Stellate ganglion block "might well work" for severe hot flashes, according to Dr. Loprinzi, but he'll reserve judgment pending the results of an ongoing randomized, double-blind clinical trial involving placebo injections of saline. ■



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