THE VAP® TEST FROM ATHEROTECH®

CLINICAL SUMMARY

"To Treat or not to Treat:" The Dilemma of PCOS

Patient 1	Patient 2
31 year old	21 year old
G1P1	Significant acne
BMI: 31	BMI: 32
Irregular periods	Hirsute
Not attempting pregnancy	Periods are regular

These patients have some indications consistent with PCOS, but do they have enough clinical or laboratory signs to warrant treatment? What encourages a physician to consider treatment beyond simply regulating menstrual cycles? Are there metabolic issues that put these patients at increased risk for diabetes and heart disease that need to be addressed?

The incidence of PCOS is estimated at 6-10 percent of reproductive age women. There are 7-10 million women with this condition, and very few are being treated, especially for the symptoms that affect their quality of life.[1] The questions remain: Is treatment indicated and what criteria should be used to determine treatment?

The Rotterdam criteria are widely used to diagnose PCOS. They are (a) oligo or anovulation, (b) clinical and/or biochemical evidence of hyperandrogenism, and (c) ultrasound confirmation of polycystic ovaries with the exclusion of other etiologies.[2] These criteria do not address the metabolic issues that actually lead to significant long-term complications for these patients.

Cardiovascular disease is the leading cause of female morbidity and mortality in the U.S.[3]

Two common risk factors for cardiovascular disease are insulin resistance and abdominal adiposity.[4] These risk factors are seen in women with PCOS, thus screening for heart disease becomes critically important. This also reinforces the need to aggressively treat the metabolic abnormalities associated with PCOS.

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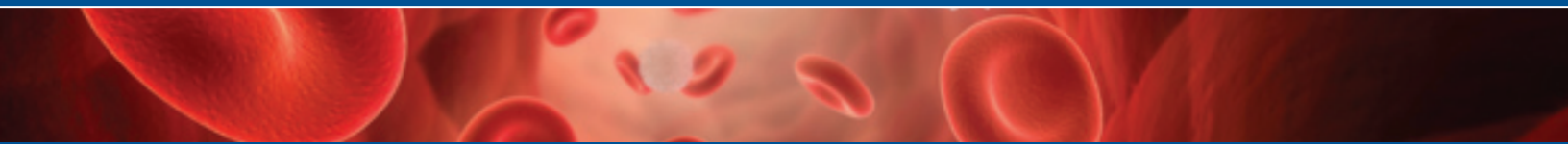
The standard lipid panel (SLP) or Friedewald is the most common test ordered by physicians to screen for cholesterol abnormalities. There are several factors that make this test inaccurate. The one that is of most concern is that a patient has to be fasting for a standard lipid panel. This is because the LDLc level is a calculation (LDLc = TC – HDLc – (TG/5)) where TC, HDLc and TGs are measured, and the LDLc is calculated using a method that was invented back in 1972 when "normal" total cholesterol was 300 mg/dL. Because of this equation, the higher the TGs are, the lower the LDLc will appear. Because a standard lipid panel only reports out four numbers—TG, TC, HDLc and LDLc—it provides a very limited view of a patient's lipid profile.

The VAP® Cholesterol Test is much more accurate and complete. The biggest advantage is that the patient does not need to fast. The LDL level is directly measured rather than calculated, making it a more accurate reflection of the patient's true lipid profile. Why does this matter to an Ob/Gyn? Because triglycerides can be significantly elevated in PCOS patients[5], thus a calculated LDL is not as accurate as one that is directly measured.

The VAP (Vertical Auto Profile) measures other factors such as Lp(a), HDL_2, and pattern size along with the HDL level and triglycerides. These values are helpful when making treatment decisions.



It also measures LDL particle size. Particle size determines risk of developing atherosclerosis (small particles = high risk). Patients with PCOS have been shown to have smaller more atherogenic LDL particles,[6] making the VAP Test very helpful in making treatment decisions.

Elevated triglycerides are a cardiovascular risk and one of the criteria necessary to diagnose insulin resistance.[7] Since many PCOS patients are also insulin resistant, abnormal triglyceride levels reinforce the need for treatment.

HDL is clearly established as the "good" cholesterol. The VAP not only measures HDL, but it also breaks it into sub-fractions of HDL_2 and HDL_3. HDL_2 is the fraction that is the most active at clearing "bad" cholesterol from your system.[8] Studies have shown that when patients have a normal HDL but a higher percentage of HDL_3 rather than HDL_2, it is not as protective, and these patients are still at high risk for cardiovascular disease.[9] Having a low HDL_2 has also been shown to be an independent risk factor for diabetes with peripheral vascular disease.[10] Having the subfraction values of HDL_2 and HDL_3 greatly aids in the treatment decision for PCOS patients.

The American Association of Clinical Endocrinologists' position paper in April 2008 stated that 80 percent of patients with irregular cycles will have abnormal lipids. The same position paper also stated that since it is impossible to accurately assess insulin resistance in a clinical setting, "all obese women should be considered insulin resistant and suffering from Insulin Resistance Syndrome." Most of these patients will not present with concerns about their risk of heart disease. Their primary complaints will be abnormal bleeding, excessive hair growth, infertility and inability to lose weight. It is a disservice to these patients to not test for and treat their metabolic abnormalities.

Historically, PCOS has been described as a primary ovarian disorder. It is now more correctly understood to be a syndrome of excess, with a high incidence of insulin resistance. Drs. Sam and Duaif refer to this condition as Syndrome XX.[11] In their article, they describe patients with Type 2 diabetes, dyslipidemia, visceral adiposity, hypertension, anovulation and hyperandrogenemia. These patients commonly are followed by Ob/Gyn physicians, and it is critical that a VAP Cholesterol Test become the standard in evaluating these patients. Once diagnosed, lipid abnormalities can be treated by the Ob/Gyn physician or referred to other specialists.

The treatment regimen followed in our office includes the use of Metformin to decrease insulin resistance. It is also essential to reduce carbohydrate intake.[12] We provide instruction and encouragement to patients utilizing a nutritional program that reduces carbohydrate intake to 50-100 gm/day and increases protein intake to 80-100 gm/day.[13] With this we have seen an increase of HDL_2 and decreased triglyceride levels as well as weight loss and return of normal ovulatory cycles.

In conclusion, "when do we treat?" Routine use of the VAP Test helps answer this question. If patients with PCOS have a normal lipid profile, it is safe to treat their symptoms of abnormal bleeding and excessive androgen production with oral contraceptives. However, if there are metabolic abnormalities, it is imperative that the issues of insulin resistance are addressed with appropriate treatment.

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