Polycystic ovary syndrome (PCOS) has been recognized as an important endocrine disorder for more than 70 yr, and its prevalence in the modern population is estimated to be between 5 and 10% of women of reproductive age (1). It is by far the most common cause of oligo- or anovulation and accounts for more than 75% of cases of anovulatory infertility (2, 3). It is also the leading cause of hirsutism, androgenetic alopecia, and persistent acne, all of which are distressing and debilitating disorders in women. In the last 30 yr, increasing emphasis has been placed on metabolic dysfunction in women with PCOS. Insulin resistance and compensatory hyperinsulinemia are central to the metabolic abnormalities of PCOS (3, 4), and the syndrome is estimated to carry a 2- to 4-fold increase in the risk of developing type 2 diabetes mellitus (5). The increasing pandemic of obesity threatens to make that figure an underestimate; obesity has a preferentially adverse effect on metabolic function in women with PCOS compared with similarly obese women without PCOS. Cardiovascular risk factors are also significantly increased in PCOS, although it remains unclear whether the incidence of cardiovascular events is similarly increased (5).

Despite the plethora of clinical and experimental data regarding this very common endocrine disorder, our knowledge of the etiology of the syndrome is, at best, incomplete. There is strong evidence for a genetic cause (6–9), but environmental factors, particularly the effect of diet, clearly play an important part in the presentation and severity of PCOS if not in the origin of the disorder itself (10). One important strategy for better understanding the etiology of PCOS has been the use of animal models. In general, the main principle underlying studies in animals has been that many of the characteristic features of PCOS arise as a result of exposure to excess androgen, the biochemical hallmark of PCOS. The observation that androgen treatment of immature rats results in abnormal antral follicle development and disrupted ovulation was made in the mid-1970s (11). Since then, there have been many studies of the effects of excess androgen on ovarian function in rodents (12–15). The relevance of rodent models in understanding the ovarian disorders in PCOS is limited, however, by the fact that ovarian development (and the nature of ovulatory cycles) in rodents differs markedly from that in women. Rats and mice are poly-ovulators and women mono-ovulators. Another important aspect of rodent models is the effect of timing of androgen exposure on reproductive phenotype. Tyndall and colleagues (16) have recently shown that whereas testosterone treatment has minimal effect on adult ovarian function if given in late postnatal life, treatment in both fetal and postnatal life causes streak ovaries in rats.

Over the last 15 yr, studies of larger species as models for PCOS have been explored and have given significant insight into the genesis of PCOS, particularly the notion that the syndrome has its origins during intrauterine development (17). Here the studies of Abbott and colleagues (17–19) in the rhesus monkey and of Padmanabhan and co-workers (20–24) in the sheep have proved particularly informative with regard to understanding the role of androgens in development of both reproductive and meta-
bolic disturbances in women. Animals exposed to high levels of androgen in utero (by giving very large doses of androgen to the mothers) develop, as adults, disrupted ovarian cycles and abnormalities of early follicle development (22, 25) that mimic those observed in women with PCOS (26, 27). Importantly, these animals also develop metabolic abnormalities, including insulin resistance and impaired glucose tolerance, again reminiscent of those seen in women with PCOS. In a recent variation of this protocol, Duncan and colleagues (28) have shown that direct fetal exposure to exogenous androgen also results in impaired glucose tolerance, again reminiscent of those seen in women with PCOS. In conclusion, although rodent models of PCOS may not be ideal with respect to understanding the ovarian abnormalities of PCOS (and are less informative than large-animal models), they may still provide important insight into the reproductive dysfunction of women with PCOS. And particularly in terms of examining the relationship between excess androgen and metabolic dysfunction, rodent models would appear to have an increasingly important part to play.

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Address all correspondence and requests for reprints to: Professor Stephen Franks, Institute of Reproductive and Developmental Biology, Imperial College London, Hammersmith Hospital, London W12 0NN United Kingdom. E-mail: s.franks@imperial.ac.uk.

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