

# Nonobese PCOS Patients Also Need the OGTT

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ORLANDO — More than 10% of non-obese adolescent girls with polycystic ovary syndrome were found to have impaired glucose tolerance in a study of 70 girls who had been referred to a specialty clinic for menstrual irregularity.

The finding suggests that all girls and women with polycystic ovary syndrome (PCOS)—not just those who are overweight or obese—should be evaluated with an oral glucose tolerance test (OGTT), said Dr. Clare A. Flannery of the Yale Multidisciplinary Adolescent PCOS Program and the department of endocrinology–internal medicine at Yale University, New Haven, Conn.

“Without an OGTT, the presence of impaired glucose metabolism is underestimated in lean adolescents with PCOS since their other parameters of insulin

**Without an OGTT, impaired glucose metabolism might be underestimated in lean adolescents with PCOS since their other parameters of insulin resistance may be normal.**

resistance may be in normal range. There is a need for a standardized OGTT for every adolescent with PCOS, regardless of weight,” she said.

The study was conducted at the Yale PCOS clinic, where patients referred for menstrual irregularity are seen by an endocrinologist, a gynecologist, and a nutritionist. All of the patients also receive a transabdominal pelvic ultrasound, androgen panel, fasting lipid testing, and a 75-g OGTT.

A group of 80 patients who were enrolled in an ongoing cohort study had a mean age of 15.6 years and a mean body mass index (BMI) of 31.4 kg/m<sup>2</sup>, but with a broad range of BMI from 19 to 46 kg/m<sup>2</sup>. Two-thirds of patients were white. Three-fourths of the patients had acne, nearly all had hirsutism, and more than half (57%) had acanthosis nigricans, signaling insulin resistance.

Because there are no established criteria for diagnosing PCOS in adolescence, two of three professional guidelines for diagnosing PCOS in adults were used for the study: The 1990 National Institutes of Health criteria (Blackwell Scientific Publications, 1992:377-84), which includes irregular menses and clinical or biochemical evidence of high androgens with the exclusion of other disorders, and the 2006 Androgen Excess Society (AES) criteria, which allow ultrasound findings of PCOS as a substitute for irregular menses (J. Clin. Endocrinol. Metab. 2006;91:4237-45). The 2003 Rotterdam criteria (Human Reproduction 2004; 19:41-7) were not used because the de-

## VITALS

**Major Finding:** Impaired glucose tolerance was found in 8 of the NIH-defined PCOS adolescent patients (14.5%) and 10 of the AES-defined group (16%). When the AES group was divided into obese and nonobese subgroups, IGT was present in 16% of both groups.

**Data Source:** A study of 70 adolescent girls referred to a specialty clinic for menstrual irregularity.

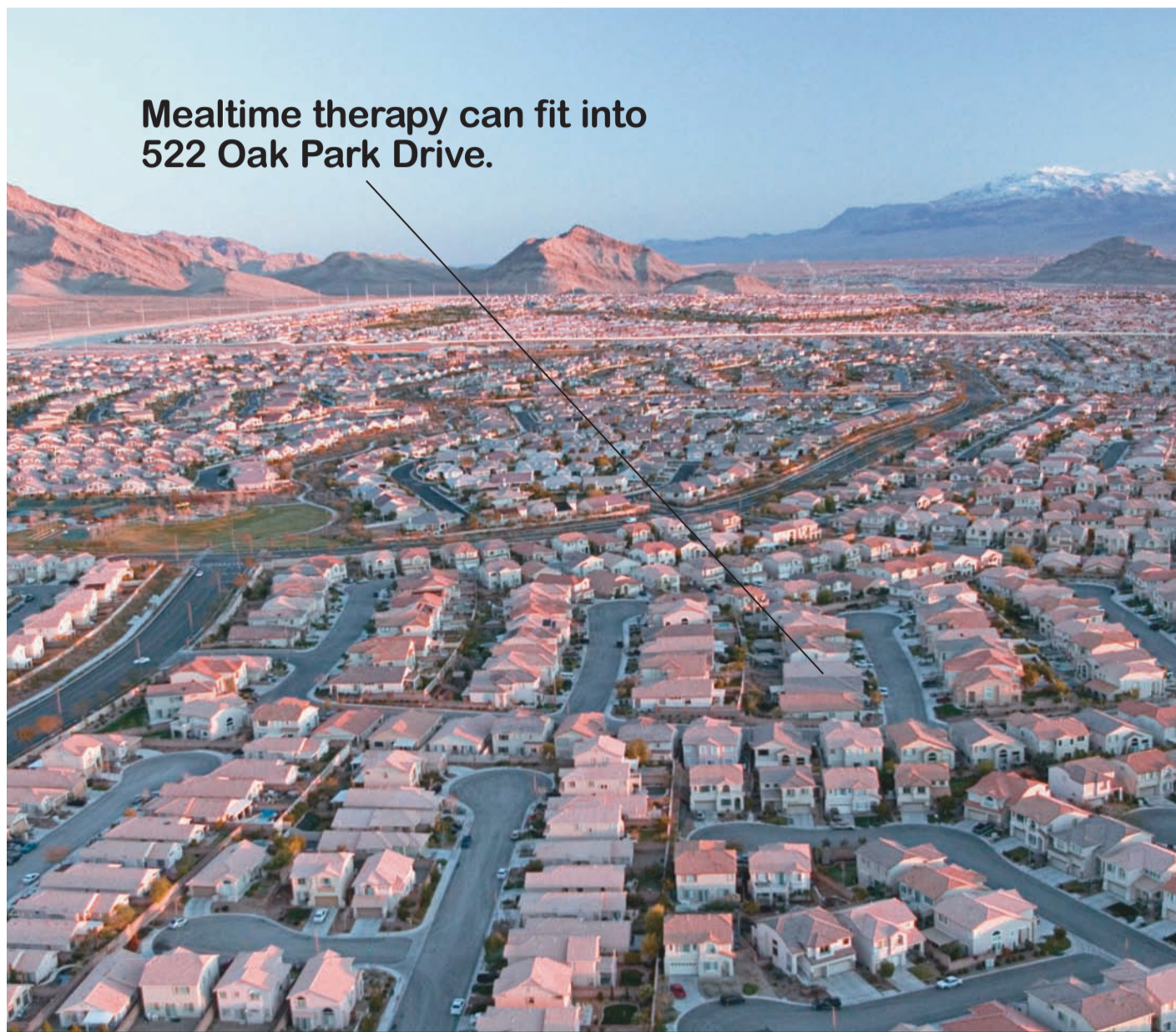
**Disclosures:** Dr. Flannery stated that she had no financial disclosures.

inition is less strict and could include adolescents with hypothalamic amenorrhea, she noted.

Ten adolescents were excluded from analysis because they were either already on metformin or had missing OGTT data. Of the remaining 70, 55 (79%) met the NIH criteria for PCOS diagnosis

and 64 (91%) met the AES criteria. One patient who met both criteria was found to have impaired fasting glucose, and another who met both definitions had type 2 diabetes. Impaired glucose tolerance (IGT) was found in eight of the NIH-defined PCOS patients (14.5%) and 10 of the AES-defined group (16%).

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Humalog is for use in patients with diabetes mellitus for the control of hyperglycemia. Hypoglycemia is the most common adverse effect associated with insulins, including Humalog.

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Among the 64 who met the AES PCOS criteria, 40 were obese (BMI of 95th percentile by age or greater). Mean BMI was 36 kg/m<sup>2</sup> for the obese group and 24 kg/m<sup>2</sup> for the nonobese. IGT was present in 16% of both groups. Two-hour serum glucose values were higher in the obese group (117 vs. 107 mg/dL in the nonobese) but that difference, which did not meet statistical significance, was primarily because of the one outlier in the obese group who met the criteria for type 2 diabetes, Dr. Flannery noted.

"The nonobese girls were just as like-

ly to have impaired glucose tolerance as their obese counterparts. If we had not indiscriminately applied the OGTT to all our patients, the abnormal glucose metabolism of the nonobese girls may have been missed," she commented.

In contrast to the OGTT finding, other metabolic characteristics did appear to be driven by obesity rather than PCOS.

Fasting glucose was found to be greater—although still within the normal range—among the obese patients (86 vs. 82 mg/dL), and there was a trend toward increased insulin resistance among those in the obese group, as measured by the homeostatic model assessment.

Lipid abnormalities and other parameters of insulin resistance also worsened as weight increased, with both dif-

ferences in C-reactive protein and high-density lipoprotein levels reaching statistical significance.

Dr. Flannery recommended that physicians use the AES guidelines for performing an OGTT in all girls and women with PCOS, regardless of age or BMI, noting that the most recent guidelines from the American Diabetes Association recommend use of OGTT only in overweight adolescents with additional risk factors.

"If we had applied the ADA guidelines, we would have missed IGT in many of our adolescents," she said. ■

### The Androgen Excess Society's guidelines should be followed for performing an oral glucose tolerance test in all patients with PCOS, regardless of age or BMI.

#### Indication

Humalog (insulin lispro injection [rDNA origin]) is for use in patients with diabetes mellitus for the control of hyperglycemia. Humalog should be used with longer-acting insulin, except when used in combination with sulfonylureas in patients with type 2 diabetes.

#### Important Safety Information

Humalog is contraindicated during episodes of hypoglycemia and in patients sensitive to Humalog or one of its excipients.

Humalog differs from regular human insulin by its rapid onset of action as well as a shorter duration of action. Therefore, when used as a mealtime insulin, Humalog should be given within 15 minutes before or immediately after a meal.

Due to the short duration of action of Humalog, patients with type 1 diabetes also require a longer-acting insulin to maintain glucose control (except when using an insulin pump). Glucose monitoring is recommended for all patients with diabetes.

The safety and effectiveness of Humalog in patients less than 3 years of age have not been established. There are no adequate and well-controlled clinical studies of the use of Humalog in pregnant or nursing women.

**Starting or changing insulin therapy should be done cautiously and only under medical supervision.**

#### Hypoglycemia

**Hypoglycemia is the most common adverse effect associated with insulins, including Humalog. Hypoglycemia can happen suddenly, and symptoms may be different for each person and may change from time to time. Severe hypoglycemia can cause seizures and may be life-threatening.**

#### Other Side Effects

Other potential side effects associated with the use of insulins include: hypokalemia, weight gain, lipodystrophy, and hypersensitivity. Systemic allergy is less common, but may be life-threatening. Because of the difference in action of Humalog, care should be taken in patients in whom hypoglycemia or hypokalemia may be clinically relevant (eg, those who are fasting, have autonomic neuropathy or renal impairment, are using potassium-lowering drugs, or taking drugs sensitive to serum potassium level).

**For additional safety profile and other important prescribing considerations, see accompanying Brief Summary of full Prescribing Information.**

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