Summary

It is of interest to realize that polycystic ovary syndrome (PCOS) has moved from a histology diagnosis of ovarian tissue to a heterogeneous clinical syndrome (characterized by abnormal menstrual cyclicity, infertility, hirsutism, and obesity), to a reproductive endocrine abnormality with elevated serum luteinizing hormone and androgen levels and, finally, to a metabolic disease characterized by hyperinsulinemia and dyslipidemia. This altered emphasis may have major implications for patient diagnosis and management, with a shift of focus from ovarian abnormalities and ovulation induction for infertility toward the prevention of long-term health consequences. This change is also represented by the involvement of other medical specialists in addition to gynecologists such as general practitioners, pediatricians, dermatologists, medical endocrinologists, and even cardiologists.

A consensus workshop organized in 2003 in Rotterdam, The Netherlands, agreed to broaden the previous National Institutes of Health criteria for diagnosing PCOS by including the ultrasound diagnosis of polycystic ovaries. This wider definition will encompass a broader spectrum of this heterogeneous condition, facilitating future metabolic and genetic studies.
INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous condition that is associated with the following clinical features: oligo/amenorrhea (caused by chronic oligo/anovulation), acne or hirsutism (resulting from hyperandrogenemia), infertility, and finally, obesity. This condition is considered the major enigma in reproductive medicine, affecting up to 7% of the female population. The clustering of PCOS in families suggests a genetic basis. Although multiple gene polymorphisms or mutations may subserve a similar clinical condition, it is generally believed that hyperandrogenism and insulin resistance represent the central endocrine and metabolic abnormalities in PCOS. The occurrence of obesity may elicit a clinical phenotype in women predisposed to develop PCOS or aggravate the clinical picture in women with a mild form of the syndrome. Recent observations establish PCOS as a polygenic condition, where multiple genes and gene–environment interactions are central in the development of a clinical phenotype. Because of the increased prevalence of obesity in the Western world, it is to be expected that the incidence of PCOS will rise even further.

The association between bilateral polycystic ovaries and amenorrhea, hirsutism, and infertility was first described by Stein and Leventhal (1). The treatment of choice was initially ovarian wedge resection, which provided material for morphological confirmation of the diagnosis. A collection of clinical data from more than 1000 patients with morphologically proven Stein-Leventhal disease firmly established the frequent occurrence of oligo/amenorrhea, infertility, hirsutism, and obesity in these women (2). After the conversion from a morphological diagnosis to a clinical syndrome, the introduction of hormone assays in clinical practice allowed an assessment of the frequency of reproductive endocrine abnormalities in these women, such as elevated serum luteinizing hormone (LH) and androgen concentrations (3,4). Subsequently, the first reports of insulin resistance in PCOS appeared (5), as well as the noninvasive assessment of ovarian morphology by ultrasound (6). In recent years, the occurrence of hypertension and an abnormal lipid profile has also been established in these women.

During different stages of life, women with PCOS may seek medical care for different reasons (Fig. 1). For childhood obesity or abnormal menstrual bleeding during puberty or adolescence, patients may visit a general practitioner or a pediatrician. For complaints of hirsutism, a dermatologist may be approached. During reproductive life, a gynecologist may be visited for menstrual cycle abnormalities, infertility, or complications during pregnancy. Finally, the internist may be consulted for obesity or signs of type 2 diabetes (see also Table 1). A recent survey suggests that the cost related to diabetes care in PCOS exceeds by far the expenses in relation to infertility treatment (7).

All these complaints are evidence of the extremely heterogeneous spectrum of the same condition, i.e., PCOS. For obvious reasons, various diagnostic procedures are chosen by the medical specialist depending on the primary complaint of the patients. The focus on metabolic conditions seems a reasonable approach in women presenting with diabetes complaints, whereas a transvaginal ultrasound scan represents the key diagnostic procedure in a woman in need of medical intervention for anovulatory infertility.