Summary

Patients with polycystic ovary syndrome (PCOS) often have coexisting insulin resistance (IR), glucose intolerance or diabetes, and metabolic syndrome. For larger epidemiological studies, detection of IR may be accomplished using surrogate measures, such as the homeostatic model assessment or the quantitative insulin-sensitivity check index. Alternatively, research studies of IR, particularly those involving a smaller number of subjects, should strive to utilize the clamp, the frequently sampled intravenous glucose tolerance test, the insulin suppression test, or oral glucose tolerance test techniques. Clinically, in PCOS the standard 2-hour oral glucose tolerance test, measuring both insulin and glucose, yields the highest amount of information for a reasonable cost and risk, providing an assessment of both the degrees of hyperinsulinemia and glucose tolerance. However, considering the current variability in insulin assays, each laboratory should set its own normal range and establish a method for periodically reevaluating the acceptability of their results. Up to 25% of nonobese patients and 50% of obese patients with PCOS will have features consistent with the metabolic syndrome. Detection of the metabolic syndrome will include obtaining a thorough medical history, waist and hip circumferences, blood pressure measures, calculation of the body mass index, a lipid profile, and either serum-fasting glucose levels or, preferably, the glucose response to a standard OGTT.

Key Words: PCOS; insulin resistance; dyslipidemia; metabolic syndrome; diabetes.
INTRODUCTION

As discussed in Chapters 1 and 2, 50–70% of patients with the polycystic ovary syndrome (PCOS) demonstrate insulin resistance (IR) and secondary hyperinsulinism (1,2), and the prevalence of the metabolic syndrome is increased compared with age- and weight-matched controls (3–5). Consequently, the rate of type 2 diabetes mellitus (DM) (6–8), and possibly cardiovascular disease (CVD) (9), is increased in PCOS. Effective methods of screening and early detection of these morbidities will be imperative in the management of the patient with PCOS. The following subheadings discuss methods of diagnosing IR, glucose intolerance and type 2 DM, and the metabolic syndrome in these women; alternatively, the detection and diagnosis of established CVD is beyond the scope of this chapter.

DETECTING INSULIN RESISTANCE IN PCOS

The definition of IR varies, with the American Diabetes Association (ADA) defining it as an impaired metabolic response to either exogenous or endogenous insulin (10), whereas some investigators define it as a common pathological state in which target cells fail to respond to ordinary levels of circulating insulin (11). Even without a common definition, IR appears to affect 10–25% of the general population, and the risk increases with obesity (12). Detectable IR occurs in 50–70% of patients with PCOS (1,2) and, because β-cell function is frequently partially or totally conserved (2), most of these women also demonstrate secondary hyperinsulinism. Detection of IR is clinically important because it is an independent risk factor for type 2 DM and CVD.

There are two general approaches to determining insulin sensitivity. The first are those direct and dynamic measures requiring an intervention (e.g., intravenous administration of glucose and insulin) that can be used to estimate the ability of insulin to dispose of glucose. Second, other methods estimate insulin action through surrogate measures utilizing the fasting values of glucose and insulin (13), or the insulin, C-peptide, or glucose responses to a physiological glucose load (e.g., oral glucose tolerance test [OGTT]). These two approaches to measuring insulin sensitivity and hyperinsulinemia will be discussed in more detail in the following subheadings.

Direct Measurements of Assessing Insulin Action In Vivo

GLUCOSE CLAMP

The glucose clamp technique is presumed to be the most accurate test available for the measurement of insulin action in vivo (14). During this test, a constant intravenous infusion of insulin is given at a rate designed to maintain a preselected steady-state insulin level, while simultaneously maintaining or “clamping” the plasma glucose concentration at the normal fasting level (the hyperinsulinemic–euglycemic clamp) by using variable intravenous glucose (or dextrose) infusion. It is assumed that at a steady state (when both the amount of glucose being infused and the circulating glucose levels are stable) endogenous glucose production is fully suppressed and the amount of total glucose being shunted intracellularly by the insulin (i.e., peripheral tissue insulin sensitivity or insulin-mediated glucose disposal) equals the glucose infusion rate. This measurement is expressed as a value termed the insulin sensitivity index (ISI or M value). Combining the clamp with tracer studies using radiolabeled glucose also allows for a