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INTRODUCTION

The Many Faces of Polycystic Ovary Syndrome

I HAVE A REPUTATION for getting people pregnant. In fact, people often seek me out specifically because they've heard from friends or co-workers: "Be careful. Don't go see Doctor Nadia unless you want to get pregnant." For couples living with fertility trouble, getting pregnant is a welcome miracle! I've now been a naturopathic doctor in clinical practice for more than 15 years, and my special focus is on helping women with polycystic ovary syndrome (PCOS) overcome infertility through dietary modifications.

PCOS is the most common reproductive disorder in the world. It affects an estimated 8 to 20 percent of women of reproductive age globally, depending upon the specific diagnostic criteria used.[1] Forty percent of patients diagnosed with PCOS suffer from infertility, and 90 to 95 percent of women in infertility clinics who cannot conceive due to lack of ovulation suffer from PCOS.

But my near-obsession with PCOS, fertility, and diet is not merely professional, it's also deeply personal. I became a naturopathic doctor after developing irritable bowel syndrome as a young adult.

Conventional medicine did not help, but I found some reprieve with naturopathic medicine. In 2004 I graduated from the Canadian College of Naturopathic Medicine and moved back to my home country of Mozambique, planning to work with the Ministry of Health in impoverished communities. I hoped to learn local traditional medicine to complement my naturopathic training. However, Mozambican politics are complicated and getting a job at the Ministry is not simple. I knocked on many doors, but I was repeatedly (and sometimes not so politely) turned away.

Eventually I requested a meeting with the Minister of Health himself, and after reviewing my curriculum vitae and listening to my story, he awarded me a license to practice naturopathic medicine privately. He advised me to go to Maputo, the capital of Mozambique and the city where I was born, where he said I would likely do well. I felt defeated that I couldn't follow my original plan, but with little alternative, and unwilling to turn my back on Mozambique, I did as he suggested.

I was initially worried that I had little to offer. To my surprise, though, my practice was completely full within six months. Instead of treating the poor and undernourished, I had clients who were affluent and overweight. They suffered from many of the same diseases affecting people in the Western hemisphere—the so-called "diseases of civilization," including type 2 diabetes, cardiovascular disease, cancer, and metabolic syndrome. They were suffering from "Western" diseases because their diet was modeled on the standard American diet, and their dominant concern was weight loss.

Mozambique, at the time, was considered the poorest country in the world and had some of the highest rates of malnutrition. But where rural people were starving, urban dwellers were overfed. Fast-food restaurants such as KFC and pizza joints had invaded the cities, and Coca-Cola was everywhere! From its inception, my medical practice focused almost exclusively on nutrition, diet, and weight loss.

My naturopathic training had not truly prepared me for this situation because I'd studied only a little nutrition, but as the only

naturopath in Maputo, I tried my best. I created diet plans for my clients, based on my medical training and common sense. Mozambicans are a wonderful and forgiving people, and they were willing to try anything I suggested. I was very thin, and they believed what I was eating must have something to do with my low body weight.

I now realize that my diet was not particularly healthy and that my thinness might have been the result of genetics and the fact that I was a very picky and poor eater. As a child, I disliked meat and vegetables, so I snacked all day long. I lived on candy, fruit, bread, lattes loaded with sugar, and Coca-Cola. If I sat down for a meal with my family, I ate refined grains with a bit of the sauce, washed it down with a Coke, and followed that with some fruit. At night I went to bed with my bag of candies, and in the morning I started the day with a latte and toast. Only a couple of hours later, I would feel shaky and eat fruit or some more candy. I always believed that I suffered from hypoglycemia, or low blood sugar, so eating sugar every few hours seemed to make sense. Little did I know that in 30 years I would develop metabolic syndrome. Only then would I learn to eat a proper meal.

Among my first patients in this small and tightknit community in Mozambique was a South African woman named Charise who wanted to lose weight. She had a long-standing addiction to soda drinks and wanted to "detox," so I counseled her on a diet I thought might help. Several months later, Charise booked an appointment along with her husband, Johann. I usually met with Charise alone, so I was a bit apprehensive about why they were coming to see me together. When they arrived, Johann announced that they were expecting a baby! He became emotional as he explained that for the first six years of their marriage Johann and Charise had been unable to conceive. They had undergone several rounds of expensive in vitro fertilization (IVF) without success and had finally accepted that they would never welcome their own biological child into this world. Instead they had joyfully adopted a child, who was now age seven. But "miraculously," they were now expecting their first biological child. Johann was confident that my "detox diet"

was the reason they were suddenly able to conceive. Over the previous three months, Charise had successfully adopted a strict diet that eliminated sugars, even the "healthy" sources like fruit and juices. Her diet encouraged protein and healthy fats such as coconut oil, avocados, eggs, butter, and olive oil. Overcome with joy, they had come to thank me.

Charise later suffered a miscarriage and lost that child. But "miraculously," she conceived for a second time and gave birth to a healthy baby boy. Johann wanted to understand the unexpected connection between this innovative diet and their newfound fertility, but I didn't have an explanation. So early in my career, I did not know myself how Charise suddenly got pregnant. I just did not understand the profound link between diet and fertility. From a practical perspective, it didn't really matter: I simply explained to patients that sometimes a bit of weight loss and a "detox" might help them bring home a little bundle of joy.

Nadia, Mozambique, 2005 (28 years old)

By age 30, I was a successful "dietician" in Mozambique. Everyone in town knew "Dr. Nadia" because I had helped many people lose weight and control their diabetes with my prescribed "Base Diet" and an occasional "detox." But I followed none of these diets myself. I kept on

eating my candies and drinking my Coke. In late 2008 when my husband and I started trying to conceive, my diet was catching up with me and I started to gain weight. My lifelong acne problem was getting a bit worse. My doctor reassured me that I was thin and healthy and in good shape to have a baby, but month after month my period showed up. I would cry for days afterward and feel miserable. By the end of 2009, I realized I must be infertile. I was devastated.

By early 2010, I had gained close to 30 pounds (13.6 kilograms) but my Body Mass Index (BMI), which is a standardized measurement of weight, was still within the normal range. My acne was terrible and my hair started falling out. Blood tests showed that my androgen (male hormone) levels were high, and an ultrasound revealed numerous cysts in my ovaries. I had stopped ovulating and, therefore, could not get pregnant. I suspected I had PCOS, and my doctor confirmed it. Because I looked thin, however, my doctor overlooked all the other symptoms and simply prescribed clomiphene citrate, a type of fertility drug. I went home and just cried. All I could think about was how much I wanted a baby. I was also upset because I didn't think my doctor was doing much to help. My husband assured me that we would get through this together, and his confidence gave me the strength to take matters into my own hands.

From my professional experience, I knew fertility improved when women lost weight because I had seen so many of my clients become pregnant. My weight wasn't an issue in my lack of fertility, I thought, but I started to follow the strictest of my own diets anyway. If that's what I had to do to get pregnant, I would do it. This extremely low-carbohydrate diet, sometimes called a ketogenic diet, meant no more candies, no more Coke, no more bread.

In the first month, I lost 5.5 pounds (2.5 kilograms). Then my acne cleared up and my menstrual cycles normalized as I began to ovulate. The night before I took my next pregnancy test, I lit a candle. I was calm and positive. I asked for nothing, but I wanted a baby. In the morning, I took the test. And after 30 seconds of agony waiting for the result, the

test was . . . positive. I was so grateful and relieved, and I immediately called my husband at work. He was ecstatic. Though he had never let on before, he admitted he had been very concerned about my physical and emotional well-being. Infertility takes a large toll on many people's work, family, and social lives. It can also drain financial resources for those people who choose to pursue IVF or other fertility treatments; I had considered IVF but it was too expensive.

While I had become pregnant, I still didn't quite understand the key role of nutrition. I threw my low-carb diet right out the window and returned to eating my candies and usual diet of small, high-carb snacks many times a day. I developed serious complications during the pregnancy, including high blood pressure and liver damage, which eventually required me to deliver the baby by cesarean section at 38 weeks. That's when my first daughter, beautiful Zinzi, came into our lives.

Unfortunately, I continued to suffer from high blood pressure and postpartum depression. One of the medications my doctor prescribed, amitriptyline, caused me to gain 20 pounds (9 kilograms) on top of the baby weight I was still carrying. Two years later, a large ovarian cyst ruptured, requiring urgent surgical removal. I was still on high blood pressure medication and having trouble sleeping. Despite my health problems, I wanted to have another baby.

When my husband and I tried to conceive a second time, the torturous journey began all over again. My doctor prescribed clomiphene once more, but by this time my BMI was in the overweight range and my health was much poorer than when I became pregnant the first time. I was eating my candies, and drinking my Coke, and taking my fertility medication. Six agonizing months later, I still was not pregnant. I remember crying constantly and feeling an overwhelming sense of doom that I would never be able to conceive again.

I stopped taking the fertility drugs and visited my friend Dr. Carolina, a Mozambican gynecologist. She told me flat out, "Of course you won't get pregnant, not even on clomiphene. You are insulin resistant!"

Until that very moment, insulin resistance related to PCOS had never crossed my mind. Much later, I realized that the low-carbohydrate diet I followed at the beginning of my first pregnancy reduces insulin, thereby improving insulin sensitivity and treating the source of my problems. But at the time, all I knew was that Dr. Carolina was right and she gave me hope. I began to take metformin, a medication to increase my insulin sensitivity—and I got pregnant the very next month.

Pateguana family, July 2018, Toronto, Canada

Pateguana girls, July 2018, Toronto, Canada

I experienced major complications during that pregnancy, likely because I didn't follow my low-carb diet. As soon as I gave birth to my beautiful second daughter, Zuri, I began to follow a low-carb diet again. A couple of months after she was born, I lost all my excess weight, came off all my medications, and saw my skin clear up and all my other PCOS symptoms disappear. My irritable bowel syndrome, food cravings, and mood swings also vanished. Adopting a strict low-carbohydrate diet—along with intermittent fasting—made a big difference for me. Today, over six years later, I still follow a low-carb diet along with intermittent fasting. I have not taken medication for hyperglycemia, hypertension, or depression again. I have no more symptoms of PCOS or irritable bowel syndrome. This lifestyle has been very sustainable for me, and I hope the same for you.

In 2013 my family and I returned to Canada, and three years later I met Dr. Jason Fung at a medical conference. I had followed his work for a few years on social media, and I knew that he and Megan Ramos had started the Intensive Dietary Management (IDM) program in Toronto, not far from where I was living at the time. Soon after, they invited me to bring my professional experience to their team, and I still proudly work with the IDM/Fasting Method program today. I am very fortunate to have Dr. Fung contribute his medical and scientific expertise to these pages.

Today, my passion in life is not only helping women get pregnant, but also assisting them to lose weight and take control of their health through natural dietary measures. I have learned many things about diet and fertility through my own journey and the journeys of the clients I see in my naturopathic practice, and I'd like to share that information so that you do not go through the same agony and heartbreak of infertility. Read on and good luck!

PART ONE

What Is Polycystic Ovary Syndrome?

The Diabetes of Bearded Women

POLYCYSTIC OVARY SYNDROME (PCOS) has only been considered a disease in the last century, but it is actually an ancient disorder. Originally described as a gynecological curiosity, it is now the most common endocrine disorder of young women and is known to involve multiple organ systems.

EARLY DEFINITIONS

IN ANCIENT GREECE, the father of modern medicine, Hippocrates (460–377 BC), described "women whose menstruation is less than three days or is meagre, are robust, with a healthy complexion and a masculine appearance; yet they are not concerned about bearing children nor do they become pregnant."[1] This description of PCOS did not exist only in ancient Greece; it is found in ancient medical texts throughout the world.

The ancient Greek gynecologist Soranus of Ephesus (c. 98–138 AD) observed that "the majority of those [women] not menstruating are rather robust, like mannish and sterile women." The renaissance French

barber, surgeon, and obstetrician Ambroise Paré (1510–1590) noted that many infertile women with irregular menses are "stout, or manly women; therefore their voice is loud and bigge, like unto a mans, and they become bearded." It's quite an accurate description from a doctor who can apparently cut your hair, cut your leg off, or deliver your children. The Italian scientist Antonio Vallisneri (1661–1730) connected these masculinizing features and the abnormal shape of the ovaries into a single disease when he described several young, married infertile peasant women whose ovaries were shiny with a white surface and the size of pigeon eggs.[2]

In 1921 French doctors Émile Charles Achard and Joseph Thiers described a syndrome that included masculinizing features (acne, balding or receding hairline, excessive facial hair) and type 2 diabetes (which used to be called adult-onset diabetes). Further cases in 1928 cemented the link between what is now called PCOS and type 2 diabetes, and these were described in the classic article "Diabetes of Bearded Women."[3] Careful observation had already revealed to these astute clinicians a syndrome that included menstrual irregularities, infertility, masculine features, and obesity with its related type 2 diabetes. The only essential feature they missed from the modern definition of PCOS was the multiple cysts in the ovary, only because they lacked the ability to carry out simple, noninvasive imaging.

DETECTION AND DESCRIPTION IN THE MODERN ERA

DRS. IRVING STEIN and Michael Leventhal ushered in the modern era of PCOS in 1935 with their description of seven women with all the modern diagnostic features: masculinization, irregular menses, and polycystic ovaries.[4] By making the connection between the lack of menstruation and the presence of enlarged ovaries, they achieved a breakthrough by merging these into a single syndrome: PCOS. The detection of enlarged cystic ovaries was difficult in the 1930s, and Stein and Leventhal achieved this either by direct surgical observation

(laparotomy) or by using a now-defunct x-ray technique called pneumoroentgenography that involved making an incision in the abdomen to introduce air and then taking x-rays. The shadow of the enlarged ovary could be seen on the film. However, in an era before effective antibiotics, this procedure was a risky one.

Dr. Stein hypothesized that some as-yet-undetermined hormonal imbalance caused the ovaries to become cystic, and he suggested that surgically removing a wedge of the ovary might help to reverse the syndrome. And indeed, this crude surgery worked. All seven women began to menstruate again and two even got pregnant. With its main features defined, interest in PCOS surged, as reflected by the large increase in PCOS articles in the medical literature.

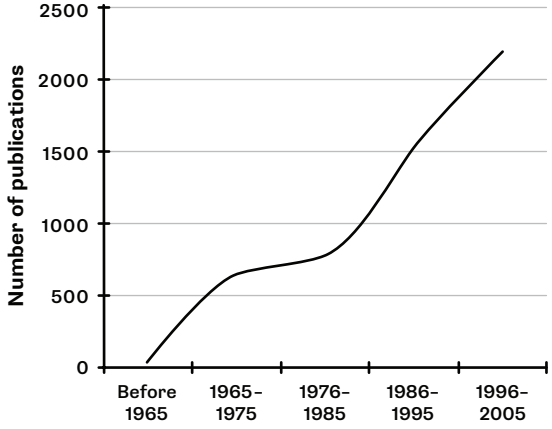

Figure 1.1. Number of publications on PCOS in the medical literature (MEDLINE)[5]

Subsequently, Drs. Stein and Leventhal performed ovarian wedge resection on another seventy-five women, restoring the menstrual cycles in 90 percent of cases and restoring fertility in 65 percent.[6] Defining the syndrome and delineating a reasonable treatment was such an accomplishment that this disease became known as Stein-Leventhal Syndrome. However, with the advent of modern medical

solutions, particularly the medication clomiphene citrate, removing a wedge of the ovary is rarely done today.

Through the 1960s and 1970s, improved lab testing allowed easier detection of the typical hormonal abnormalities of PCOS. Researchers discovered that an excess of male sex hormones called *androgens*, of which testosterone is the best known, causes the masculine appearance in women. Features associated with an excess of androgens, such as acne, male-pattern baldness, and facial hair growth, are often obvious in women, but measuring these hormones is not as useful for the diagnosis of PCOS as you may think. Androgen levels in women with PCOS are only modestly elevated and vary throughout the day and throughout the menstrual cycle, so it is difficult to make a diagnosis of PCOS based on biochemical analysis alone.

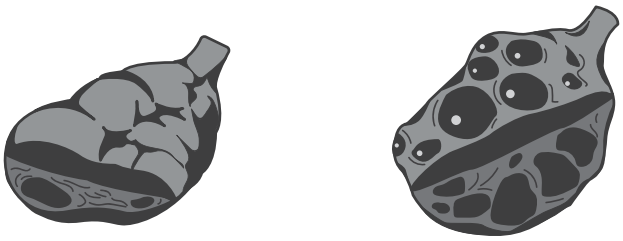

Figure 1.2. The normal ovary compared with the polycystic ovary. From *Polycystic Ovary Syndrome*, 2nd ed., Gabor T. Kovacs and Robert Norman, © Cambridge University Press, 2007. Reproduced with permission of the Licensor through PLSclear.

By the 1980s, the increasing availability of real-time ultrasound revolutionized the diagnosis of PCOS, because it meant laparotomy was no longer necessary to confirm the enlargement of the ovaries. In 1981 the ultrasound definition of polycystic ovaries was standardized, which allowed researchers to easily compare different cases.[7] Further refinements included the introduction of transvaginal ultrasound (an ultrasound in which the probe is inserted into the vagina),

which detects ovarian cysts with more precision because the probe is closer to the ovaries. This technology soon made clear that many otherwise-normal women also had multiple cysts on their ovaries. In fact, almost a quarter of women of reproductive age had polycystic ovaries without any other symptoms. Thus, it is important to distinguish between the presence of polycystic ovaries alone and polycystic ovary syndrome.

The 1980s also saw a revolution in our understanding of the underlying cause of PCOS. The root cause of the disease was originally ascribed to excessive exposure of female fetuses to androgens, but this hypothesis was ultimately refuted. Instead, studies increasingly linked PCOS to hyperinsulinemia, literally "too much insulin in the blood," a condition commonly seen in association with insulin resistance. Because the syndrome was still known by a multitude of different names—polycystic ovaries disorder, a syndrome of polycystic ovaries, functional ovary androgenism, hyperandrogenic chronic anovulation, polycystic ovarian syndrome, ovarian dysmetabolic syndrome, sclerotic polycystic ovary syndrome, and so forth—researchers did not always know if they were talking about the same disease. To move forward in properly identifying and diagnosing the disorder, the terms would need to be standardized.

Attendees of the 1990 National Institute of Child Health and Human Development (NICHD) conference on PCOS took the first step when they agreed by consensus on the following specific criteria:

1. Evidence of excess androgens (symptomatic or biochemical)
2. Persistent rare or absent ovulatory cycles

Because these symptoms are not specific to PCOS, other diseases would still need to be ruled out. However, these so-called National Institutes of Health (NIH) criteria were a giant leap forward because proper classification allowed international collaboration between universities and researchers. Interestingly, the NIH criteria do not require evidence of polycystic ovaries, which obviously presented a problem for a disease known as polycystic ovary syndrome.

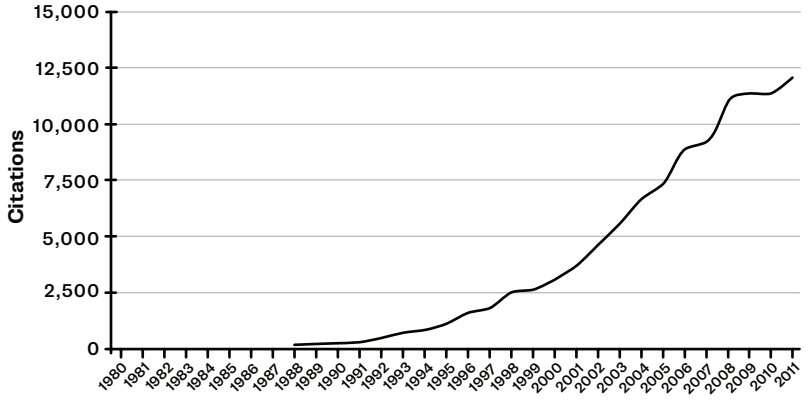

Figure 1.3. The number of scientific articles linking PCOS and insulin resistance increased from one in 1980 to about 12,000 in 2011[8]

In 2003 the second international conference on PCOS was held in Rotterdam, the Netherlands. Two new features were added to the NIH criteria. First, the mention of polycystic ovaries was introduced. It took a mere 14 years to correct that little oversight! Second, PCOS was recognized as a spectrum of disease in which not all symptoms may appear in all patients, and it was decided that a patient could be diagnosed with PCOS if they showed two of three criteria. The updated criteria, published in 2004, became known as the Rotterdam criteria:

1. Hyperandrogenism: literally, a state of too many androgens. The prefix "hyper" means "too much" and the suffix "ism" means "a state of."
2. Oligo-anovulation: literally, few or no ovulatory menstrual cycles. The prefix "oligo" means "few" and the prefix "a" means "absence of."
3. Polycystic ovaries: literally, many cysts in the ovaries. The prefix "poly" means "many."

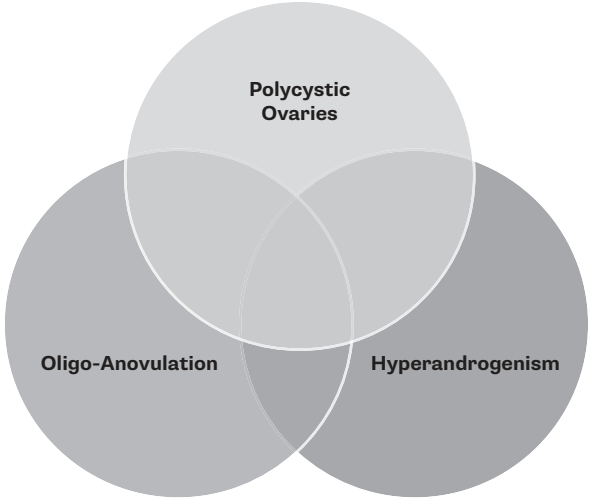

Figure 1.4. Diagnostic criteria[9]

In 2006 the Androgen Excess Society (AES) recommended that hyperandrogenism be considered the clinical and biochemical hallmark of PCOS. Without evidence of hyperandrogenism, they suggested, a person simply could not receive a diagnosis of PCOS. The AES recommendation of making hyperandrogenism a necessary criterion for PCOS diagnosis focused researchers and doctors on the underlying cause of disease rather than merely on the presence or absence of polycystic ovaries.

Today, the NIH criteria are rarely used. In 2012, an NIH Expert Panel recommended that the Rotterdam criteria be used for diagnosis. And being fairly similar to those criteria, the AES 2006 recommendations are commonly used as well.

Table 1.1. Criteria for the diagnosis of polycystic ovary syndrome[10]

NIH/NICHD[a] 1992	ESHRE/ASRM[b] (Rotterdam criteria) 2004	Androgen Excess Society 2006
Exclusion of other androgen excess or related disorders Includes all of the following: • Clinical and/or biochemical hyperandrogenism • Menstrual dysfunction	Exclusion of other androgen excess or related disorders Includes two of the following: • Clinical and/or biochemical hyperandrogenism • Oligo-ovulation or anovulation • Polycystic ovaries	Exclusion of other androgen excess or related disorders Includes all of the following: • Clinical and/or biochemical hyperandrogenism • Ovarian dysfunction and/or polycystic ovaries

[a] National Institutes of Health/National Institute of Child Health and Human Development

[b] European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine

It is important to note here that although obesity, insulin resistance, and type 2 diabetes are commonly found in association with PCOS, they are not part of the diagnostic criteria.