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Polysystic Ovarian Syndrome (PCOS)

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Polycystic ovarian syndrome (**PCOS**) is the most common endocrine disorder in women of reproductive age, affecting 10% or more of premenopausal women, depending on the diagnostic criteria used. It is a cluster of symptoms that often include irregular menstrual periods, acne, weight gain, excess hair growth, thinning scalp hair, difficulty becoming pregnant, and blood sugar dysregulation, among other possibilities. 'Polycystic' refers to a large number of normal follicles or eggs in the ovary, not to large painful cysts, so the word is confusing. The ovaries can grow up to three times the size of normal ones and are covered with cysts (sacs) containing immature eggs. These cysts produce an excess amount of androgen hormones—considered 'male' hormones such as testosterone—that interrupt the normal menstrual cycle and prevent normal ovulation. The pancreas, brain, liver, blood vessels, muscle and fat tissues may all be affected. Indications of PCOS can start as early as the teen years. An estimated three out of four women women with PCOS may not know they have it. Since physical symptoms and lab test results can strongly resemble other conditions, even Cushing's syndrome or congenital adrenal hyperplasia, women typically see several doctors before getting the proper diagnosis. [1]

A functional ovarian cyst (the most common) is a result of follicle malfunction. A **follicle** is a sac that contains an egg (oocyte) surrounded by fluid and epithelial (follicular) cells before it's released during ovulation. During normal ovulation, the follicle grows to a certain size and then ruptures, releasing the egg. The follicle then becomes larger and develops the corpus luteum within it which secretes estrogen and progesterone needed to promote proper growth and maturation of the uterine lining during the second half of the menstrual cycle. This makes certain that either normal menstruation takes place or, if pregnancy occurs, that the uterus is prepared to sustain a fetus. An ovarian **cyst** forms when the follicale continues to grow instead of releasing the egg and dissolving as it's supposed to do. Cyst formation means **failed** ovulation; there is no corpus luteum and no proper hormonal secretion. In PCOS the ovary's outer layer (cortex) is like a thickened and hardened capsule that prevents ovulation. The cortex contains many 2- to 6-mm cystic follicles with a sheath of excessive cells, accounting for the ovary's polycystic appearance. As there are fundamental differences between polycystic and normal ovaries in early follicular development, an **abnormality** in ovarian function is suggested. [2]

PCOS is not a disease since it is not a specific and constant set of symptoms and physical characteristics. It is a **syndrome,** a cluster of various possible symptoms, physical indications and biochemical irregularities. There are two consistent aspects: high levels of androgen hormones and a lack of or infrequent ovulation. Androgens such as testosterone and androstenedione (a precursor of testosterone) produce or stimulate the development of male characteristics (masculinization). Women normally have androgens but in far lesser amounts than men. Common in PCOS are: a lack of or infrequent ovulation usually resulting in an absense of menstruation (amenorrhea) or scanty or infrequent menstrual flow (oligomenorrhea); excess hair growth or hair in unusual places (hirsutism); acne; multiple ovarian cysts; infertility; and obesity. More than 95% of women who have three classic signs—obesity, hirsutism and irregular menses—have PCOS. Still, some women have the syndrome but don't have all three of these classic signs. More than 50% of women with PCOS are overweight or obese; the general increase in obesity incidence is linked to the increase in PCOS prevalence. But not all women with PCOS are overweight. Some are of normal weight or even underweight, have no excess hair growth on the face, chest or legs, and may even have semi-regular menses. Obese women with PCOS have much higher average levels of testoterone and androsterone than non-obese women with PCOS. Obesity may contribute to hormone imbalances. High androgen levels can manifest, not only by excess hair growth, but also by hair thinning. Not all women with PCOS are infertile as there may be random unpredictable ovulation.

It can be difficult to come up with a definitive diagnosis as there are so many variables in this syndrome. Yet it is probably the most common cause of a lack of ovulation, leading to abnormal menstrual cycles and infertility. There have been some variations in the stipulations for diagnosis since the first mention of this condition in 1935. The **current** diagnostic criteria are that at least two of the following three features must exist (and other causes of the high androgen hormones and/or lack of or infrequent menses must be excluded):

- Scanty or infrequent menstrual flow (oligomenorrhea) or absence of menstruation (amenorrhea).
- Elevated androgen hormone levels evident in clinical presentation (hirsutism and/or other signs of masculinization) or from laboratory findings.
- Polycystic ovaries (12 or more follicles measuring 2 to 9 mm in diameter or volume of more than 10 ml).

In addition to elevated androgens (testosterone and androstenedione, a steroid hormone converted to testosterone), there is usually **also** a reduction of sex-hormone-binding globulin, elevations of luteinizing hormone and prolactin, plus high insulin levels and/or insulin resistance. Testosterone testing is not always accurate in women. For one thing, the range of normal has not been clearly established. **Other** problems related to PCOS or that develop due to it can include abnormal levels of: blood fats (elevated LDL, reduced HDL, elevated triglycerides), elevated insulin, elevated blood sugar, and high blood pressure. There are increased risks of developing type 2 diabetes, cardiovascular disease, and uterine (endometrial) cancer. Underlying causes of PCOS are complex and not completely clear. It is known that there are: 1) elevated secretions of androgens from the ovaries and/or adrenal glands that prevent the conversion of these androgens to sufficient amounts of estrogen. 2) An abnormal ratio of the pituitary hormones, luteinizing hormone (LH, too high) to follicle stimulating hormone (FSH, relatively too low). 3) Failure of the monthly maturing of a follicle in the ovaries. 4) Resistance to insulin. 5) Disturbed action of insulin. High androgen levels are found in 60% to 80% of cases. Insulin resistance occurs in at least 80% of cases and is more severe in women with severe PCOS, including those who are overweight or obese. Insulin resistance is a prediabetic state that can lead to diabetes, obesity, cardiovascular disease and more. About 40% of women with PCOS develop type 2 diabetes by the age of 40. Women who meet two of the three criteria for PCOS and are lean or have milder manifestations generally have less severe insulin resistance or insulin elevations. The elevation of androgens persist in women with PCOS after menopause; there are both higher adrenal and higher ovarian androgen levels, although the adrenals probably contribute more in postmenopausal women. [3]

While overweight or obese people often have high insulin levels and insulin resistance or metabolic syndrome, women with PCOS who are not obese can nevertheless have insulin resistance and metabolic syndrome. So abnormalities in blood sugar metabolism may contribute to PCOS development. Diet **quality** and nutritional needs are no doubt involved. High insulin levels may suppress ovulation, cause drops in blood sugar, increase risk of weight gain, and affect sex-hormone ratios. There is evidence that high insulin levels can promote high androgen levels **and** that high androgen levels can promote insulin resistance. The question is 'which came first, the chicken or the egg?'—it can be difficult to know. **Insulin** might stimulate androgen production because: 1) Ovaries have insulin receptors. 2) Insulin decreases the serum level of sex hormone binding globulin (SHBG), the primary protein that carries estradiol or testosterone to cell membrane receptors in target tissues. When SHBG levels decrease, more unbound testosterone is allowed to circulate, amplifying its effects. 3) Insulin-like growth factors (IGF) may stimulate production of androgens and growth of the ovaries. IGFs are proteins with similarities to insulin. Among the many factors that may cause IGF-1 variations are excess stress, nutritional needs, excess weight, low estrogen, and xenobiotic intake. IGF-1 may work with luteinizing hormone (LH) and insulin to produce androgen hormones. Insulin reduces levels of the primary binding protein for IGF (IGVBP-1), making more IGF available. 4) Insulin may affect the anterior pituitary by increasing LH, creating a relative decline in follicle stimulating hormone (FSH) which leads to ovarian tissue thickening and increasing androgen production. 5) Elevations of androstenedione and DHEA (dehydroepiandrosterone, an adrenal hormone with about one fifth the potency of androsterone, an androgen product) can have androgen-producing effects. Many women with PCOS have a significant increase in adrenal androgen levels in addition to increased ovary levels. The adrenal component may be more prevalent in younger and leaner women. [4]

Long-term use of oral contraceptives (a common medical treatment for PCOS) can contribute to insulin resistance. Reduced levels of nutrients such as glutathione, vitamin C and vitamin E plus GST (glutathione-S-transferase) enzyme have been found in non-obese women with PCOS and are unrelated to insulin status. A number of other nutrient deficiencies are found in women with the syndrome. Obviously, many components can contribute to PCOS. [4,5] There is evidence that environmental factors can play a role. Some research, for example, indicates that exposure to bisphenol A (BPA), a chemical used in plastics and linings of food cans and known to be a hormone disruptor, could be a contributing cause. Blood levels of BPA were more than 30% higher in overweight women with PCOS and nearly 60% higher in lean women with the syndrome compared

with a control group. As BPA levels increased, so did concentrations of testosterone and androstenedione. There is also an association between BPA levels and insulin resistance. BPA is being replaced by other chemicals, but they are turning out to be just as bad or even worse. Excessive stress triggers stress hormones, especially cortisol, which place glucose stores on "red alert" for the fight, flight or freeze response. High insulin levels tend to increase cortisol levels so a woman's body may be flooded with both insulin and cortisol. [6]

Therefore, possible basic causes of PCOS include: 1) Excess weight gain. 2) Insulin resistance. 3) Ovarian dysfunction (low estrogens and high androgens). 4) Adrenal dysfunction. 5) Hypothalamic-pituitary axis dysfunction (elevated LH and lower FSH). 6) Environmental factors (including exposure to toxins such as hormone disruptors). All of these can benefit from nutritional and other lifestyle improvements.

Conventional **medical** treatments include a number of **drugs** due to the many systems affected. Metformin is commonly prescribed to treat insulin resistance and glucose intolerance. But weight and obesity influence the effectiveness of metformin and the drug can cause gastrointestinal disturbances that interfere with nutrient bioavailability. Metformin helps about 23% of women with PCOS to ovulate, but it doesn't fix the underlying problem in blood sugar metabolism. Oral contraceptives (estrogen and progestin) are used to treat symptoms of elevated androgens such as acne, hirsutism, and hair loss. These drugs often produce myriad side effects (increased appetite, mood swings, weight gain, nausea, etc.), cannot be used by women who are trying to conceive, and frequently worsen insulin resistance. GnRH (gonadotropin-releasing hormone) agonists such as leuprolide are used to suppress the pituitary-ovarian axis to cause a decrease in ovarian secretion of estrogen and androgens; these drugs can cause bone loss. Anti-androgens such as spironolactone are used to treat symptoms such as acne and hirsutism; they can cause menstrual abnormalities. Eflornithine, a topical drug for hirsutism, inhibits an enzyme in the skin to decrease the rate of hair growth. Clomiphene (Clomid, Serophene), an anti-estrogen, is used to increase LH and FSH to induce ovulation and enhance fertility. Clomid can lead to multiple-birth pregnancies and increase risk for major birth defects. All these drugs have side effects—some very serious such as increased cancer risk—and can lead to more hormonal disturbances without approaching the underlying causes of PCOS. Giving women synthetic hormones "violates the basic principle of healing." Instead, diet, nutrients, herbs, physical activity and other lifestyle changes can often balance hormones. [7]

Alternative therapies should focus on a woman's specific problems, address underlying causes, and provide long-term strategies to prevent future sequels such as diabetes, cardiovascular disease or endometrial cancer. Goals include: 1) lowering androgens and easing symptoms of excess, 2) establishing regular ovulation and menstruation (and restore fertility) by improving female hormone balance, 3) improving insulin resistance and lowering excessive insulin secretion, 4) reducing weight if the woman is overweight or obese, and 5) maintenance of health. Lifestyle intervention—diet and exercise—is the first line of treatment. A Cochrane summary concluded that following a healthy lifestyle "reduces body weight and abdominal fat [in women who are overweight], reduces testosterone and improves both hair growth and insulin resistance." Lifestyle approaches should include minimizing exposure to hormone-disrupting chemicals. [8]

Dietary changes and weight loss have profound effects on the symptoms of PCOS. Research shows that in overweight women even modest weight loss improves insulin sensitivity, menstrual-cycle regularity, and fertility; increases SHBG; and decreases circulating androgens. Weight loss is found to decrease ovarian volume, number of follicles, and spontaneous abortion rates. Improved dietary changes affect blood-sugar control as well. As little as 5% to 10% weight loss can have significant impact on insulin sensitivity and risk factors for cardiovascular disease and type 2 diabetes. It is important to achieve a stable weight without weight gain in all women with PCOS—lean, overweight, or obese. A healthy diet encourages improved hormone balance. Recommended dietary **changes** involve reducing refined carbohydrates while increasing vegetables, fruits, nuts, seeds, whole grains and legumes. Wholesome proteins include organic (preferably pasture-raised) meats and poultry and eggs, ocean fish, organic and raw milk products. Plant proteins are also supportive such as legumes, whole grains, and vegetables. Nuts such as almonds and walnuts can improve metabolic and endocrine parameters. Increasing healthful proteins and reducing refined carbohydrates can lead to reduced body weight and androgen levels, increased insulin sensitivity and decreased C-reactive protein (lowered inflammatory processes). A "low glycemic index" diet has been shown to help which basically means avoiding refined carbohydrates. (Some items high on the glycemic index are foods that will not cause disturbances, but

the general idea of eating low on the glycemic index is to avoid refined, over-processed carbohydrates.) Eating a lot of refined sugars results in higher insulin levels, insulin resistance, and stimulation of cortisol and DHEA secretion from the adrenal glands. Fats and oils should be unaltered and unrefined; natural fats do not need to be avoided and, in fact, a number of fatty acids are needed for proper hormone production and utilization. Steroid hormones such as progesterone and estrogen are made from cholesterol. The liver produces most of the body's cholesterol but some cholesterol in the diet is also helpful. "In the case of PCOS, the starvation of the ovaries causes them to become cystic, swollen and eventually unable to regulate the synthesis of their hormones," says Tom Cowan, MD. Women who follow a low-fat diet or who consume altered, refined or fake fats inevitably eat excessive amounts of refined carbohydrates—they crave sugars and refined flour products. This in itself causes hormonal shifts. The pivotal point is to consume **real** foods the way nature made them and avoid nonfoods the way food manufacturers concoct them. Additionally: "No one diet works for everyone. Each diet must be tailored to suit the individual." Some women need more animal protein than others or more fats or more plant foods including vegetables and fruits. [9]

Women with PCOS who adhere to a regular **exercise** program experience general weight loss and reductions in waist-to-hip ratio, insulin sensitivity and homocysteine levels. Weight loss for overweight women reduces insulin and testosterone levels, often providing dramatic relief from many symptoms. Regular exercise is a crucial in regulating menses and reducing cardiovascular and diabetes risks. Yoga may help reduce facial hair, and improve menstrual frequency, hormone concentrations, and glucose metabolism. **Acupuncture** can assist insulin sensitivity and glucose balance, weight loss, inflammation reduction, hormonal balance, and regular ovulation induction. Reducing **stress** levels may be needed. "In response to stress," says Angela Hywood, ND, "the adrenals release cortisol, inducing an elevation in prolactin…and increased androgen synthesis, which in turn leads to menstrual cycle dysregulation, especially anovulation, characteristic of PCOS." Herbs (such as ashwagandha, American or Asian ginseng, licorice, rhodiola, and schisandra) and nutritional support (such as vitamin B complex; minerals including calcium, magnesium and potassium; vitamin C complex, and others) in addition to relaxation techniques (exercise, biofeedback, meditation, aromatherapy, yoga, etc.) can decrease stress hormones and improve blood sugar, hormone balance and anxiety. Excessive or regular **alcohol** consumption may reduce the liver's ability to metabolize hormones and disrupt blood sugar regulation. [10]

Herbs. Flaxseeds contain lignans that increase SHBG, lower blood testosterone levels and reduce the effects of elevated androgens; 2 tablespoons of freshly ground seeds per day is recommended. Saw palmetto inhibits activity of an enzyme (5-alpha reductase), helping to lessen conversion of testosterone to its more potent form, dihydrotestosterone. This can reduce acne, excess facial and body hair, and hair loss from the scalp. Licorice root high in glycyrrhizin may decrease testosterone secretion probably due to the block of testosterone by two enzymes Chaste tree berry and dong quai root may assist in restoring normal menses, decrease elevated prolactin levels, improve fertility and improve the body's progesterone-producing process. White peony may decrease androgens, decrease LH, and improve hirsutism. Blue cohosh has a traditional use among Native North Americans and was used by women as a remedy for amenorrhea and profuse menstruation, both common in PCOS. It is particularly useful to bring on menses. Black cohosh can reduce luteinizing hormone (LH) levels, progesterone levels, and improve ovulation. A reduction in LH has a potent effect on androgen excess in women with PCOS, allowing for more regular ovulation. Maitake mushroom extract was able to induce ovulation in women with PCOS by an impressive 76.9%. Cinnamon can improve menstrual cycle frequency. Gymnema sylvestre at 400 mg daily improves blood sugar control and decreases elevated lipid levels. Fenugreek seed also can lower serum glucose and lipids. Bitter melon and Panax ginseng have been used traditionally to reduce elevated glucose levels. [11]

Nutrients. Nutritional deficits or imbalances can contribute to faulty ovarian follicle development in women. **Chromium** helps blood-sugar balancing, glucose tolerance and insulin sensitivity in people with high blood sugar. It enhances the action of insulin and helps glycemic control by increasing the glucose disposal rate. Chromium in its trivalent form is found in many foods such as whole-grains, egg yolks, coffee, nuts, nutritional yeast, meats, green beans, broccoli, and more. When supplemented with chromium, obese women with PCOS have shown improved glucose tolerance and improved insulin sensitivity. **Zinc** is a required cofactor for numerous biochemical reactions. For one, it affects glucose transport and insulin levels. Evidence indicates that zinc supplementation can improve glucose tolerance and increase insulin-induced glucose transport into

cells. **Calcium** and **vitamin D** affect hormones. Women with PCOS who were supplemented with calcium and vitamin D showed improved weight loss, follicle maturation, menstrual regularity, and androgen levels. Vitamin D plays a role in glucose metabolism; supplementation has been shown to improve glucose tolerance, insulin sensitivity, triglyceride levels and menstrual frequency in women with PCOS. A deficit of vitamin D may be more frequent in women with PCOS than in those without the syndrome. [12]

Alpha-lipoic acid, a coenzyme used in carbohydrate metabolism and production of adenosine triphosphate (ATP) for cellular energy, can improve insulin sensitivity and increase metabolic clearance of glucose. Essential **fatty acids**—omega-3s (docosahexaenoic acid and eicosapentaenoic acid) and omega-6s (such as linoleic acid) are required for physiologically active molecules, to support proper inflammation and repair processes, reduce excess blood clotting, reduce high triglycerides and increase low HDL. The body can convert linoleic acid to gamma linolenic acid (GLA), but it needs magnesium, zinc, vitamin C, vitamins B_3 and B_6 for that conversion. GLA helps resolve inflammation and aids in avoiding insulin resistance and obesity; it is especially rich in borage seed, evening primrose, and black currant seed oils. Omega-3 supplementation is associated with significant decreases in body mass index (BMI), glucose, insulin, total cholesterol, LDL, triglycerides, serum luteinizing hormone (LH) and testosterone levels as well as increases in sex hormone-binding globulin (SHBG) levels. Improvement in hirsutism, blood pressure, HDL-cholesterol and insulin resistance are found. The fat content in the liver is lowered, enabling it to metabolize hormones better. [13]

Inositols and compounds related to them in foods work together to help insulin resistance. Jillian Stansbury, ND, says, "They support signal transduction, the ability of a cell to receive insulin and then tell the nucleus of the cell to respond to it." Myo-inositol, a carbohydrate form, was once considered to be a member of the vitamin B complex. But because it can be produced in the body from glucose (with supportive nutrients), it is no longer considered 'essential.' Isolated myo-inositol has been used as an insulin-sensitizing agent; it lowers circulating insulin and serum total testosterone as well as improves metabolic factors. Some scientists suggest that the insulin resistance in PCOS is partly due to a deficiency of myo-inositol's associates, D-chiro-inositol (DCI) and inositol-phosphoglycan, both mediators of insulin actions. Another theory is that women with PCOS have a higher urinary clearance of DCI. At least two studies showed that giving women with PCOS either myo-inositol or DCI reduces androgen levels, enhances restoration of ovulatory function, lowers blood pressure, and decreases triglycerides. DCI naturally occurs in buckwheat and has been shown to reduce circulating insulin, decrease serum androgens and ameliorate some metabolic abnormalities (high blood pressure and high triglycerides). Other research indicates that myo-inositol may help restore ovarian activity and fertility in most women with PCOS. Pinitol (3-O-methyl-D-chiro-inositol), structurally similar to DCI with similar biochemical actions, appears to mediate insulin activity, decrease testosterone levels, and may restore ovulation. Myo-inositol and folic acid increased ovulation and conception rates in infertile women with PCOS. A combination of DCI and myo-inositol has been effective in treating PCOS. However, these treatments use separated, often nonfood sources of inositols that are more pharmaceutical than nutritional. Obtaining real food sources with their natural supportive companions would be better. These include alfalfa, brown rice, legumes (lentils, peas, beans, and carob), citrus fruits, buckwheat, astragalus, and licorice. [14]

B vitamins such as B_1, B_6, B_{12} and folic acid (folate) benefit the metabolic profiles of women with PCOS by reducing homocysteine, improving insulin resistance and balancing cholesterol levels. Women with PCOS tend to have significantly higher levels of homocysteine compared to women who do not have PCOS. **Vitamin C** complex can increase ovulation and may improve progesterone levels. It has been shown to enhance endothelial-dependent vasodilation which is abnormal in many women with PCOS. Hypothyroidism is found in some cases of PCOS. With signs and symptoms of an under-functioning **thyroid**, nutritional support with a glandular (Thytrophin PMG), iodine, essential fatty acids and other nutrients may result in improvements. [15]

N-acetylcysteine given to women with PCOS resulted in small decreases in body mass index (BMI) and waist-to-hip-ratio, improvements in hirsutism, fasting blood sugar, insulin, insulin resistance and serum testosterone. Regular menses (ovulation induction) increased; total and LDL cholesterol levels decreased. The mechanism is not yet known. N-acetylcysteine is used as a pharmaceutical drug (IV, inhalant or oral) and as a 'nutritional' supplement (oral). The IVs and inhalants have many adverse effects. The oral version can cause nausea, vomiting, rashes, rhinorrhea, and fever. It is not a food; it's more of a drug. It is a **derivative** of the amino acid

cysteine which the body can produce from methionine; both are sulfur-containing amino acids. Methionine is an essential amino acid (must be obtained from food) and requires certain enzymes and B vitamins to be processed. Meats, poultry, dairy, eggs, quinoa and buckwheat are rich sources; smaller amounts occur in plants such as broccoli, Brussels sprouts, red and yellow bell peppers, onions, and garlic. Decreased total **l-carnitine** levels are found in women with PCOS. A lower sex hormone-binding globulin (SHBG) level in PCOS is a strong predictor of lower serum total l-carnitine levels. Lower levels may accompany high androgens and/or insulin resistance. Carnitine is produced in the body from the amino acids methionine and lysine. The highest concentrations are in red meats. Lower levels appear in many foods such as nuts, seeds, legumes, vegetables (artichokes, asparagus, beet greens, broccoli, Brussels sprouts, collards, garlic, mustard greens, okra, parsley, kale, etc.), fruits (apricots, bananas, etc.), corn, millet, oats, rice, rye, whole wheat, nutritional yeast, carob, and bee pollen. Evidently, obtaining sufficient amino acids is essential in PCOS. [16]

Two primary areas demand attention in PCOS. **One** is metabolic, relating to excess weight and/or blood sugar processing. Benefits come from lifestyle improvements (diet, physical activity) plus supplemental support to reduce insulin resistance and improve blood sugar balance. The **second** area is endocrine imbalance or dysfunction. Assistance can come from diet and supplemental support to the ovaries, pituitary, adrenals, and perhaps thyroid. Supplements as real whole food concentrates rather than isolated or synthetic 'nutrients' provide the full spectrum of the hundreds and perhaps thousands of food components that all work together. Since each woman with PCOS has some differing issues, an individualized program should be designed. Nevertheless, the metabolic and endocrine issues seem to be constant for all women with this syndrome, even those who are not overweight.

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