# PCOS
## 360 Guide

by **Dr. Oybek Rustamov**

This is not another run-of-the-mill blog on PCOS. It is a **comprehensive article** which explains the cause of PCOS, how each symptom develops, and how you can diagnose it.

More importantly, the article equips you with the knowledge of how to **prevent** the symptoms from developing into stressful problems. If you already have PCOS-related issues, you can address them using the **solutions** I recommend in the article and by obtaining medical help.

You can bookmark this as your **guide** for dealing with PCOS. If you do not find an answer to your questions, please ask emailing us on **admin@dr-rusty.com** and I will try to answer promptly.

# What is PCOS?

Polycystic ovary syndrome, or PCOS, is a common <u>reproductive health</u> problem that affects **1 in 10 women.**

As the name suggests, women with PCOS have an **excess amount** of small fluid-filled sacs in their ovaries, which look like small <u>cysts</u>. In fact, these "cysts" are growing follicles containing eggs, called antral follicles.

Normally, all women have antral follicles during reproductive ages. However, women with PCOS have an excess amount. These follicles can be **counted** using an ultrasound, a method called <u>Antral Follicle Count</u> (AFC). This count should be **less than 20** in each ovary, or less than 40 in total.

Women with PCOS usually have a higher AFC. It appears that the **high number** of antral follicles is responsible for the other symptoms of PCOS, which include irregular menstrual cycles and high levels of male hormones.

Antral follicles produce the Anti-Mullerian Hormone (AMH), a hormone **responsible** for regulating ovulation. At any given time, there are many <u>antral follicles</u> in the ovaries. However, in each menstrual cycle, only **one (1)** follicle should grow larger and ovulate. This means that the remaining antral follicles should be kept suppressed, which is the role of AMH.

In PCOS, the amount of <u>AMH</u> is so high that it keeps **all** of the follicles suppressed. Even one (1) leading follicle cannot escape the suppression of AMH and hence, ovulation does not occur.

For the menstrual period to occur, women should produce estrogen in the **first 14 days** of the menstrual cycle and produce progesterone after <u>ovulation</u>. Since ovulation does not occur **every month** in PCOS, women do not produce progesterone and do not have their monthly menstrual period.

Ovulation may occur once every 2 to 3 months, which means that women with PCOS often have their <u>menstrual</u> period once every few months. Similarly, due to the lack of regular ovulation, they do not release an egg every month – leading to infertility.
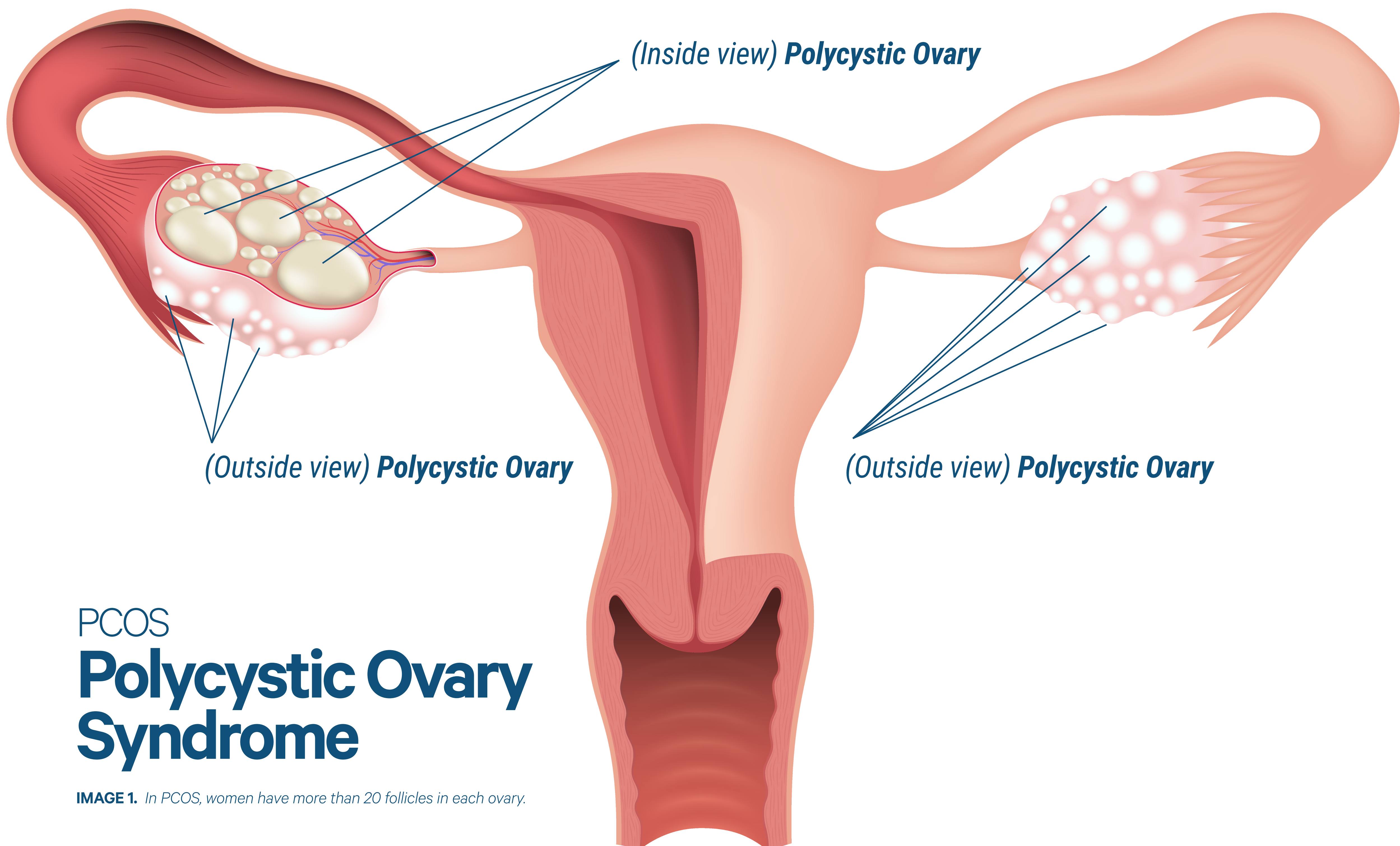


*(Inside view)* **Polycystic Ovary**

*(Outside view)* **Polycystic Ovary**

*(Outside view)* **Polycystic Ovary**

## PCOS
# Polycystic Ovary Syndrome

**IMAGE 1.** *In PCOS, women have more than 20 follicles in each ovary.*

# Cause of PCOS

The official cause of PCOS is **unknown**. However, we know the following things about the condition.

- More common in some families, indicating genetic origin.
- Symptoms start after puberty, showing a link to reproductive function.
- Symptoms associated with ovarian hormones, associated with pathology of ovarian function.
- Women with PCOS have high AMH and AFC, showing a link to high egg reserves.
- Women with PCOS have longer reproductive life and late menopause, caused by high egg reserves.
- Symptoms settle after menopause, showing a strong link to ovarian function.

Based on the facts above, we can assume that women with PCOS are born with high egg reserves. They have an excessive number of growing follicles that produce too many male hormones. This causes high levels of <u>androgens</u> in the blood. In addition, due to the high levels of the Anti-Mullerian Hormone, growing follicles are suppressed and cannot ovulate. Finally, the lack of ovulation causes **irregular** menstrual cycles and infertility.
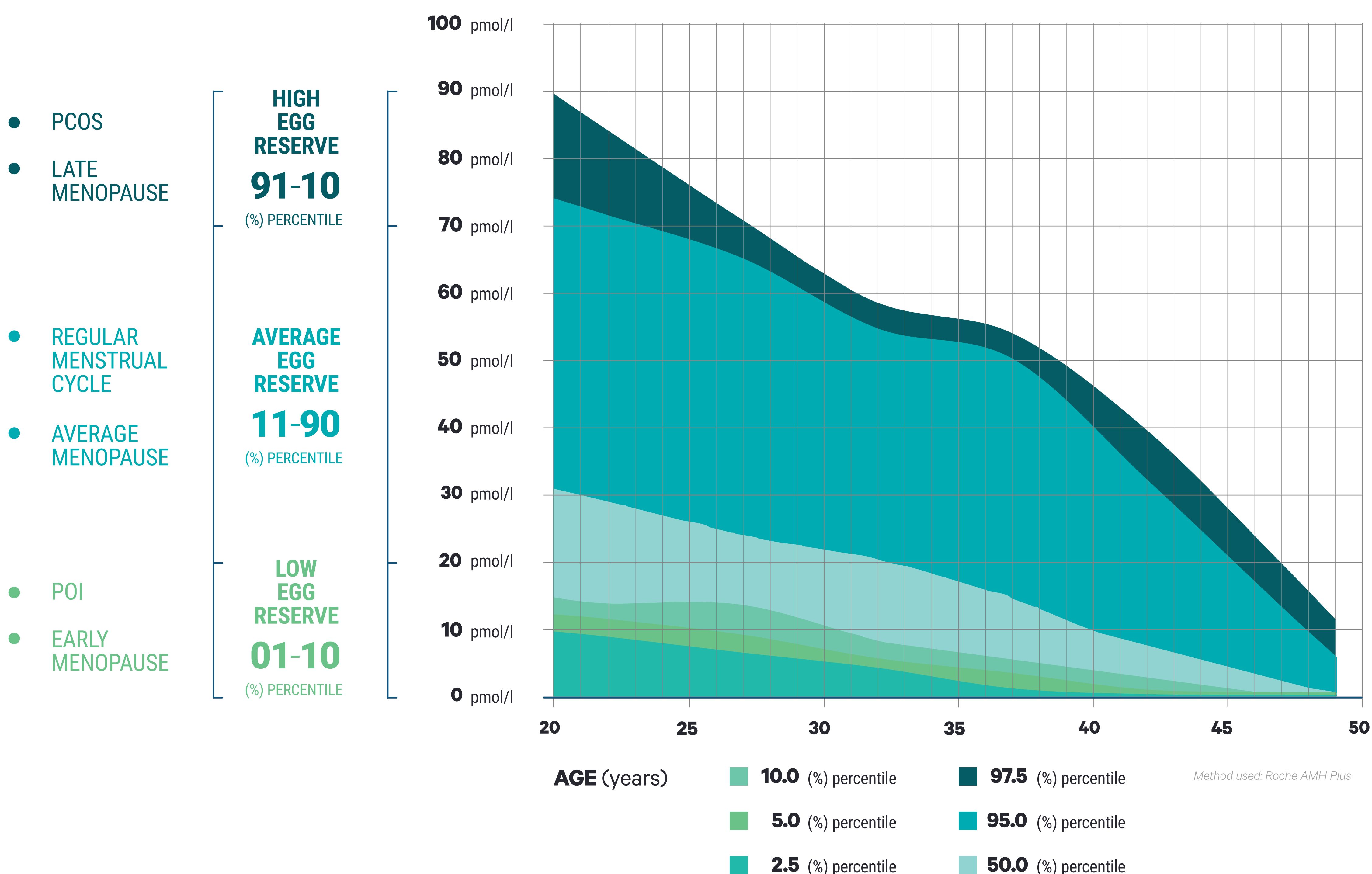


**IMAGE 2.** *Women with PCOS are born with very high egg reserves. Hence, they have very high Antral Follicle Counts (AFC), very high Anti-Mullerian Hormone (AMH) levels, and late menopause.*

# Diagnosis

If you have **two or all** of these symptoms, you can be diagnosed with PCOS. PCOS diagnosis is based on three (3) following symptoms:

1. Symptoms of excess androgens.
2. Signs of no ovulation, or "anovulation".
3. Polycystic ovaries seen on ultrasound.

There are **four types** of PCOS:

- **TYPE A**: All three symptoms present, known as Classic PCOS.
- **TYPE B**: Excess androgen and anovulation.
- **TYPE C**: Excess androgen and polycystic ovaries seen on ultrasound.
- **TYPE D**: Anovulation and polycystic ovaries seen on ultrasound.
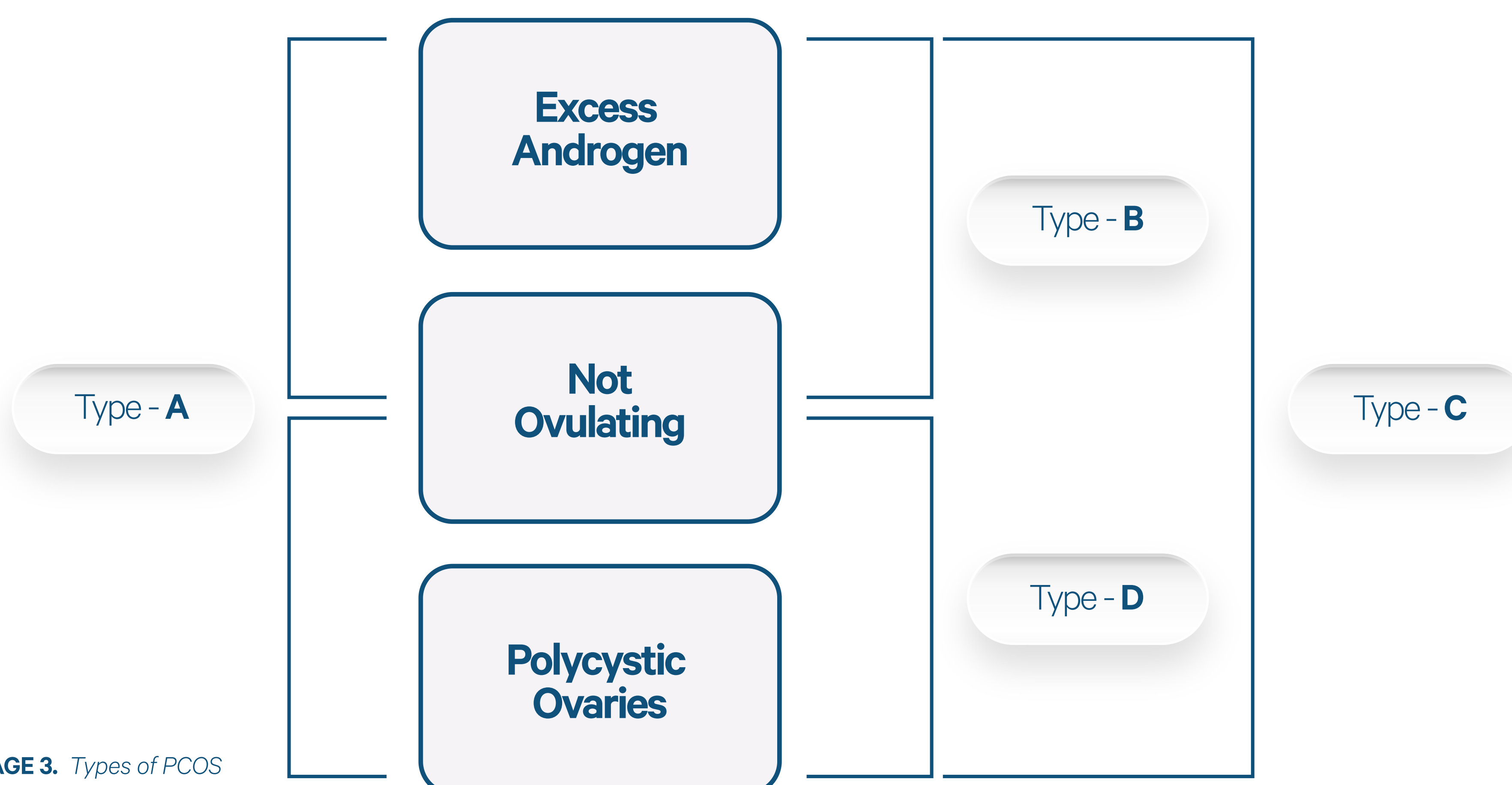
TYPES OF PCOS
# PCOS Phenotypes



**IMAGE 3.** *Types of PCOS*

# How do you diagnose excess androgen?

Excess androgen can be diagnosed **based** on symptoms or a blood test for male hormones. For the diagnosis of PCOS, either is fine. To diagnose on the basis of symptoms, you should look for signs of high amounts of <u>male hormones</u>. This usually **manifests** as excess hair growth, acne, and the loss of scalp fair.

**Hirsutism** is the excess growth of body and facial hair. The best diagnostic tool for hirsutism is the Modified Ferriman-Gallwey Score (mFG Score). An <u>mFG</u> score of 6 or more is considered as an indication of excess androgen in PCOS. For the **severity** of hirsutism, an mFG score of 6 to 15 is mild, 16 to 24 is moderate, and more than 25 is severe.

You can check your mFG Score using the PCOS Quiz on this page!

Excess androgen can also be diagnosed using a **blood test** that measures the amount of the following male and <u>steroid hormones</u>: free testosterone, androstenedione, and Sex Hormone Binding Globulin (SHBG).

- **Total Testosterone:** 0.3-1.8 nmol/L
- **Free Testosterone:** 7-48 pmol/L
- **Free Androgen Index (FAI):** 0.4% -8.0%
- **SHBG:** 26-110 nmol/L
- **Androstenedione:** 0.7 to 3.1 ng/mL

Active androgen levels are measured by the <u>Free Androgen Index</u> (FAI). This can be calculated by **comparing** the Total Testosterone (TT) and Sex Hormone Binding Globulin (SHBG) levels.

# Modified Ferriman-Gallwey Score (mFG Score)

The Ferriman-Gallwey score for hirsutism.  A score of 1 to 4 is given for nine areas of the body. A total score less than 8 considered normal; a score of 8 to 15 indicates mild hirsutism; and a score greater than 15 indicates moderate to severe hirsutism. A score of 0 indicates absence of terminal hair.



**IMAGE 5.** *Modified Ferriman-Gallwey Score (mFG Score)*

## How do you diagnose anovulation?

Anovulation can be diagnosed using symptoms or performing a blood test. A regular menstrual cycle occurring approximately every **28 to 35 days** is a very reliable sign of ovulation. Irregular menstrual cycles lasting longer than 35 days indicate that ovulation is not taking place every month.

We can reliably diagnose anovulation in women with irregular periods. Not having periods for **longer than 6 months**, known as amenorrhea, also confirms anovulation. Anovulation can also be diagnosed using LH kits, though, they may give false readings.

Progesterone level is a very **accurate** test for ovulation.

Since the only source of progesterone is an ovulated follicle, high levels of progesterone confirm ovulation. Progesterone gradually increases to its peak on the **7th day** after ovulation. With that, it is **important** to time progesterone correctly. In 28-day cycles, ovulation occurs around the 14th day of the menstrual cycle and progesterone level should be measured on the 21st day. In 35-day cycles, progesterone is measured on Day 28 of the cycle. Also, progesterone levels higher than 30 nmol/L confirms ovulation.

## How do you diagnose Polycystic Ovaries?

Polycystic ovaries are **diagnosed** using an internal pelvic ultrasound scan. The sonographer counts the antral follicles, measures the volume of the ovaries, and looks for **specific features** of polycystic ovaries. If any of the features below are present, a sonographer can diagnose polycystic ovaries:

1.  Antral Follicle Count more than 20 in each ovary or more than 40 in total.
2.  Volume of either or both ovaries larger than 10 cm^3.
3.  "String of pearls" sign. Due to the hardening of the ovaries' outer layer, the follicles are arranged around the surface of ovaries. In the ultrasound, this looks like a string of pearls.

# Screening for PCOS

You can check if you have symptoms of PCOS using symptom checker **questionnaires**. Since women with PCOS have very high levels of AMH, the AMH test can be used as a reliable tool for screening.

# Categories of Related Problems

Polycystic ovary syndrome causes three different **categories** of problems:

1. Metabolic
2. Skin
3. Reproductive

## PCOS Problem

|  | Metabolic | Skin | Reproductive |
|---|---|---|---|
| CAUSE | INSULIN RESISTANCE | ANDROGEN EXCESS | ANOVULATORY CYCLES |
| PROBLEMS | EXCESS WEIGHT | EXCESSIVE HAIR | IRREGULAR PERIOD |
|  | DIABETES | ACNE | INFERTILITY |
|  | BLOOD PRESSURE | HAIR LOSS | ENDOMETRIAL CANCER |

**IMAGE 5.** *Categories of PCOS Problems.*

## Metabolic Problems

In PCOS, for unknown reasons, the body cells become **resistant** to insulin.

Insulin, a hormone produced from the pancreas, **transports** blood glucose into the muscle, fat, and liver cells where it will be used for energy. With insulin resistance, the cells do not take up glucose easily, leaving a **high amount** of sugar in the bloodstream. In response, the pancreas produces more insulin to push the glucose into the cells.

Provided that the pancreas keeps up with the insulin production, the level of glucose in the blood remains normal. Gradually, the pancreas can **fail** to provide enough insulin. Resulting in blood sugar, it can lead to prediabetes and later, type II diabetes.

High amounts of circulating sugar can enter visceral fat cells in excess amounts and cause a cascade of metabolic changes. The fat surrounding the internal organs in the abdomen and around the tummy is called visceral fat. This has different properties than fat in other parts of the body.

Visceral fat, or belly fat, produces hormones and various substances that cause **generalised inflammation**. Chronic generalised inflammation worsens insulin resistance and leads to further weight gain, high blood pressure, and heart diseases. Additionally, insulin resistance can cause a specific skin feature, like brown skin tags. Some areas of the skin, such as the armpit or the back and sides of the neck, can also darken which is called **acanthosis nigricans**.

In severe forms of insulin resistance, women develop **metabolic syndrome** which has the following symptoms:

1. Elevated waist circumference: >80 cm
2. Elevated blood pressure: Systolic BP >130 or Diastolic >85
3. Elevated fasting glucose level: > 5.6 mmol/L
4. Elevated triglycerides: >1.7 mmol/L
5. Reduced High-Density Lipoprotein Cholesterol (HDL-C: <1.3 mmol/L)

Metabolic syndrome can be diagnosed in women with three or more of the above **symptoms**.

# Skin Problems

PCOS-related skin problems are caused by **high levels** of male hormones or androgens.

Normally, women produce a **small amount** of male hormones, like testosterone, dihydrotestosterone (DHT), androstenedione, dehydroepiandrosterone sulphate (DHEAS). These hormones are **necessary** to maintain reproductive function, provide energy, and maintain metabolism.

To understand the cause of hormonal problems in PCOS, we should review how these hormones are produced. For this, we should look into ovarian follicles, the **main source** of production of the male hormones.

Sleeping eggs and their surrounding nursing cells together are called **primordial follicles**.

Women are typically born with around half a million primordial follicles in their ovaries, known as the **egg reserve**. However, women with PCOS genes are born with three to four times more eggs in their ovaries. This is a starting point that determines who will have PCOS.

Almost all primordial follicles rest in a **non-active state** until their activation. Hence, they are called "sleeping eggs". Once the time for each egg comes, they activate and start growing.
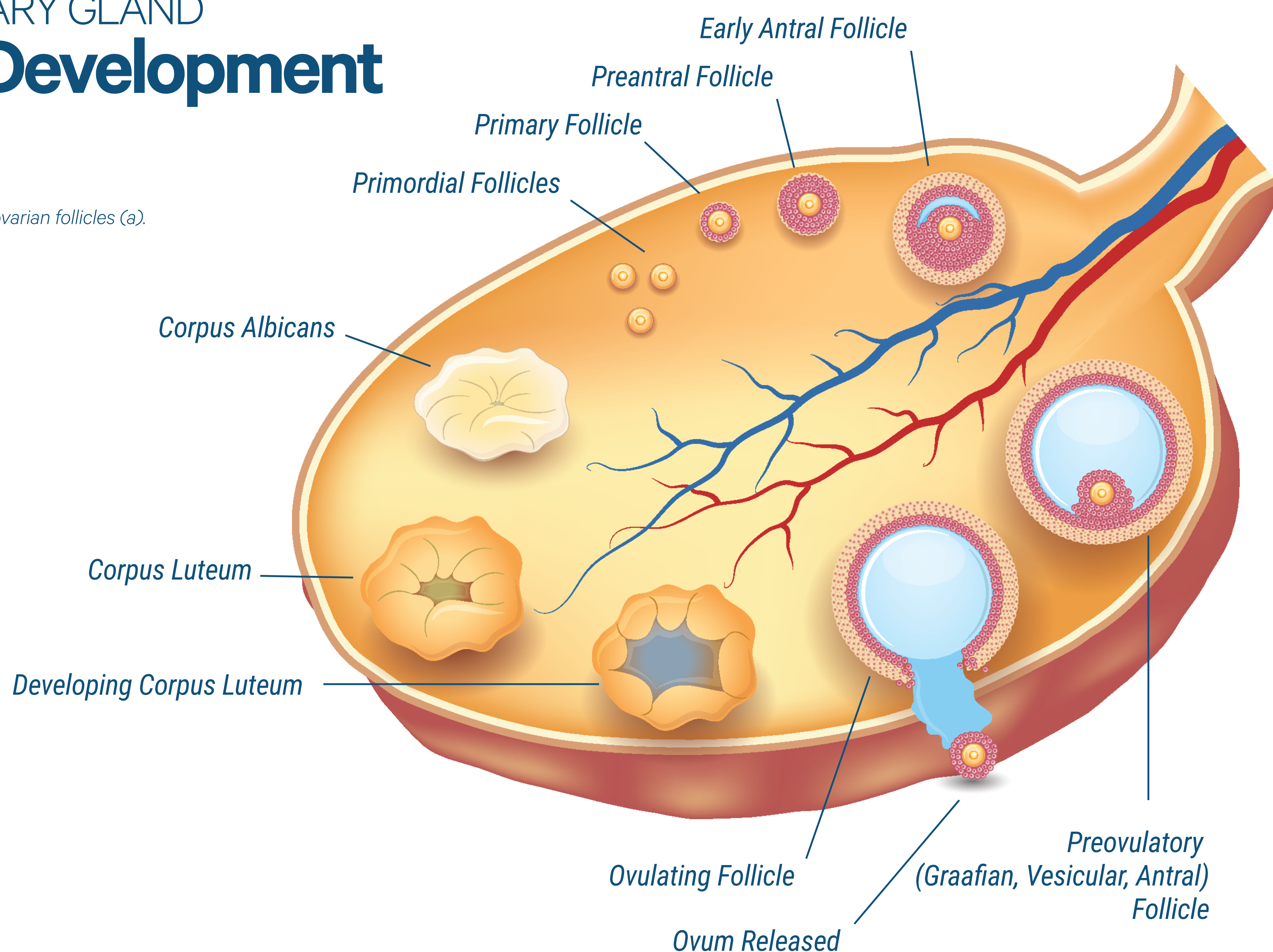
The time from activation to full growth, or follicle development, takes approximately **three months**. Towards the end, activated eggs and their surrounding nursing cells, called granulosa cells, undergo rapid changes.

The size and number of granulosa cells increase and start producing hormones such as estrogen and AMH. This stage is called the **Pre-Antral Follicle stage**. Later, the fluid-filled cavity or "Antrum" in Latin, accumulates between the layers of the egg and its surrounding granulosa cells. Hence "Antrum", we call this the **Antral Follicle stage**.

During this period, the follicles measure **2 to 10 mm** in size and are visible on an ultrasound scan. One of the antral follicles is selected to become a dominant follicle when it grows to **17 to 20 mm** in size and ovulates the egg. The remaining pre-antral and antral follicles stop developing, are broken down by immune cells, and taken away from the ovaries.

## OVARY & PITUITARY GLAND
# Follicular Development Ovulation

**IMAGE 6.** *Stages of development of ovarian follicles (a).*



Early Antral Follicle

Preantral Follicle

Primary Follicle

Primordial Follicles

Corpus Albicans

Corpus Luteum

Developing Corpus Luteum

Ovulating Follicle

Ovum Released

Preovulatory
(Graafian, Vesicular, Antral)
Follicle

Having discussed the structures of ovaries that produce female and male hormones, we can now discuss the actual production of these hormones. More importantly, we will try to understand **why** women with PCOS produce both female and male hormones in excess amounts and what we can do about it.

The main female hormone is called estrogen and the male hormone is called testosterone. They are also called sex hormones.

Both female and male hormones are mainly produced from the sac of growing antral follicles in the ovaries. Women without PCOS have approximately **15 to 20** antral follicles in their ovaries. Given this is an average number, they produce a normal amount of sex hormones. However, women with PCOS have an antral follicle count (AFC) of **more than 40**, meaning they have 2 to 3 times more follicles. A large number of growing follicles in ovaries produce a much higher amount of male hormones than necessary.
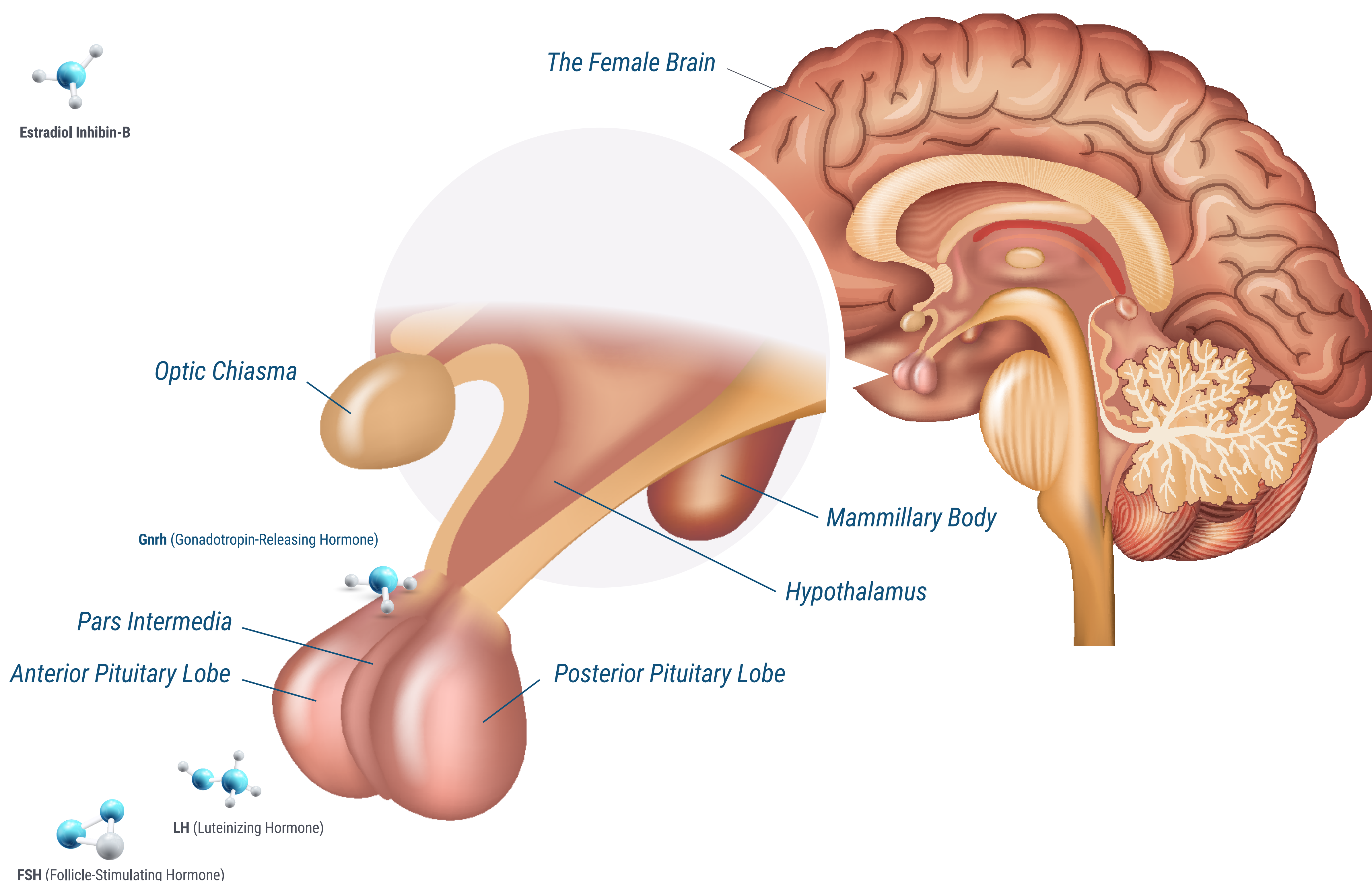
There are **two** more sources of male hormone production in women.

**Adrenal glands** produce different types of male hormones called DHEAS and androstenedione. The role of these hormones is not significant in women of reproductive age as they play important roles after menopause.

The other important source of production of male hormones is fat tissue. The enzymes produced from the fat cells can **convert** estrogen into testosterone. So, fat transforms a male hormone from a female hormone, especially belly fat.

OVARY & PITUITARY GLAND
# Interrelationships bet. Ovarian & Pituitary Hormones

**IMAGE 6.** *Stages of development of ovarian follicles (b).*



Estradiol Inhibin-B

*The Female Brain*

*Optic Chiasma*

**Gnrh** (Gonadotropin-Releasing Hormone)

*Mammillary Body*

*Pars Intermedia*

*Hypothalamus*

*Anterior Pituitary Lobe*

*Posterior Pituitary Lobe*

**LH** (Luteinizing Hormone)

**FSH** (Follicle-Stimulating Hormone)

PCOS increases the activity of an enzyme called **5-alpha reductase** which converts testosterone to a more potent form of a male hormone, dihydrotestosterone (DHT). High levels of androgens stimulate skin glands to produce more sebaceous fluid which can increase **oiliness** of skin and cause acne.

With regards to **hair growth**, testosterone and DHT affect different parts of the body differently. To understand it, we should explore normal hair growth in women. Generally, there are two different types of hair in the body: vellus and terminal hair.

In women of reproductive age, the scalp, armpit, and pubic area are covered with thick terminal hair. The rest of the body is covered with fine vellus hair. **Prolonged exposure** to high amounts of androgens turns follicular into terminal hair in all parts of the body. It has the **opposite effect** on the scalp's terminal hair, making the scalp hair thinner and finer, turning into vellus hair. Later, vellus hair starts falling off which causes alopecia.

## PCOS Frequency of Problems

| Problem | Frequency |
| --- | --- |
| EXCESSIVE HAIR | 85% |
| INFERTILITY | 75% |
| EXCESS WEIGHT | 70% |
| HIGH BLOOD PRESSURE | 20% |
| DIABETES | 10% |

**IMAGE 7.** *Frequency of problems in women diagnosed with PCOS.*

## Reproductive Problems

PCOS-related problems of the reproductive system are **linked** to not ovulating regularly. In fact, women with PCOS have high egg reserves and long fertility.

For instance, women with normal egg reserves run out of eggs at the age of 40 to 47 and stop having menstrual periods at the **age** of 45 to 52. Women with PCOS run out at the age of 48 to 55 and become menopausal the age of 53 to 60 years. They can release eggs in their mid to even late forties. However, with age, the quality of eggs become **poorer** which reduces the odds of conception.

If women with PCOS have high egg reserves and long fertility, why do they **struggle** to conceive? Good question.

This is something to do, again, with the amount of antral follicles they have in their ovaries. To understand this, we need to take a journey into the follicles and **eggs** in the ovaries. If it is too technical, you can skip this section.

As we discussed, growing antral follicles produce the AMH hormone. One of the roles of AMH is to prevent all antral follicles from becoming **dominant** and ovulating. This is nature's way of preventing the ovulation of multiple follicles at once. This ensures that only a **single follicle** can ovulate to prevent twins, triplets or even higher order pregnancies.

The amount of AMH in the ovaries and blood determines how much **suppression** takes place.

Women with normal egg reserves and normal amounts of antral follicles produce an average amount of AMH. This is just enough to keep all follicles suppressed, except the one leading follicle. Once the **leading follicle** enters the dominant stage, it starts producing hormones, like estrogen and inhibin which sends a **signal to** the pituitary gland.

Subsequently, the pituitary gland slows down FSH production and stops stimulating the remaining follicles. So, in concert with other ovarian and pituitary hormones, AMH plays the **role** of suppressing antral follicles and ensuring only one follicle ovulates. In other words, AMH is the **gatekeeper** of follicles.

Women with PCOS have a large number of antral follicles and produce very high levels of AMH. High AMH concentration in the ovaries suppresses **more** follicles than necessary. As a result, **none** of the follicles manage to escape the suppression and cannot grow into the dominant stage. Unless follicles grow into their dominant phase, they cannot ovulate.

As a result, we have a **paradox** of PCOS.

Women have lots of follicles but do not release them. In this strange situation, women have very high fertility as they have a high number of eggs, but are **temporarily infertile**. Why temporarily? Because they become fertile later. How come? Because as PCOS women age, their egg reserve **declines**, their antral follicle count reduces, and their AMH becomes normal.

The normal AMH does not suppress the growing follicles as much and women start ovulating. So paradoxically, women with PCOS are infertile in their twenties to early thirties and become fertile in their late thirties and early forties.

The time they start ovulating and become fertile **depends** on the severity of PCOS. Women with mild PCOS start having normal AMH in their late twenties to mid-thirties and start ovulating. AMH levels of women with severe PCOS become normal in their late thirties to mid-forties and ovulating.

However, ovulation does not necessarily mean they have a normal fertility. As age affects the quality of eggs, their **overall fertility** declines with age. Hence, women with PCOS should not wait until their ovaries start ovulating. They should start trying to conceive when they are ready. Though, they may **need** fertility treatment, which we will discuss later.

# Treatment of PCOS

There are two types of **treatment** for problems caused by PCOS: General Treatment and Targeted Treatment.

**General treatment** includes weight loss, metformin, and the hormonal pill. These treatments help correct the underlying metabolic and hormone changes caused by PCOS. Targeted treatment is directed to relieving symptoms of each individual PCOS-related problem. Both treatments are important to improve the **overall symptoms** of PCOS and achieve the desired effect.

## General Treatment

### WEIGHT LOSS

When it comes to weight, PCOS women pulled the short straw. It is **not easy** to keep their weight down.

This is because of how your metabolism works. For women with PCOS, it is **easy** to gain weight. Even if they eat an average amount of food, they can easily put weight on. But it is very **hard** to shed any weight. Due to insulin resistance, they always have higher levels of blood sugar.

Instead of distributing sugar to cells as an energy source, they convert most of the sugar into **fat**. In addition, they disproportionately transport higher amounts of sugar into visceral fat which is **notoriously** difficult to lose. While other parts of the body convert sugar into predominantly healthy High-Density Lipoproteins (HDL), visceral fat stores it as unhealthy cholesterol, triglyceride (TGL).

Excess amount of body weight, particularly increase in tummy fat, creates metabolic changes in the body and **triggers** other symptoms of PCOS. An increase in the level of unhealthy triglycerides can cause the collection of fatty cells inside the blood vessels, called **atherosclerosis**. If weight loss is not achieved, this can lead to heart diseases in later life.

The conversion of estrogen to testosterone in fat tissue can **increase** the amount of male hormones in the bloodstream. This can cause skin symptoms, such as excess hair growth and acne.

There is a link between body fat and ovarian function, but the mechanism is not fully understood. However, it is likely to be related to **insulin resistance** and the production of enzymes and androgens from fat cells. This mechanism is responsible for the **change** in ovarian function when body weight is increased or reduced.

Women with PCOS stop ovulating once their body weight increases. Similarly, once they lose weight, they start ovulating again. Studies show when PCOS women with obesity lose **10 percent** of their body weight, they start ovulating. For instance, a 10-kg weight loss is sufficient for a woman of 100 kg to start ovulating. This **regulates** her periods, restores fertility, and improves metabolic and skin problems.

So, we all agree gaining weight is easy for women with PCOS and often, it is not their fault. Increased **weight** causes multiple PCOS symptoms. Losing weight is very important in dealing with PCOS. Now, we know why we should focus on weight loss and know that there is no way around it. I know it is harder for women with PCOS, but it is **achievable** and the reward is immense.

It will transform all aspects of your health and wellbeing – it is **worth** the effort.

## METFORMIN

Earlier, we explored how insulin resistance **causes** a cascade of metabolic changes which results in increased blood sugar, weight gain, hormonal changes, blood pressure, and heart disease.

Metformin is a drug that counteracts these pathological processes by making cells more **sensitive** to insulin. As a result, circulating sugar in the bloodstream can easily enter the cells to be used as an energy source.

Due to the generalised effect of metformin on one's whole metabolism, it improves all symptoms of PCOS. However, metabolic changes are slow processes and the benefits are gained through long-term use.

You can start metformin tablets in **lower doses** and gradually increase the number of tablets you take. Initially, you take a 500 mg tablet once a day for a week. Next week, a 500 mg tablet twice a day for a week. Then, you can increase it to three to four times a day.

Metformin **side effects** include feeling sick, vomiting, diarrhea, stomach pain, loss of appetite, and a metallic taste in the mouth. Usually, side effects gradually settle. Taking metformin can cause Vitamin B12 deficiency, which can cause tiredness, mouth ulcers, and problems with vision. If you have these symptoms, you should **check** the Vitamin B12 levels in your blood.

## HORMONAL PILL

The pituitary gland and ovarian hormones govern the reproductive system.

FSH and LH hormones produced from the pituitary stimulate ovaries to grow antral follicles into dominant follicles and ovulate the egg. Growing antral follicles produce estrogen and testosterone. In return, estrogen levels regulate FSH and LH production by **sending** feedback signals. This chain of **feedback interactions** can be broken by administering artificial estrogen hormone.

**Combined Oral Contraceptive Pills (COCP)** contain artificial estrogen and progesterone hormones. Administration of COCP blocks the pituitary gland from producing FSH and LH. With low levels of FSH and LH, antral follicles are not stimulated and prevent the growth of a dominant follicle and ovulation. Further, the production of estrogen, and more importantly testosterone, from the follicles remain very low.

Like we discussed earlier, some PCOS symptoms are fuelled by the production of estrogen and testosterone in high levels. Reducing estrogen and testosterone levels improve most PCOS symptoms, including **skin problems**.

In PCOS, high and prolonged estrogen production causes the uterine lining to **continuously** grow. Since ovulation does not take place regularly, women with PCOS do not produce progesterone. To have a menstrual period, the uterine lining should get progesterone. An increase and **subsequent** reduction in progesterone levels causes menstrual period.

In PCOS, the lack of progesterone causes the uterine lining to **build up**, causing unscheduled and prolonged bleeding. As COCP contains both artificial estrogen and progesterone, despite not having ovulation, women have a regular menstrual period. This allows the regular **renewal** of uterine lining which is important in preventing unexpected heavy and prolonged menstrual periods.

Since hormonal pills stop ovulation and have contraceptive effects, this treatment is **not ideal** for women trying to conceive.

## PCOS General Treatment

| | Metabolic | | Skin | | Reproductive | |
| --- | --- | --- | --- | --- | --- | --- |
| | **EXCESS WEIGHT** | **DIABETES** | **EXCESSIVE HAIR** | **ACNE** | **IRREGULAR PERIOD** | **INFERTILITY** |
| WEIGHT LOSS | VERY EFFECTIVE | VERY EFFECTIVE | VERY EFFECTIVE | VERY EFFECTIVE | VERY EFFECTIVE | VERY EFFECTIVE |
| METFORMIN | VERY EFFECTIVE | VERY EFFECTIVE | EFFECTIVE | EFFECTIVE | EFFECTIVE | EFFECTIVE |
| COCP | EFFECTIVE | EFFECTIVE | EFFECTIVE | EFFECTIVE | VERY EFFECTIVE | CONTRAINDICATED |

**IMAGE 8.** *General Treatment. .*

## Targeted Treatment

In targeted treatment, we will discuss how you can **manage** each symptom of PCOS.

### EXCESS WEIGHT

We can assess **body weight** by measuring Body Mass Index (BMI) and waist circumference.

- **Underweight:** BMI < 18.5
- **Normal Weight:** BMI 18.5-24
- **Overweight:** BMI 25-29
- **Obese:** BMI 30-35
- **Morbidly Obese:** BMI > 35

**Waist circumference** is obtained by placing a tape measure halfway between your lowest rib and the top of your hip bone. This is roughly in line with your belly button. You can **breathe normally** while measuring. Waist circumference is used to estimate tummy fat to assess your risk of metabolic diseases, like diabetes, blood pressure, and heart diseases. The risk can be calculated in three categories:

- **Normal risk:** Waist < 80 cm
- **High risk:** Waist 80-87 cm
- **Very high risk:** Waist > 88 cm

Women with PCOS should try to keep their weight within a **normal BMI** and waist circumference of less than 80 cm. Given they are at risk of metabolic and hormonal changes, an increase in body weight and tummy fat triggers the development and **worsening** of PCOS symptoms. So, keeping weight in the normal range should be the priority.

There are **five ways** to lose weight and keep it under control:

- Diet
- Exercise
- Weight loss tablets
- Weight loss injections
- Bariatric surgery

Healthy diet and regular physical exercise are the **necessary** parts of your weight loss project.

A healthy diet provides necessary amounts of nutrients that are essential for your overall **well being**. Regular physical exercise increases your metabolic rate and helps you lose weight faster and improve your physical as well as mental well being.

Medical treatment of weight loss includes tablets and injections. These treatments are **available** for women with a BMI of over 30. The treatment can be prescribed to women with a BMI of over 27 if they have one of the following: diabetes, high blood pressure or dyslipidemia.

**Dyslipidemia** is diagnosed using a blood test for fasting lipid profile. High levels of unhealthy cholesterol (LDL cholesterol > 3.3 mmol/L or triglycerides >1.7 mmol/L) or low levels (HDL cholesterol < 1.5 mmol/L) is the diagnosis of dyslipidemia.

Using diet, physical exercise, and medications, most women achieve **target weight**. If these interventions are not successful, bariatric surgery can be considered in women with a BMI of over 35. The common forms of weight loss **surgeries** are intragastric balloon (Orbera), sleeve gastrectomy, single anastomosis gastric bypass, and RY gastric bypass.

Bariatric surgery may provide significant weight loss and improvement of health. Since it involves a significant **surgical** intervention, bariatric treatment is recommended only when other treatments have not been successful.

## Weight Loss Medication

| Tablets | Effectiveness (Loss of % of body weight after 12m) | Mechanism of Action | Cost (AUD a month) |
|---|---|---|---|
| METFORMIN | 3-5% | LOWERS BLOOD GLUCOSE LEVEL | $ 8.00 |
| DUROMINE | 7.50% | REDUCES GLUCOSE RELEASE FROM THE LIVER | $ 120.00 |
| XENICAL | 5-10% | REDUCES FAT ABSORPTION | $ 120.00 |
| CONTRAVE | 5-10% | SUPRESSES HUNGER | $ 240.00 |
| INJECTIONS | | | |
| SAXENDA | 5-10% | SUPRESSES APPETITE | $ 400.00 |
| WEGOVY | 15-17% | SUPRESSES APPETITE | ? |

**IMAGE 9.** *Weight Loss Treatment*

## UNWANTED HAIR

To diagnose excess hair, we should use objective tools for assessment. The **Modified Ferriman Gallwey (mFG)** Score is the best tool for diagnosis and monitoring the effects of treatment.

Unwanted hair is directly linked to abnormal metabolism, increased weight, and excess androgen. Hence, general treatment to **improve** insulin resistance, weight loss, and reduction in androgen production is essential. In addition to these, treatments that reduce the effect of androgens and local treatment of excess hair are **recommended**.

The first line treatment to improve insulin resistance is **metformin**. The effect of metformin can be monitored using blood tests for fasting sugar levels. If the fasting blood sugar level is more than 5.6 mmol/L, the glucose tolerance test (GTT) gives a more **accurate** assessment of insulin resistance and development of pre-diabetes and diabetes.

If metformin is **not effective**, a more potent treatment, such as Ozempic and Saxenda, can be prescribed.

Since increased body fat contributes to excess androgen production, achieving and maintaining normal weight is essential. Weight loss also improves metabolism and insulin resistance which **reduces** unwanted hair.

## HORMONAL TREATMENT

Androgen production in the ovaries is stimulated by a **cyclical change** in FSH and LH hormone, which is produced during the menstrual cycle by the pituitary gland. Combined Oral Contraceptive Pills (COCP) contain estrogen and progesterone that suppress FSH and LH production.

In addition, COCP increases the protein in blood called the Sex Hormone Binding Globulin (SHBG). This protein **binds** sex hormones and reduces the amount of free androgen hormones in the blood. Therefore, COCP can reduce the amount of androgens in the blood and improve symptoms of **unwanted hair**.

The effect of COCP on hirsutism can be seen after taking it at least for **6 months or longer**.

## ANTI-ANDROGENS

Cyproterone Acetate (CA) is commonly used as an anti-androgen for hirsutism. It blocks the binding of testosterone and DHT to androgen **receptors** of the hair follicles. Essentially, hair follicles do not fully "sense" androgens in the blood when you take CA.

**Cyproterone acetate** can be used in doses of 50 to 100 mg daily. Also, you can take it as part of the Diane-35 tablet containing COCP and Cyproterone Acetate. Side effects include headache, weight gain, breast tenderness, and depression. It can have a **toxic effect** on the liver in some patients, therefore women should have the liver function test (LFT) periodically while on CA. Cyproterone acetate can also be used for treatment of alopecia.

**Spironolactone** is the most effective anti-androgen for treating hirsutism, acne, and alopecia. It blocks androgen receptors, so testosterone and DHT cannot stimulate growth of body and facial hair. Spironolactone can be started with a 25 mg tablet a day and progressively increased to 100 mg per day over a **week**. It can cause the following side effects: tiredness, dizziness, and low blood pressure.

**Flutamide** reduces androgen production and blocks androgen receptors. The daily dose of flutamide is 250 to 750 mg. It is effective for hirsutism, acne, and alopecia. However, it can have hepatotoxic effects in some women. Therefore, monitoring **liver** function is necessary.

Finasteride blocks the conversion of testosterone to a more active androgen DHT. Due to the reduction of DHT levels, it can improve symptoms of hirsutism **significantly**.

Using anti-androgens strictly contraindicates during **pregnancy**. Anti-androgens can cause serious abnormalities in the fetus. With that, women on anti-androgens must use very effective contraception, like COCP or long-acting reversible contraceptives.

## LOCAL TREATMENT

**Local treatment** of hirsutism includes waxing, bleaching, laser removal, and anti-androgen cream (Vaniqa).

## PCOS Treatment of Excessive Hair

| Hormonal | Anti-Androgens | Local |
|---|---|---|
| COCP | CYPROTERONE ACETATE | WAXING |
| DIANE-35 (COCP + CYPROTERONE) | SPIRONOLACTONE | BLEACHING |
| | FLUTAMIDE | LASER |
| | FINASTERIDE | VANIQA (EFLORNITHINE) |

**IMAGE 10.** *Treatment of unwanted hair*

## INFERTILITY

In PCOS, infertility is mainly caused by anovulation. However, conceiving requires **optimal functioning** of both female and male reproduction. Therefore, it is important to conduct a full assessment of fertility. If all other causes of infertility, such as male factor, tubal disease, severe endometriosis, and uterine pathologies, are **excluded**, treatment of anovulation can be started.

Women with PCOS have plenty of follicles in their ovaries. Due to high levels of AMH and other ovarian hormones, they **do not** ovulate regularly. To achieve ovulation, you need a higher level of FSH and LH hormones.

This can be achieved in **two** different ways.

1. **Clomid or Letrozole tablets**. Increases your own FSH and LH production from your pituitary gland.

2. **FSH and LH Injections**. These treatments are called Ovulation Induction (OI). Its effectiveness is approximately 10 percent per month. Provided ovulation is achieved, it is recommended to continue OI 4 to 6 months, giving approximately 35 percent chance of a successful pregnancy. If OI is not effective, it is assumed there may be other causes of infertility. Then, IVF Treatment is recommended.

## LONG-TERM HEALTH PROBLEMS

Due to metabolic changes, PCOS increases your risk of developing diabetes, high blood pressure, and heart disease. Therefore, you should undergo a **PCOS Annual Check-up** which includes the following:

- Medical history
- Measurement of blood pressure
- Measurement of BMI
- Measurement waist circumference
- Blood tests for lipid profile
- Screening for diabetes: Fasting Blood Glucose Level and HbA1C level

If necessary, your doctor will provide you with advice on **lifestyle modifications** and treatment for metabolic problems. The main objective of the annual check-up is identifying **risk factors**, early detection of symptoms of metabolic syndrome and prevention of diabetes and cardiovascular diseases.

In PCOS, continuous estrogen production without progesterone can cause excessive growth of the uterine lining, called unopposed estrogen. Long-term unopposed estrogen for years can cause changes in the uterine lining and increase the risk of **endometrial cancer**.

# Conclusion

**Polycystic Ovary Syndrome (PCOS)** is a common condition that is linked to ovarian function, excess androgen production, increased insulin resistance, and metabolic abnormalities. PCOS causes metabolic, skin, and reproductive problems which can be very **distressing**.

PCOS can be diagnosed if women have two or all three of these **symptoms**: irregular period, excess androgens, and polycystic ovaries. Effective treatment of PCOS has two strategies: generalised and targeted treatment. Most women benefit from generalised treatment which includes maintaining body weight in normal range, metformin to improve insulin resistance, and taking COCP.

**Specific symptoms**, such as unwanted hair, acne, and infertility can also be treated using effective targeted treatment.

To **prevent** diabetes, blood pressure, heart disease, and endometrial cancer, women should have an annual check-up.

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