

Long-Acting Methods Are Contraception's Future

BY SHERRY BOSCHERT

EXPERT ANALYSIS FROM THE ANNUAL MEETING
OF THE AMERICAN COLLEGE OF
OBSTETRICIANS AND GYNECOLOGISTS

SAN FRANCISCO — Fifty years after the introduction of oral contraceptives, physicians are looking to long-acting removable contraceptives to provide the next leap forward in preventing unintended pregnancy.

Three themes emerged in interviews with multiple physicians who gave separate presentations on contraception in sessions at the meeting.

First, nothing in the future of contraception is likely to match the revolutionary impact of oral contraception. Second, the great advances in contraception over the past half-decade still are accompanied by an unacceptably high rate of unintended pregnancies. And third, when asked to imagine what contraception might look like 50 years from now, most physicians looked to greater use of long-acting removable contraception (LARC) such as intrauterine devices (IUDs) or implants.

Long-acting removable contraception is the wave of the future, said Dr. Sarah Prager of the University of Washington, Seattle. Their advantage is that once the devices are inserted, they don't require patient participation in contraception, which has been one of the major stumbling blocks in contraceptive failures.

Not that physicians haven't kept trying new ways to get patients to remember to take their daily contraceptive pill. One prize-winning poster at the meeting reported on a randomized study that sent

reminders by text messages on cell phones. It didn't help, reported Dr. Melody Y. Hou of Boston University and her associates. Among the 82 women, objective pill counts showed an average of five pills missed per cycle in both groups randomized to get or not get text messages.

The next 50 years probably will see improvements in long-acting removable contraceptives, Dr. Prager added. "Our longest-acting LARC method only lasts for 10-12 years," she noted.

Dr. Joseph Anthony Ogburn of the University of New Mexico, Albuquerque, shared the same vision for the future. Approximately half of U.S. pregnancies are unintended, giving the United States the worst unintended pregnancy rate among developed countries, he noted.

Only about 1%-2% of U.S. women on contraception use an IUD, and less than 1% have a contraceptive implant. "If we could increase those numbers significantly, I think we could have a dramatic impact on the unintended pregnancy rate," he said. Advances in the next 50 years probably will entail tweaking existing long-acting removable contraceptives to make them more acceptable.

Dr. Pouru Bhiwandi was more enthusiastic. "It's a very, very exciting time for all of contraception," said Dr. Bhiwandi, an ob.gyn. in Raleigh, N.C., and an international consultant in women's health. "We have so many choices today, which we've never had before."

Since the first oral contraceptive was approved in 1960, women's options grew with approval of more than 40 birth

control pills and the development of other forms of hormonal contraception in transdermal patches, the vaginal ring, implants, and intrauterine devices (IUDs).

Modifications in dosing since the first oral contraceptives, which contained nearly four times the amount of estrogen and nearly 10 times the amount of progestin as today's formulations, have made the Pill safer and more acceptable, as has the development of newer estrogens and progesterones, she added. Newer regimens mean women no longer have to bleed while on hormonal contraception.

On the horizon are "exciting possibilities" for new products in barrier contraception that are both spermicidal and microbicidal to prevent sexually transmitted infections, plus "a whole range of new IUDs, a 1-year vaginal ring with a new progestin, and other products," Dr. Bhiwandi said.

The U.S. should emulate Europe, where longer-acting methods of birth control, including IUDs and contraceptives are much more prevalent, said Dr. Andrew Kaunitz, professor of ob.gyn. at the University of Florida, Jacksonville.

Although U.S. clinical trials report a failure rate of 1%-2% with oral contraceptive use, in "typical practice" it's much higher, Dr. Kaunitz said—around nine women per 100 couples annually have unintended pregnancies on the Pill. "That's too high," he said.

Dr. Bliss Kaneshiro of the University of Hawaii, Honolulu, noted that long-acting contraceptive devices are expen-

sive and not always covered by insurance. "One of the big challenges, I think, is cost," she said. "Our challenge for the next 50 years is improving access to those good contraceptive methods."

Dr. David Plourd of the Naval Medical Center, San Diego, said he hopes to see more options in long-acting removable contraceptives in the next 50 years, such as "a flexible IUD, not the semi-rigid T-shaped ones we have currently."

The development and use of contraception methods targeted to men should play more of a significant role, he added. "For decades, there's been ongoing research developing hormonal, testosterone-based, [gonadotropin-releasing hormone-based] preparations that are very effective at inhibiting spermatogenesis," Dr. Plourd noted.

"That said, there seems to be some barriers to its acceptance in this country. I hope that in the next 50 years that is another option on the table for contraception."

Dr. Kaunitz disclosed financial relationships with Teva Pharmaceuticals, Bayer, Ortho (Johnson & Johnson), Merck, Procter & Gamble, Becton Dickinson, Sanofi-Aventis, and Medical Diagnostic Laboratories. Dr. Ogburn has been a consultant for Organon/Schering-Plough. Dr. Bhiwandi disclosed financial relationships with Teva Pharmaceuticals, Warner Chilcott, Boehringer Ingelheim, and Watson Pharmaceuticals. Dr. Plourd has been a speaker for Merck, Novartis, Sanofi-Aventis, Graceway, and Warner Chilcott.

Dr. Prager and Dr. Kaneshiro said they have no conflicts of interest. ■

Ovarian Cancer Screen Promises Earlier Disease Detection

BY DOUG BRUNK

FROM AN AMERICAN SOCIETY OF
CLINICAL ONCOLOGY PRESSCAST

A staged algorithm that incorporates the CA-125 assay to screen postmenopausal women for ovarian cancer has a near-perfect specificity of 99.9%, according to the results of a single-arm, multicenter study that enrolled more than 3,200 women at average risk of the disease.

If confirmed in larger studies, this approach could be used to detect ovarian cancer in its early, more curable stages, lead author Dr. Karen Lu said during a press briefing sponsored by the society.

"Ovarian cancer is the most lethal gynecologic cancer," said Dr. Lu, professor of gynecologic oncology at the University of Texas M.D. Anderson Cancer Center, Houston.

"Greater than 75% of cases present with advanced stage disease, when cure rates are less

VITALS

Major Finding: The specificity of a new screening approach developed for postmenopausal women at average risk for ovarian cancer was 99.9%.

Data Source: A single-arm, prospective, multicenter study of 3,252 women aged 50-74 years.

Disclosures: One of the study authors, Dr. Herbert A. Fritsche, disclosed that he received research funding from Roche Diagnostics. Another study author, Dr. Robert C. Bast Jr., disclosed that he serves as a consultant and adviser to Fujirebio Diagnostics, Inc. He also receives other remuneration and royalties for helping to invent the CA-125 assay.

than 30%. If caught at an early stage, cure rates are 60%-90%, but at the current time there are no effective screening methods."

For the 9-year study, which was presented at the annual meeting of ASCO in Chicago, Dr. Lu and her associates enrolled 3,252 women aged 50-74 years with no significant family history of breast or ovarian cancer to be screened with the Risk of Ovarian Cancer Algorithm (ROCA). She described ROCA as a mathematical model that takes into account a woman's age as

well as changes in the values of her CA-125 assay over time.

"From here there are three possibilities," she explained. "Those individuals who have a low ROCA score are told to come back at 1 year for a repeat CA-125. Those who have an intermediate ROCA score are told to come back at 3 months for another CA-125, and those who have a high ROCA score are triaged to a transvaginal ultrasound and referral to a gynecologic oncologist."

After following the women for 9 years, the researchers

found that the average annual rate of referral for CA-125 assays every 3 months was 6.8% and that the average annual rate of transvaginal ultrasound and referral to a gynecologic oncologist was only 0.9%. "Each year the overwhelming majority of women were triaged to the low-risk category—an annual CA-125," Dr. Lu said.

Cumulatively, 85 women (2.6%) received transvaginal ultrasound and subsequent referral to a gynecologic oncologist. Of these, eight required surgery: three for invasive ovarian cancers (two stage 1C and one stage IIB), two for borderline ovarian tumors, and three for benign ovarian tumors. This translated into a positive predictive value of 37.5%. "This means that three operations would be necessary to detect one case of invasive ovarian cancer," Dr. Lu said.

The combined specificity of ROCA followed by transvaginal ultrasound was 99.9%,

"which means that there were very few false positive."

Dr. Lu emphasized that while results of the ROCA screening strategy are encouraging, "they are not practice changing at this time. We need to await the results of a definitive ovarian cancer screening trial that uses mortality as an end point, and uses the same ROCA algorithm." That trial of more than 200,000 women is underway in the United Kingdom, she said. Results are expected in 2015.

ASCO President Douglas W. Blayney said that the ROCA algorithm "represents yet another example of personalized medicine. Here, we have a personalized screening strategy for a vicious type of cancer. This also represents a more refined application of known technology. The CA-125 is widely available, as is transvaginal ultrasound, which is intrusive and technologically somewhat difficult to interpret. Here, we have a staged application." ■