

# Understanding Polycystic Ovarian Syndrome



Emily S. Edmondson, MPAS, PA-C\*

## KEYWORDS

- Polycystic ovarian syndrome • Ovarian cysts • Obesity • Insulin resistance
- Hyperandrogenism • Metabolic syndrome • Gestational diabetes

## KEY POINTS

- Polycystic ovarian syndrome is a condition that crosses multiple specialties and, with a wide range of presentations, should be understood by the entire medical community.
- The cause and pathogenesis of polycystic ovarian syndrome are not entirely known and therefore require more evidence-based research to be better understood.
- Polycystic ovarian syndrome diagnosis and treatment are focused on the patient's symptoms, and there is no one treatment that is accepted as superior.
- Early diagnostic approach and symptomatic treatment by the patient's health care team can make it possible for appropriate management and a promising prognosis.

## INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a heterogeneous disease that affects many aspects of the patient's endocrine system, and the patient's reproductive, dermatologic, and psychological systems.<sup>1</sup> PCOS was first explained in 1935 when American gynecologists Dr Irving F. Stein, Sr. and Dr Michael L. Leventhal recounted seven female patients who presented with symptoms of hyperandrogenism and oligomenorrhea or amenorrhea. These patients also had bilateral polycystic ovaries. When these gynecologists performed a bilateral wedge resection on the patients' ovaries, there was a therapeutic effect: the patients' irregular menses and issues with fertility were normalized. Therefore, the two gynecologists concluded that the cause of the disease lay in the dysfunction of polycystic ovaries, hence the name "polycystic ovarian syndrome."<sup>2</sup>

PCOS is one of the most common metabolic disorders in premenopausal women.<sup>3</sup> It is estimated that the prevalence rate of this disease is 5% to 10%. However, there is also evidence that this rate is actually underestimated. This could be caused by

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Vineyard Primary Care, UPMC Hamot, 2060 North Pearl Street, North East, PA 16428, USA  
\* 3952 Ridge Parkway, Erie, PA 16510.

E-mail address: [edmondsone2@upmc.edu](mailto:edmondsone2@upmc.edu)

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providers underdiagnosing the disease.<sup>1</sup> Regardless, what must be pointed out and kept in mind when discussing this disease is the relevance it has today. According to the Centers for Disease Control and Prevention, the obesity rate in the United States is 34%. Although that statistic has been steady since 2007, it still includes a large number of American citizens. Combined with the prevalence of overweight individuals, that statistic jumps up to around 66% of Americans who are above their ideal weight. These statistics impact the discussion regarding PCOS because diseases associated with obesity and being overweight, such as type 2 diabetes mellitus (T2DM) and risk factors for cardiovascular disease, are also associated with PCOS.<sup>4,5</sup>

## CAUSE AND PATHOGENESIS

### *Cause*

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The cause of PCOS is unknown. It is thought that there are many factors influencing the ultimate outcome of a female developing the disease. However, there is believed to be a strong genetic influence in the development of PCOS. Various animal models have shown evidence that fetal exposure to increased maternal androgen is associated with the development of PCOS later in life. Also, studies done on families of adolescent girls with PCOS found that their fathers had an obesity rate of 94% and a metabolic syndrome (MetS) rate of 79%. In that same study, the mothers of those patients had a 54.4% rate of being obese and a 34% rate of having MetS. This links the significance of today's obesity rates and the genetic influence on the development of PCOS.<sup>2</sup>

Another idea is that changes or exposures that occur during childhood and puberty may play a role in the development of the condition. The production of steroids by the ovaries is thought to play a role in the development of PCOS, specifically in infancy during periods of increased insulin-like growth factor 1 production. Hormonal changes during puberty are also thought to play a role in the cause of PCOS, either because of the increase in androgen production during puberty or simply atypical brain development. The latter is thought to result in atypical puberty and therefore abnormal hormonal production.<sup>6</sup>

### *Pathogenesis*

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There is no definite pathogenesis that has been uncovered in all patients with PCOS. As with the cause, there seems to be many genetic and environmental factors that cause the metabolic and reproductive changes associated with PCOS. However, one characteristic that many patients with PCOS possess is insulin resistance. Insulin resistance, and subsequent hyperinsulinemia, are prevalent in 50% to 70% of patients with PCOS. Hyperinsulinemia has a negative effect on regulation of lipid metabolism, protein synthesis, and modification of androgen production, resulting in some of the typical signs and symptoms associated with PCOS.<sup>3</sup>

Androgen production modification is a result of the dysregulation of luteinizing hormone. Luteinizing hormone is dysregulated at the central level when there is an increased amount of insulin in the bloodstream. This dysregulation occurs because increased insulin levels support an increase in the activity of cytochrome P-450 C17 in the liver, which results in an increase in androgen secretion by the ovaries.<sup>7</sup>

The modification of androgen production leads to androgen excess in the body. That androgen excess results in hypersensitivity of the androgen receptor gene that is located on the X chromosome. The androgen receptor gene codes for an androgen receptor protein that contains repeats of the nucleobases CAG. These CAG repeats are polymorphic and range from 8 to 35 repeats. It has been shown that the fewer

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