

## Arteries Show Signs of Early Aging in Young PCOS Patients

BY BETSY BATES  
Los Angeles Bureau

SAN DIEGO — Young women with polycystic ovary syndrome have evidence of endothelial dysfunction and low-grade, chronic inflammatory markers characteristic of much older patients, researchers reported at the annual meeting of the Endocrine Society.

Dr. Evanthia Diamanti-Kandarakis and associates at Laiko Hospital of the University of Athens compared endothelial function and inflammatory cytokines in 25 women with PCOS and 20 age-matched controls with similar body mass index (BMI) measurements and waist-hip ratios. The women were in their mid-to-late 20s and had BMIs of about 26-29 kg/m<sup>2</sup>.

Endothelial function was assessed by flow-mediated dilatation of the brachial artery on ultrasound, plus plasma endothelin-1. Numerous cytokines were measured to assess arterial inflammation.

Subjects with PCOS had significantly lower percentages of flow-mediated dilatation than controls (3.47% vs 9.26%). Nitrate-induced dilatation, measured to exclude smooth muscle cell injury, was not significantly different in the two groups.

Significantly higher levels of endothelin-1, intracellular adhesion molecules, vascular cell adhesion molecules, and C-reactive protein were found in PCOS subjects, compared with controls.

In PCOS "the lining of the arteries is affected and at the same time, the molecules are sticking to each other and to the vessel wall, leading to a compromised circulation as would be seen in a woman much older" than these subjects, Dr. Diamanti-Kandarakis said at a press conference during the meeting.

As expected, testosterone levels were significantly elevated in women with PCOS. When asked to advise clinicians on how to use the information, she pointed out that a multiple regression analysis determined that the best predictors of endothelial damage in PCOS subjects were elevated levels of testosterone and CRP. Young PCOS patients with high levels of both should be closely followed for cardiovascular consequences of the syndrome, particularly if they are obese.

"It they are obese, this risk is multiplied," she said. "We cannot assume that all women with PCOS have [endothelial dysfunction]. There are different subtypes of the disease," she said. ■

## Treating Apnea May Lower Cortisol Levels in PCOS

BY BETSY BATES  
Los Angeles Bureau

SAN DIEGO — A small but intriguing study has found that treating obstructive sleep apnea in patients with polycystic ovary syndrome lowered their cortisol levels not only at night, but during the daytime as well.

Obstructive sleep apnea symptoms also greatly improved in five nondiabetic PCOS patients who received continuous positive airway pressure (CPAP) for 8 weeks as part of a study presented at the annual meeting of the Endocrine Society.

Previous research has determined that the risk of obstructive sleep apnea is 30-fold to 40-fold higher in women with PCOS compared with weight-matched controls. It has been theorized that there may be a link between obstructive sleep apnea and the metabolic and hormonal abnormalities associated with the disease.

"These findings strongly suggest that obstructive sleep apnea is likely to contribute to elevated cortisol levels in women with PCOS and could play a role in the risk for adverse metabolic alterations in this patient population," concluded researchers Eve Van Cauter, Ph.D., and Dr. Esra Tasali, of the de-

partment of medicine at the University of Chicago, who presented a poster at the meeting.

Subjects in the study were in their early to mid-30s and had a mean body mass index (kg/m<sup>2</sup>) of 51. Three of the five had impaired glucose tolerance. CPAP treatments were administered for 8 weeks at the patients' homes, with compliance confirmed by built-in monitors.

Following therapy, mean 24-hour cortisol levels fell from 10.2 mcg/dL to 7.7 mcg/dL. Daytime cortisol levels fell from 10.3 mcg/dL to 7.9 mcg/dL, whereas nighttime cortisol dropped from 10.1 mcg/dL to 7.5 mcg/dL. These decreases were all statistically significant.

The cortisol nadir declined by 40%. "Interestingly, this decrease in the nadir was associated with the severity of patients' sleep apnea," Dr. Tasali, a pulmonologist and sleep researcher at the university, said in an interview at the meeting.

CPAP may emerge as a treatment modality in some patients, not only to alleviate symptoms of obstructive sleep apnea, but also to independently target hormonally and metabolically driven symptoms, said Dr. Van Cauter, a professor of medicine at the university. ■

## Statins Improve Endocrine, Metabolic Aspects of PCOS

BY BRUCE DIXON  
Chicago Bureau

MONTREAL — The addition of simvastatin to an oral contraceptive regimen significantly reduces hirsutism and elevated levels of total testosterone in women with polycystic ovary syndrome, according to a study conducted by Dr. Antoni J. Duleba, of Yale University, New Haven, Conn., and associates.

"This is the first report that simvastatin improves a clinical end point of treatment of polycystic ovary syndrome/hirsutism," Dr. Duleba, the lead investigator, said in an interview.



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DR. DULEBA

The data were presented by another investigator in the study, Dr. Beata Banaszewska, at the conjoint annual meeting of the American Society for Reproductive Medicine and the Canadian Fertility and Andrology Society.

Oral contraceptive pills "do reduce testosterone levels, but in this crossover study, we can appreciate that statins have a greater power to this effect," Dr. Banaszewska, of Poznan University of Medical Sciences in Poland, said at the meeting.

"We still don't have satisfactory medical treatments for PCOS; symptomatic treatments only partly improve the situation, and

long term, these patients are at increased risk of cardiovascular problems," he said.

The study randomized 48 PCOS patients (mean age 24 years) into two treatment groups. One group received oral contraceptive pills (OCP) alone (20-mcg ethinyl estradiol and 150-mcg desogestrel) for 12 weeks, after which 20-mg simvastatin was added to their regimen daily for 12 more weeks. The other group first received the

combined drug regimen for 12 weeks and then were given OCP alone for 12 weeks. Clinical, endocrine, and metabolic evaluations were performed at baseline, at crossover (12 weeks), and at 24 weeks.

"Simvastatin induced a decrease of total testosterone by 18% below the effect of OCP," Dr. Duleba said. "This effect was paralleled by a 16% decrease of free testosterone below the effect of OCP. We also found that the hirsutism declined, and there was a strong trend toward an improvement in acne."

A simvastatin-attributable decline of hirsutism was modestly but significantly greater than with OCP alone; this 4% difference was statistically significant. ■

Kate Johnson of the Montreal Bureau contributed to this report.

## Fitness Attenuates Metabolic Syndrome Mortality in Women

BY BRUCE JANCIN  
Denver Bureau

DALLAS — Physical fitness cancels out the excess mortality risk associated with the metabolic syndrome in asymptomatic women, Dr. Martha Gulati, said at the annual scientific sessions of the American Heart Association.

This finding from the large observational St. James

Women Take Heart Project has important clinical implications: It suggests that as part of a primary cardiovascular prevention strategy, physicians ought to routinely

assess cardiorespiratory fitness in asymptomatic women who meet criteria for the metabolic syndrome (MS). If risk is stratified in this manner, the unfit can be targeted for more aggressive interventions, explained Dr. Gulati of Northwestern University, Chicago.

She reported on 5,721 asymptomatic women age 35-86 years who participated in the St. James Project, a prospective observational study whose primary purpose was to assess the value of exercise stress testing in asymptomatic women. The mean age of participants was 52 years. Thirty percent met National Cho-

lesterol Education Program (NCEP) criteria for the MS.

The MS has been shown to confer at least a twofold increased risk of all-cause and cardiovascular mortality. That's why the condition received prominent attention in the NCEP Adult Treatment Panel III guidelines. The impetus for Dr. Gulati's study was a recognition that the impact of physical fitness upon this mortality risk

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DR. GULATI

hadn't previously been studied in women.

In 1992, participants underwent a symptom-limited Bruce protocol exercise stress test, then were followed prospectively through

2000. During a mean 8.4 years of follow-up, 180 women died, with one-third of the deaths being due to cardiac causes.

An unadjusted analysis showed that women with the MS were at least 1.5 times more likely to die from any cause, compared with those without it, and at least twice as likely to die from cardiac causes. Upon adjustment of the data for cardiorespiratory fitness, however, the MS was no longer an independent risk factor for mortality. "What this ultimately means is that fitness is more important than the presence or absence of the metabolic syndrome," Dr. Gulati said. ■

