

# Some Oral Contraceptive Side Effects Irreversible

BY MIRIAM E. TUCKER  
Senior Writer

WASHINGTON — The hypoandrogenic effects of oral contraceptives may not be completely reversible after discontinuation of their use, Claudia Panzer, M.D., reported at the annual meeting of the American Association of Clinical Endocrinologists.

Oral contraceptives (OCs) are known to decrease serum testosterone levels by decreasing ovarian production of testosterone and increasing production of sex hormone-binding globulin (SHBG) by the liver. Higher SHBG levels lower the amount of free testosterone that reaches the tissues. Such changes have been associated with decreases in sexual interest, arousal, vaginal lubrication, and frequency of sexual intercourse.

It has long been assumed that these changes are reversible after discontinuation of OC use, but findings from a review of 124 premenopausal women with female sexual dysfunction suggest otherwise, said Dr. Panzer, an endocrinologist at Boston University.

Among the subjects were 62 current OC users, 39 former users, and 23 who had never used OCs. None of the subjects had used OCs for reasons other than birth control. The "never users" were older than the current users (36 vs. 32 years), and had a longer duration of sexual dysfunction than both current and former OC users (9 years vs. 6 years in both OC groups).

Those who had never used OCs also scored higher on the Female Sexual Function Index, indicating better function (21 points, vs. 15 points for the current OC users and 10 points for the former users). Women on OCs had lower scores in the domain of sexual desire, compared with those who had never used them, and also complained more about sexual pain.

Of the 101 OC users, 39 said that the knowledge that the pill might cause sexual dysfunction would convince them to

stop taking it. "I guess that is pretty good evidence that they were impacted enough to change things," Dr. Panzer told this newspaper.

There were no differences between the groups in body mass index, Beck Depression Index scores (means were all in the normal range), or scores on the Sexual Distress Scale (means for all indicated moderate distress).

Baseline SHBG levels were four times higher in the current OC users (157 nmol/L) and the former users (161 nmol/L) than in the never users (41 nmol/L). Although SHBG levels did decrease after discontinuation of OC use, they remained elevated after 49-120 days (62 nmol/L) and again at more than 120 days (63 nmol/L), compared with the never users, for whom SHBG measured after 120 days was 35 nmol/L, she said.

The fact that the SHBG value after 120 days in the group that had discontinued OCs had fallen into the normal reference range despite being twice as high as for the never-users suggests that the currently used SHBG reference range may be too wide. A narrower range might better reflect hormonal changes seen in women who use OCs, Dr. Panzer commented.

Total testosterone levels at baseline did not differ between the three groups, but the never users had significantly higher free androgen indexes than did the current and former OC users (3.7 vs. 0.8 for both OC groups), calculated free testosterone levels (6.2 pg/mL vs. 2 pg/mL for both OC groups), and calculated bioavailable testosterone (146.5 pg/mL vs. 47.8 pg/mL for former users and 46.7 pg/mL for current users).

These data suggest that total testosterone is a poor test to evaluate androgen status in OC users and that assessments of free or bioavailable testosterone are superior, Dr. Panzer said.

Physicians who prescribe OCs should warn patients of possible sexual side effects associated with their use, she recommended. ■

# New Drospirenone OC Provides Effective Premenstrual Relief

BY KATE JOHNSON  
Montreal Bureau

SAN FRANCISCO — A new drospirenone-based oral contraceptive awaiting approval by the Food and Drug Administration is effective in relieving premenstrual symptoms because it is given in a low dose and for an extended regimen, according to new research.

Drospirenone is a progestin derived from spironolactone, and thus has a diuretic effect that other progestins do not, Gloria Bachmann, M.D., reported at the annual meeting of the American College of Obstetricians and Gynecologists.

Drospirenone is used in an FDA-approved OC (Yasmin, manufactured by Berlex) in a formulation of 30 mcg of ethinyl estradiol (EE) and 3 mg of drospirenone given in the typical OC regimen of 21 days, followed by 7 hormone-free days.

But the newer low-dose formulation (20 mcg of EE/3 mg drospirenone) given over a 24-day period with only 4 hormone-free days can significantly reduce symptoms of premenstrual dysphoric disorder (PMDD), compared with placebo, said Dr. Bachmann, associate dean for women's health and professor of obstetrics and gynecology at Robert Wood Johnson Medical School, New Brunswick, N.J.

"In the usual OC cycle of 21 hormone days and 7 days off, women begin to get symptomatic even before the pill-free in-

terval because their ovaries are not totally suppressed," she said in an interview.

"By giving an extended number of days of hormone, you have better ovarian suppression and thus fewer symptoms during the shorter pill-free interval," she added.

Dr. Bachmann presented a double-blind study, funded by Berlex, in which 83 women with PMDD were randomized to either the low-dose drospirenone-based extended OC regimen (42 women) or placebo (41 women) for three cycles of treatment followed by a washout cycle. The women then crossed over to the other arm of treatment for another three cycles.

PMDD symptoms were assessed using the Daily Record of Severity of Problems (DRSP) scale, which includes 21 symptoms and three functional impairment measures.

Active treatment was significantly more effective than placebo in relieving emotional and physical symptoms of PMDD, and the effects were similar to those seen when PMDD is treated with selective serotonin reuptake inhibitors (SSRIs), Dr. Bachmann said.

"If you're deciding between an SSRI and an OC [to treat women with PMDD], you have the added benefit of birth control. You're actually improving the gynecologic health of women as well, so it's a win-win situation," according to Dr. Bachmann. ■

**'If you're deciding between an SSRI and an OC [to treat women with PMDD], you have the added benefit of birth control.'**

# St. John's Wort Does Not Mitigate Antiandrogenic Effects of OCs

BY JANE SALODOF MACNEIL  
Southwest Bureau

LOS ANGELES — St. John's wort does not appear to interfere with the antiandrogenic effects of oral contraceptive pills, Robin Fogle, M.D., said at the annual meeting of the Society for Gynecologic Investigation.

She reported that testosterone levels decreased, while a marker of androgen metabolism increased, in 15 healthy women treated with St. John's wort and Loestrin 1/20 (norethindrone/estradiol) during a 4-month study.

Although the changes did not reach statistical significance, the outcomes strongly suggest St. John's wort will not interfere with the oral contraceptives' pill's effectiveness when used as a primary treatment for hirsutism rather than for birth control, said Dr. Fogle, of the University of Southern California, Los Angeles, in an interview.

The study was undertaken because reports have shown the over-the-counter

herbal remedy, commonly used for depression and inflammation, induces cytochrome P450 activity. This can interfere with the efficacy of some drugs, including oral contraceptives, Dr. Fogle and her coinvestigators wrote in a poster presented at the meeting.

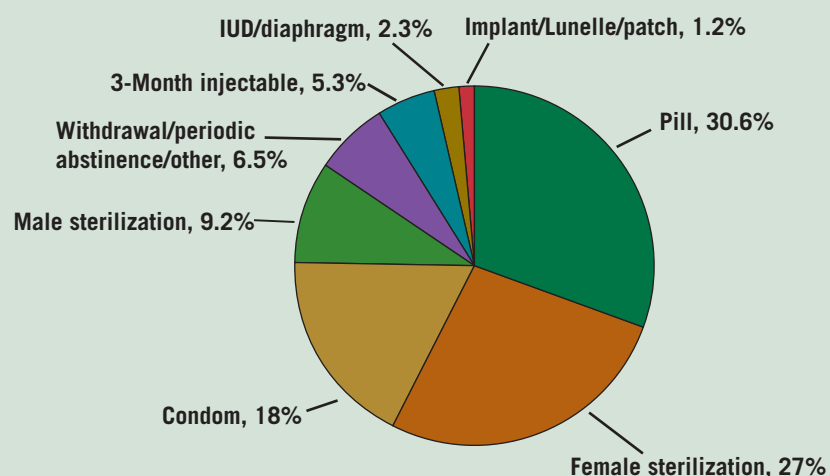
None of the women in the study had hirsutism. They took Loestrin 1/20 for four consecutive 28-day cycles. During the last two cycles, the protocol added 300 mg of St. John's wort taken three times daily.

Mean testosterone decreased 10.7% (from 44.8 ng/dL to 40.0 ng/dL), and free testosterone dipped 15.8% (from 0.38 ng/dL to 0.32 ng/dL) after the addition of St. John's wort. Conversely, 3 $\alpha$ -androstane diol glucuronide, the marker of androgen metabolism, increased 6.5% from 2 ng/mL to 2.13 ng/mL.

"Thus, it appears that St. John's wort enhances androgen metabolism and does not interfere with the antiandrogenic properties of oral contraceptive pills," the investigators concluded. ■

## DATA WATCH

### Contraceptive Methods Used by Women Aged 15-44 Years



Note: Numbers may not equal 100% because of rounding.  
Source: 2002 data, Centers for Disease Control and Prevention