

**Effects of Western and Eastern Fertility Treatment Modalities on Conception in Women
with Polycystic Ovary Syndrome**

By

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ABSTRACT

Polycystic ovary syndrome (PCOS) can be considered the most common endocrine abnormality in women of reproductive age. With links to infertility, metabolic disorder, and some life-threatening diseases, it is a major public health concern worthy of extensive research. This is a qualitative, retrospective research study based on the case studies of two infertile women with PCOS who achieved pregnancy and live birth. The study entailed the collection and analysis of data from two medical charts. Both patients were treated by a practitioner of Traditional Chinese medicine and a reproductive endocrinologist (a different pair in each case). Each patient went through numerous Western fertility treatment cycles, employing a variety of drugs and procedures, and was also treated with a combination of acupuncture and herbs. The two cases demonstrate how infertile women with PCOS can become pregnant using a combination of Western and Eastern medicine. The differences and similarities between the cases are detailed in chart and narrative form. The information gleaned in this study can potentially guide health practitioners in treating this difficult malady, although further research is needed to determine optimal fertility treatments using a combination of Western and Eastern medicine.

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CHAPTER 1: INTRODUCTION

There is a saying often quoted in Chinese medical texts: “The treatment of women is ten times more complicated than that of men” (Lyttleton, 2004). One reason for that is childbearing. As natural as it may seem, the making of a baby is a complex endeavor. Many things must go right, and a lot can go wrong. The whole process is like an orchestra with numerous instruments playing a wide array of notes. When it goes well, it’s a beautiful symphony. When it does not, it can be a long, tedious ordeal for the approximately 10-15% of couples who are touched by infertility (Speroff & Fritz, 2005).

All gynecological disorders and a number of non-gynecological disorders can cause infertility, which can potentially be treated by both Eastern and Western medicine. Traditional Chinese medicine (TCM), with its use of acupuncture, herbs, and nutrition, and Western fertility medicine, with its use of drugs, intrauterine insemination (IUI), *in vitro* fertilization (IVF) and other procedures, attempt to overcome infertility in very different ways. The fact that they are so different means they have the potential to complement or enhance each other’s results (Lyttleton, 2004).

Polycystic ovary syndrome (PCOS), also known as polycystic ovarian syndrome, “can be considered one of the most common disorders of humans, and the single most common endocrine abnormality of women of reproductive age” (Azziz et al., 2009). It is a baffling and multi-dimensional condition, with many and varied opinions on the subject. It is a malady of great importance to our society because it is often accompanied by infertility. In addition, PCOS

frequently involves metabolic syndrome, which can include glucose intolerance, insulin resistance, obesity, an increased risk of Type 2 diabetes and cardiovascular disease (Beilby, 2004). The prevalence of PCOS in the general population is approximately 5% to 10% of women of reproductive age. It is, therefore, a major public health concern worthy of extensive research and clinical attention (Pfeifer & Kives, 2009). This study has the potential to benefit the larger community by shedding light on PCOS as a whole, and exhibiting solutions to the infertility dilemma that plagues it.

The purpose of this study is to identify successful treatment modalities combining Eastern and Western medicine for infertile PCOS females who achieve full-term pregnancies. This will be done by comparing and contrasting two case studies, and using the literature as a reference guide to analyze the data. There is a wealth of information on PCOS, spanning the period from 1935, when the syndrome was first described by two gynecologists in Chicago (Stein & Leventhal, 1935), to the famous Rotterdam conference in 2003, when a group of experts in the field of PCOS created a consensus to diagnose the syndrome (Franks, 2006), to the present day, with widespread interest due to its high prevalence, mysterious nature, and link to insulin resistance and diabetes. Western medicine typically treats PCOS with drugs and surgery, while TCM uses various tools including acupuncture, herbs, nutrition, and lifestyle changes.

The aim of the present study is to answer the following question: What are the effects of combined Western and Eastern fertility treatment modalities on conception in women with PCOS? It is hypothesized that an infertile woman with PCOS who is treated on a consistent basis with weekly acupuncture treatments and daily herbal intake for at least three months will

conceive sooner, with fewer Western medicine fertility cycles, than a woman who undergoes similar TCM treatment for less than three months.

There are various reasons for conducting this study. Due to the magnitude of its prevalence and potentially devastating effects, it is important to investigate if women with PCOS might be successfully treated for infertility with both Western and Eastern modalities. It is also beneficial to explore how TCM might aid Western medicine protocols to increase the rate of pregnancy success for women with PCOS. In addition, it is important to document the progress that both Western and Eastern medicine are making to better understand this complicated syndrome.

The goal of this study is to document and discuss ways for infertile PCOS women to get pregnant and deliver a baby. The information gleaned in this study can potentially be a guide for health practitioners (both Western and Eastern) to treat this difficult and widespread malady.

CHAPTER 2: LITERATURE REVIEW

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder with a diverse and complex presentation. Its etiology is uncertain, and its definition and diagnostic criteria remain controversial (Franks, 2006). PCOS affects 5% – 10% of women of reproductive age. It is characterized by hyperandrogenism, chronic anovulation, and infertility. However, it is not only a reproductive endocrinopathy. It is also considered a metabolic disorder associated with multiple cardiovascular risk factors including insulin resistance, diabetes mellitus, dyslipidemia, and hypertension (Pamuk et al., 2010).

This literature review will first cover PCOS from a Western medical perspective, and then it will delve into PCOS from a Traditional Chinese Medicine (TCM) point of view. There will be information about the condition as a whole, with treatment strategies to follow.

The Western Medicine Perspective on PCOS

The History, Definition, and Diagnosing of PCOS

References to what we now recognize as PCOS can be found in scientific publications dating back to the 19th century (Franks, 2006). It was first recognized as a medical disease in 1845 in France (Lewis, 2004). In 1935, two gynecologists from Chicago, Irving F. Stein and Michael L. Leventhal, first clearly described this symptom complex in a classic paper published in the *American Journal of Obstetrics and Gynecology* (Stein & Leventhal, 1935). The two doctors wrote about seven patients (four were obese) with amenorrhea, hirsutism, and enlarged,

polycystic ovaries. There was evidence of androgen excess, but not all patients had hirsutism, and three showed evidence of recent ovulation. Nevertheless, the combination of hyperandrogenism and chronic anovulation became the standard definition of PCOS for the next fifty years. This widely accepted definition was then published in the proceedings of an international workshop on PCOS held at the National Institutes of Health (NIH) in 1990. At that time, PCOS was defined as chronic anovulation associated with clinical and/or biochemical hyperandrogenism, assuming other potential diagnoses with a similar clinical presentation to PCOS are ruled out (Franks, 2006).

Ovarian morphology was not part of these early definitions, even though, during the 1980s, ultrasound imaging of the ovaries helped to show that polycystic ovaries were commonly associated with hirsutism and hyperandrogenism in women with regular, ovulatory cycles (Franks, 2006). Gradually, there was increasing awareness that the clinical expression of PCOS might be broader than that defined by the 1990 NIH criteria (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004). In May of 2003, a group of experts in the field of PCOS met in Rotterdam (The Netherlands) for a conference jointly sponsored by the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) (Franks, 2006). The end result was the creation of a consensus called the 2003 Rotterdam criteria to diagnose PCOS (Pfeifer & Kives, 2009). The Rotterdam criteria took into account the broad range of presenting features that could be attributed to PCOS, including women with androgen excess, but regular menses, and those with menstrual irregularities without androgen excess (Franks, 2006). It also included polycystic

ovarian morphology to be determined by transvaginal ultrasound. This was an important change from the 1990 NIH criteria (Rotterdam, 2004).

The following is a summary of the various criteria for diagnosis: According to the 1990 NIH criteria, a diagnosis of PCOS would depend on both of the following: 1) Chronic anovulation, and 2) Clinical and/or biochemical signs of hyperandrogenism, plus exclusion of other etiologies. In contrast, according to the 2003 Rotterdam criteria, a diagnosis would depend on 2 out of 3 of the following: 1) Oligo- or anovulation, 2) Clinical and/or biochemical signs of hyperandrogenism, and 3) Polycystic ovaries, plus exclusion of other etiologies (see table #1). Other disorders that might be confused with PCOS and need to be ruled out include Cushing's syndrome, congenital adrenal hyperplasia, androgen-secreting tumors, and hyperandrogenic-insulin resistant-acanthosis nigricans syndrome (Rotterdam, 2004).

<i>Table #1 – Diagnostic criteria for PCOS according to the 1990 NIH conference and the revised criteria from the ESHRE/ASRM sponsored consensus meeting, Rotterdam 2003.</i>	
NIH 1990	Rotterdam 2003
1) Chronic anovulation	1) Oligo- or anovulation
2) Clinical and/or biochemical signs of hyperandrogenism	2) Clinical and/or biochemical signs of hyperandrogenism
	3) Polycystic ovaries
The NIH definition requires both criteria to make the diagnosis. The ESHRE/ASRM requires two of three. For both, the diagnosis assumes exclusion of other diagnoses with a similar clinical presentation to PCOS (Franks, 2006).	

There is widespread belief that PCOS is most definitely a syndrome, and is therefore recognized as a collection of signs and features with no single test being diagnostic. Establishing a clear definition is important for both clinical and research purposes. The use of a broader definition (e.g. Rotterdam 2003) versus more restrictive criteria (e.g. NIH 1990) can lead to a

significant increase in the number of women seemingly affected by this disorder. However, a diagnosis of PCOS should not be given lightly as it can imply a number of serious issues including an increased risk of infertility, dysfunctional bleeding, endometrial carcinoma, obesity, insulin resistance/hyperinsulinemia, Type 2 diabetes mellitus, dyslipidemia, hypertension, and possible cardiovascular disease (Azziz et al., 2009). This paper will continue to explore the various issues that revolve around this complex syndrome, its diagnostic procedures, and treatment options.

Polycystic Ovaries

The classic image of the polycystic ovary is one that is enlarged, with a thickened ovarian stroma and an increased number of small follicles arranged peripherally around the ovarian cortex like a “string of pearls” (Buckett, Bouzayen, Watkin, Tulandi, & Tan, 1999; Elmashad, 2011). Various features can be used to assess the presence of polycystic ovaries. They include follicle size and number, and ovarian size and volume (Azziz et al., 2009). The Rotterdam criteria defines polycystic ovaries by the presence of 12 or more follicles in each ovary, with each follicle measuring 2-9 millimeters in diameter, and/or an increased ovarian volume of more than 10 milliliters. Only one ovary fitting this definition is sufficient to define polycystic ovaries. However, if a dominant follicle of more than 10 millimeters is detected, or there is evidence of a corpus luteum, the ultrasound should be repeated in the next menstrual cycle. This definition of polycystic ovaries does not apply to women on the oral contraceptive pill since the pill modifies ovarian morphology in normal women, and presumably does the same in women with PCOS (Rotterdam, 2004).

One study conducted at two Italian universities, assessed ovarian morphology in 326 women with an average age of 25 (Carmina et al., 2005). They had been diagnosed with PCOS using the clinical criteria of hyperandrogenism and chronic anovulation. Normal ovarian size in their control group of ovulating women was first calculated to be 1.9 to 7.5 centimeters. Compared to these controls, 60% of the PCOS women had an ovarian size of more than 7.5 centimeters, and 51% had an ovarian size of more than 10 centimeters. This shows a high percentage of enlarged ovaries in these two PCOS groups. It should be noted that the PCOS diagnosis used in this study was anovulation and not oligo-ovulation. Results may have shown a lower percentage of enlarged ovaries if the diagnosis was oligo-ovulation (Carmina et al., 2005). It should also be noted that other researchers have used an ovarian size of more than 5.5 centimeters to indicate the possibility of a positive PCOS diagnosis (Jonard et al., 2003).

The sole presence of polycystic ovaries has limited diagnostic value. Although approximately 20% of women with polycystic ovaries have PCOS (a number that is threefold higher than that found in the general population), polycystic ovaries are also common in young, healthy women (Azziz et al., 2009; Polson, Adams, Wadsworth, & Franks, 1988). Two English studies showed that women between the ages of 20 and 25 who considered themselves to be normal and had not sought treatment for menstrual irregularities or infertility exhibited polycystic ovaries 22% (Clayton et al., 1992) and 33% (Michelmore, Balen, Dunger, & Vessey, 1999) of the time. However, these numbers appear to decrease with age, with women older than 35 exhibiting polycystic ovaries only 7.8% of the time (Koivunen et al., 1999). Interestingly, a study on diabetic women in India showed a 52% higher prevalence of polycystic ovaries (Rodin,

Bano, Bland, Taylor, & Nussey, 1998). Similarly, another study demonstrated that women with a history of gestational diabetes had polycystic ovaries 52% of the time (Kousta et al., 2000).

Other studies have noted mild abnormalities in androgen secretion in asymptomatic women with polycystic ovaries (Norman, Hague, Masters, & Wang, 1995; Carmina et al., 1997). All in all, there appears to be a significant connection between polycystic ovaries and deviations in androgen levels, glucose metabolism, and insulin sensitivity (Azziz et al., 2009).

Ovulation Dysfunction: Anovulation/Oligo-ovulation

Ovulation dysfunction includes anovulation (the absence of ovulation) and oligo-ovulation (infrequent or irregular ovulation). There are women with PCOS that ovulate and those that do not (Azziz et al., 2009). Anovulation is not always chronic. Intermittent or even prolonged episodes of regular, ovulatory cycles can interrupt a pattern of anovulatory vaginal bleeding or amenorrhea (Franks, 2006). What appears to be a history of regular periods may actually be ovulatory dysfunction. Ricardo Azziz, and his fellow researchers, analyzed 20 separate studies, which provided an opportunity to observe data on 6,978 patients with PCOS. Within that pool, 79.11% had oligomenorrhea, which can be defined as “vaginal bleeding episodes” that are more than or equal to 35 days apart, or less than 10 bleeds per year (Azziz et al., 2009).

The theory of follicular arrest might explain the process of anovulation to some degree. The theory states that the natural progression of small antral follicles to selected follicles, and then eventually to a dominant follicle, does not proceed normally in PCOS (Jonard et al., 2003).

Normally one dominant follicle continues to grow and release an egg, while the others undergo atresia. Instead, the polycystic ovary has multiple follicles that grow to half or less than normal size. These immature follicles produce an abundance of estrogen, which tells the pituitary gland to decrease Follicle stimulating hormone (FSH) and produce Luteinizing Hormone (LH) in readiness to ovulate. However, none of the follicles are mature enough to ovulate, and so a stalemate is reached (Lyttleton, 2004). This phenomenon is related to hyperinsulinism (Jonard et al., 2003). The link between metabolic disturbance and anovulation is paramount to understanding the mechanism of arrested antral follicle development in anovulatory women with PCOS. Studies have shown that obese women with PCOS are more likely to be anovulatory than lean, hyperandrogenemic women, and that weight gain increases the chance of chronic anovulation (Franks, 2006).

The presence of anovulation can be determined by measuring serum progesterone (P4) on day 20 to 24 of the menstrual cycle. Serum P4 levels below 3 or 4 ng/mL can help indicate the presence of anovulation (Azziz et al., 2009). In one study, researchers measured P4 levels to determine which subjects ovulated and which did not. When levels dropped below 3 ng/mL, the diagnosis was anovulation. In patients with normal menses, at least two consecutive cycles were studied. Low levels of P4 in both cycles indicated chronic anovulation (Di Fede, Mansueto, Pepe, Battista Rini, & Carmina, 2010).

Hyperandrogenism

Hyperandrogenism affects around 7% of reproductive-aged women, and within that large group, the majority are diagnosed with PCOS. Many women with PCOS have both clinical and biochemical signs of androgen excess (Huang, Brennan, & Azziz, 2010).

Clinical Signs of Androgen Excess

The chief clinical signs of androgen excess are hirsutism, acne, and male pattern hair loss (A. Huang et al., 2010). The Rotterdam experts felt that hirsutism was the primary clinical indicator of hyperandrogenism, however the sole presence of acne was also thought to be a potential marker (Rotterdam, 2004).

Hirsutism is defined as the presence of terminal hairs on the face and/or body of a female in a male-type pattern. There is a visual scoring method commonly used to assess hirsutism. It is a modification to what was originally reported by Ferriman and Gallwey in 1961 (Ferriman & Gallwey, 1961). It consists of nine body areas, including the upper lip, chin, chest, upper back, lower back, upper and lower abdomen, upper arm, and thigh. Each area is assigned a score of 0-4 based on the density of terminal hairs. A score of 0 represents the absence of terminal hairs. A score of 1 represents minimal hair growth, and a score of 4 represents extensive hair growth. Various “cutoff values” have been used to diagnose hirsutism, such as 6 or more, 7 or more, or 8 or more (Azziz et al., 2009). For example, one study of 716 patients with PCOS found that 72%

had hirsutism based on a modified Ferriman-Gallwey (mFG) score. They used a cutoff value of 6 or more to help determine their results (DeUgarte, Woods, Bartolucci, & Azziz, 2006).

It should be noted that race and ethnicity are important factors when evaluating hirsutism. One study observed hirsutism to be more prevalent and more severe among PCOS patients of South Asian ancestry than among Whites (Wijeyaratne, Balen, Barth, & Belchetz, 2002). However, prevalence is less likely among those of East Asian descent. Overall, hirsutism is an important feature of PCOS, affecting approximately 65% to 75% of patients with PCOS, including Whites, Blacks, and Southeast Asians (Azziz et al., 2009).

It is not unusual to document some degree of acne as a result of androgen excess (Chang, 2004), although it varies with ethnicity. It affects approximately 12% to 14% of White PCOS patients, with increased percentages in certain races, such as Asian Indians (Wijeyaratne et al., 2002). Overall, acne affects 15% to 25% of PCOS patients, but it is hard to determine the significance of this since there is a high prevalence of acne in the general population (Azziz et al., 2009).

Androgenic alopecia is another term for male pattern hair loss. It is a recognized sign of PCOS, but its prevalence is unclear. In one study of 257 PCOS patients, only 12 (4.7%) complained of hair loss (Azziz et al., 2004). Estimates for this feature vary widely. More studies are needed to define prevalence (Azziz et al., 2009). Even less prevalent are virilization and clitoromegaly, extreme manifestations of androgen excess that are not typically found in PCOS (Chang, 2004).

Biochemical Signs of Androgen Excess

Assessing clinical hyperandrogenism may be subjective, but evaluating hyperandrogenemia is not. The most useful test to detect hyperandrogenemia is the free testosterone (T) level, when using a high quality, sensitive assay (A. Huang et al., 2010). The principle dehydroepiandrosterone (DHEA) metabolite is dehydroepiandrosterone sulfate (DHEAS) (Lobo, Paul, & Goebelsmann, 1981). The measurement of DHEA for the diagnosis of PCOS has limited diagnostic use (Azziz et al., 2009). DHEAS, on the other hand, has been the preferred method of assessing *adrenal* androgen production and has been traditionally used as the marker for adrenal androgen excess (Lobo et al., 1981). However, free T is more sensitive than DHEAS or total T in detecting hyperandrogenemia (Huang et al., 2010). Although some researchers have relied on the sole measure of total T, it turns out to have limited value (Hatch, Rosenfield, Kim, & Tredway, 1981). The combined measurement of free T, total T, and DHEAS appears to provide a reasonable evaluation of PCOS (A. Huang et al., 2010).

Even though PCOS has a prevalent *ovarian* androgen secretion, serum DHEAS is also elevated in many of these PCOS women. Increased circulating DHEAS levels can indicate the existence of hyperandrogenism. Two studies found increased DHEAS levels in about 50% of women with PCOS (Carmina, Rosato, & Janni, 1986; Wild, Umstot, Andersen, Ranney, & Givens, 1983). Other studies found increased DHEAS levels in lower numbers of PCOS women, such as 27% (Orio et al., 2003) and 22% (Chang, Knochenhauer, Bartolucci, & Azziz, 2005). “In PCOS, increased DHEAS is generally associated with increases in other circulating androgens”

(Chang et al., 2005). However, “DHEAS should be used with caution as a marker of adrenal androgen secretion, particularly in PCOS, as DHEAS levels may not always reflect alterations in adrenocortical steroidogenesis” (Azziz et al., 2009).

Metabolic Syndrome, Insulin resistance & Hyperinsulinemia

Polycystic ovarian syndrome is a complex metabolic disorder related to infertility and obesity (Maciel et al., 2004). Obesity occurs in about half of PCOS women. The type of obesity can be described as android, with an increased waist-to-hip ratio (Chang, 2004). Android or truncal obesity is typically more prevalent in men, whereas gynoid or lower-body obesity occurs more in women. Upper-body obesity creates a greater risk for cardiovascular disease than lower-body obesity regardless of gender (Vega, 2002).

Although the pathogenesis of PCOS is still unclear, it is now thought that insulin resistance and compensatory hyperinsulinemia play a critical role (Romualdi et al., 2010). Insulin resistance results in a compensatory increase in insulin secretion by the pancreas in order to maintain normal glucose homeostasis (Azziz et al., 2009). The current thinking is that hyperinsulinemia may contribute to the etiology of hyperandrogenism (Romualdi et al., 2010). There are a variety of theories that explain how insulin stimulates the release of androgens. There are both direct and indirect mechanisms (Pfeifer & Kives, 2009). Several studies have suggested that insulin stimulates the cytochrome P450c17 α , which in turn increases androgen production by the theca and adrenal cells (Maciel et al., 2004). In other words, abnormal hyperactivity of

this enzyme alters steroidogenesis in the ovaries and adrenal glands prompting a hyperandrogenic state (Speroff & Fritz, 2005).

Another theory for how insulin causes hyperandrogenism involves sex hormone-binding globulin (SHBG), which is a protein carrier of the major sex steroids, including testosterone. SHBG is produced in the liver (Speroff & Fritz, 2005). In a normal state, testosterone circulates in the blood bound to SHBG, and only the unbound or free fraction testosterone enters the tissues (Azziz et al., 2009). However, when hyperinsulinemia is present, the excess insulin acts directly on the liver to decrease synthesis of SHBG, which then increases available and active androgens (Kasa-Vubu, Jain, & Welch, 2010; Pfeifer & Kives, 2009; Romualdi et al., 2010). The decrease in SHBG is associated with an increase in free testosterone (Speroff & Fritz, 2005). Obesity decreases SHBG (Chang, 2004). Women with PCOS often have low circulating levels of SHBG, and therefore serum SHBG might be a simple and effective method to document insulin resistance (Azziz et al., 2009; Speroff & Fritz, 2005).

Another factor in the insulin to androgen story involves insulin-like growth factors, which resemble insulin in structure and function (Speroff & Fritz, 2005). Insulin increases androgen levels by stimulating insulin-like growth factor 1 (IGF-1) secretion (Romualdi et al., 2010). Insulin and IGF-I may act as “co-gonadotropins” in the ovary, stimulating theca cell production of androgens (Kasa-Vubu et al., 2010).

Theories have focused on LH stimulation and the role of insulin in hyperandrogenism. It is said that insulin directly increases production of LH and androgens by activating its own

receptor on the ovary, adrenal, and pituitary. Elevated LH levels increase production of androgens from the theca cell of the ovary (Pfeifer & Kives, 2009).

Insulin-lowering/sensitizing medications have been shown to benefit ovulation and fertility (Franks, 2006). Studies in PCOS patients have demonstrated that Metformin reduces serum levels of insulin, LH, and testosterone, improves insulin resistance, decreases the number of antral follicles, and improves ovulation (Bayrak et al., 2007). Furthermore, one study showed that Metformin was effective in decreasing hyperandrogenemia and increasing ovulatory frequency in non-obese PCOS women who were not insulin resistant (Baillargeon, Jakubowicz, Luorno, Jakubowicz, & Nestler, 2004).

Other Diagnostic Markers

For women who present with oligo/anovulation, the initial workup should include an assessment of hormones, including FSH and Estradiol (E₂). This is key in ruling out hypogonadotropic hypogonadism (central origin of ovarian dysfunction), and premature ovarian failure as distinguished by low E₂ and high FSH (Rotterdam, 2004).

It may be useful to test for LH as both the absolute level of circulating LH, as well as its relationship to FSH, are significantly elevated in PCOS (Rotterdam, 2004). Patients with persistent anovulation have high LH, but low or low-normal levels of FSH (Speroff & Fritz, 2005). PCOS is often associated with an increased LH-to-FSH ratio (Svendsen, Madsbad, & Nilas, 2010). This shift in gonadotropins is due to an increased amplitude and frequency of LH

pulses. Research has shown that elevated LH levels (above the 95th percentile of normal) were observed in around 60% of women with PCOS, whereas the LH/FSH ratio was elevated in up to 95% of subjects, if those who had recently ovulated were excluded (Rotterdam, 2004).

A study was done in Michigan to analyze the impact of higher adiposity (“fatness”) and LH secretion in adolescent females (Kasa-Vubu et al., 2010). The researchers noticed that the adolescent population had been growing heavier, and that the number of females affected with PCOS had been increasing as well. Younger patients had been presenting with signs of PCOS, such as oligomenorrhea, insulin resistance, and excess androgens. Adolescence is a transitional time, one of instability in the hypothalamic-pituitary-ovary axis. The onset of fertility disorders related to obesity can begin during this transition. The researchers postulated that heavier adolescents would secrete LH with increased pulse frequency. They found that higher adiposity, as reflected by body fat percentage or by the measure of leptin (the adipocyte hormone that is a biochemical marker of obesity), has a stimulatory effect on the hypothalamic GnRH pulse generator, thereby leading to an increased number of LH pulses during a 24 hour period (Kasa-Vubu et al., 2010).

Most experts who attended the Rotterdam conference thought that prolactin should be routinely measured when evaluating hyperandrogenism and PCOS. Many patients with androgen excess have prolactin levels that are slightly above normal or in the upper normal limit (Rotterdam, 2004). Since menstrual irregularities can also be due to hyperprolactinemia, it is important to rule that out. Therefore, hyperprolactinemia is an exclusion criterion for the diagnosis of PCOS (Escobar-Morreale, 2004).

Another important condition to rule out is 21-Hydroxylase-deficient non-classic adrenal hyperplasia, which is one of the most common autosomal recessive disorders. Nonclassic adrenal hyperplasia and PCOS present very similarly in the clinic. They can both exhibit ovulatory and menstrual dysfunction, hirsutism, acne and alopecia, as well as increased androgen levels. However, unlike PCOS, non-classic adrenal hyperplasia can be simply diagnosed with serum elevations of 17-hydroxyprogesterone (17-OHP) (Pall, Azziz, Beires, Pignatelli, 2010).

Other disorders that might be confused with PCOS and need to be ruled out include Cushing's syndrome, androgen-secreting tumors, and hyperandrogenic-insulin resistant-acanthosis nigricans syndrome (Rotterdam, 2004). Hyperandrogenism and insulin resistance are often associated with Acanthosis nigricans, a gray-brown discoloration of the skin, usually at the neck, groin, axilla, and under the breasts (Speroff & Fritz, 2005). This disorder is common in obese PCOS women (Chang, 2004), but it can also be seen in normal women (Speroff & Fritz, 2005). Cushing's syndrome, a situation of excess cortisol production, can also present with obesity, hirsutism, acne, and menstrual irregularity. However, additional characteristics of Cushing's include a moonlike face, buffalo hump, and abnormal cortisol secretion, which can help distinguish it from PCOS. Androgen-producing neoplasms can also present with hirsutism, acne, irregular menstrual cycles or amenorrhea, but these tumors can also create virilization, clitoromegaly, and lowering of the voice. The difference between a "functional hyperandrogenic syndrome" such as PCOS and the neoplastic process is the rapid and dramatic onset (possibly within a matter of months). That most important clue helps pin down a diagnosis (Chang, 2004).

Western Medical Treatment of PCOS

Subfertility in PCOS women is mainly due to anovulation. Therefore, the main treatment for infertile women with PCOS is ovulation induction. (Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008). However, a primary treatment strategy for PCOS involves weight loss, diet, and exercise. A weight loss as small as 5% can make a significant difference in lowering androgen levels, improving hirsutism, resuming normal menses, and decreasing insulin resistance, although it may take months to see these results (Heiman, 2009).

Clomiphene citrate (CC, Clomid) is a first-line drug for treating anovulation (Pfeifer & Kives, 2009). It is an orally administered nonsteroidal ovulatory stimulant, one of a group of drugs characterized as selective estrogen receptor modulators (SERMs). Clomid is one of the drugs given most frequently for infertility. It is used to induce ovulation in anovulatory patients, and also help correct irregular ovulation (Lewis, 2004). Clomid is an anti-estrogen that is the treatment of choice for ovulation induction in anovulatory women with PCOS (Thessaloniki, 2008). Approximately 75% to 80% of women ovulate in response to Clomid (Pfeifer & Kives, 2009). However, Clomid accumulates in the body because of its long half-life, and as a result, may have a negative effect on the quality and quantity of cervical mucus, and on endometrial development (Mitwally & Casper, 2001). Clomid has also been known to produce hot flashes, headaches, and visual disturbances (Thessaloniki, 2008).

The recommended starting dose for Clomid is generally 50 milligrams a day for five days, starting on cycle day (CD) 2, following a spontaneous or progestin-induced withdrawal

bleed. The maximum suggested dose is 150 milligrams a day, as studies were not able to show increased effectiveness at higher doses. The Food and Drug Administration (FDA) recommends a maximum of 750 milligrams per treatment cycle. Additionally, treatment is generally limited to six cycles (Thessaloniki, 2008).

With insulin resistance now thought to play a major role in PCOS, insulin-sensitizing agents are often used. Metformin is the most widely studied of all insulin-sensitizing drugs. It inhibits hepatic glucose production and increases peripheral tissue sensitivity to insulin. With 1500 to 2000 milligrams a day, Metformin has been shown to decrease androgens, decrease insulin, improve ovulatory rates, and resume menstrual regularity (Pfeifer & Kives, 2009). Metformin has been proposed as a first-line treatment in obese or overweight women with both PCOS and hyperinsulinemia (Romualdi et al., 2010). It has also been shown to decrease hyperandrogenemia and increase ovulatory frequency and in non-obese PCOS with normal insulin levels (Baillargeon et al., 2004). Some researchers believe that a combination of Metformin and Clomid should be considered first-line therapy for infertile women with PCOS who want to achieve a live birth (Jungheim & Odibo, 2010).

Surgery is another treatment option for women with PCOS. Laparoscopic ovarian drilling (LOD) has been used to treat anovulatory infertility in Clomid resistant women with PCOS. The mechanism of action is unclear, but LOD may decrease ovarian androgen production by reducing stromal mass or disrupting parenchymal blood flow. The idea is to change the ovary from an unfavorable androgenic environment to an estrogenic one in order to stimulate follicular development and ovulation. However, there are two drawbacks with LOD: the risks involved

with any surgical procedure, and the issue of adhesion formation, which can potentially interfere with fertility (Mercorio et al., 2008).

A consensus compiled in 2007 on infertility treatment related to PCOS stated that, in principle, anovulation is not an indication for IVF. The logical therapy for PCOS is ovulation induction, especially with clomiphene citrate. If that fails, exogenous gonadotropin therapy can be used. Many PCOS women are very sensitive to the use of ovulation induction agents. One major complication is a 10% multiple pregnancy rate, especially with gonadotropin therapy. Another major problem is the risk of ovarian hyperstimulation syndrome (OHSS), a complication that also occurs with the use of gonadotropin stimulation (Thessaloniki, 2008). OHSS is characterized by ovarian enlargement, pleural effusion, ascites, oliguria, and potential for thromboembolism, and possibly (albeit rarely) death (Griesinger, 2010). The incidence of OHSS in patients with PCOS has been reported to be as high as 30% (Huang, Chian, & Tan, 2010). Careful monitoring is essential to reduce the risk of both OHSS and multiple pregnancies in both IVF and IUI cycles. The use of IVF with a single-embryo transfer is a reasonable option for markedly reducing the risk of multiple pregnancies (Thessaloniki, 2008).

More recent advances in Western fertility medicine include *in vitro* maturation (IVM), which has been an established treatment option in many centers worldwide for over a decade (J. Huang et al., 2010). IVM avoids the risks and side effects of ovarian stimulation (namely OHSS) by retrieving immature oocytes from unstimulated ovaries. The immature oocytes are then cultured, matured, and fertilized *in vitro*. The best embryos are then selected for transfer in the same way as conventional IVF. There has been significant progress improving clinical

pregnancy and live-birth rates with IVM, but there is still much to learn about maturation, fertilization, and implantation rates (Reinblatt & Buckett, 2008).

The Traditional Chinese Medicine Perspective on PCOS

Traditional Chinese medicine (TCM) is an ancient medical system that heals by improving homeostasis in the body. In TCM theory, Qi (vital energy, life force) moves through pathways that are associated with organs and systems. Qi can be manipulated to encourage balance within the body. Ancient texts profess that Jing (seed of life, life essence) is responsible for fertility. This substance that is “most closely associated with life itself” is stored in the Kidney, which is why the Kidney organ system is said to contain “potential for life activity” (Stone, Yoder, & Case, 2009). The Kidney governs birth, growth, reproduction and development (Maciocia, 1989), and is therefore responsible for all functions related to the uterus, fallopian tubes, ovaries, and hypothalamic-pituitary-ovarian axis (Maciocia, 1998).

Diagnosing PCOS in TCM Terms

There is no mention of PCOS in the ancient TCM texts (Song, Yan, Wu, & Hou, 2006), but PCOS, a disruption of the ovaries, is thought to be the result of Kidney disharmony (Lyttleton, 2004; Stone et al., 2009). It is mainly considered to be a condition of Kidney deficiency, possibly accompanied by Blood stasis, Phlegm-Damp, and/or Liver Qi stagnation (Song et al., 2006; Jin, 1998).

Phlegm-Damp accumulation is a TCM diagnosis often associated with PCOS. The enlarged polycystic ovaries could be a consequence of accumulated damp, which then transforms into phlegm. Phlegm-Damp is a complex phenomenon that includes congealing of fluids, which then creates stagnation and disrupts function. It is often associated with obesity, or at least a tendency to gain weight. Phlegm-damp typically develops as a result of other pathologies, such as Kidney Yang deficiency and/or Spleen Qi deficiency (Lyttleton, 2004).

PCOS can show up in many forms, be it a mild, moderate or severe case, or a thin, fat, or normal weight body. The Kidney Yin deficient type of PCOS might stem from Qi and Blood deficiency, or Qi stagnation. This type of PCOS woman might be thin, wiry, and restless, ovulate irregularly or infrequently, and have high testosterone. In contrast, the Kidney Yang deficient woman may have stopped ovulating altogether (Lyttleton, 2004).

Some clinics in China use the ratio of LH-to-FSH in serum to aid their PCOS TCM diagnosis. An LH-to-FSH ratio greater than 2.5 indicates Kidney Yang deficiency and Phlegm-Damp accumulation, whereas an LH-to-FSH ratio less than 2 indicates a predominance of Kidney Yin deficiency. In general, the treatment of Kidney Yang deficiency is more successful in terms of ovulation and conception rate than the treatment of Kidney Yin deficiency (Lyttleton, 2004).

Treating PCOS with Chinese Herbs

Chinese medicine treats ovulation disorders by trying to re-establish regular menstrual cycles. The process of achieving ovulation may require clearing excess, such as phlegm-damp or blood stasis, and/or strengthening deficiencies, such as building up the blood, yin, and yang. As signs of ovulation develop, the Kidney Yang can be bolstered to promote successful ovulation. (Lyttleton, 2004)

Pharmacological studies in China, both clinical and experimental, have confirmed that Kidney strengthening herbs have hormonal-like effects. Chinese herbs that replenish the Kidney, combined with activating herbs that circulate blood and remove stagnation, were found to improve blood flow to the ovaries, promote follicular development, induce ovulation, and encourage luteum formation (Song et al., 2006).

One study published in Chinese and reviewed by Song et al. (2006) consisted of 76 PCOS patients who had been diagnosed with Spleen and Kidney Yang deficiency (Hua, Wu, & Zhang, 2003). According to Song et al. (2006) the women in the Hua et al. (2003) study were given a Chinese herbal formula that included the following herbs: Dodder Seed (Tu Si Zi) (12 g), Plantain Seed (Che Qian Zi) (10 g), Epimedium (Yin Yang Huo) (10 g), Eucommia Bark (Du Zhong) (10 g), Chinese Angelica (Dang Gui) (10 g), Peach Kernel (Tao Ren) (10 g), fresh Job's tears seeds (fresh Yi Yi Ren) (10 g), and Chuan Xiong (3 g), plus other herbs that were not listed in the research article. The control group included 31 PCOS patients who were treated with Clomid. Results showed that both treatments reduced serum levels of LH and testosterone, but

the Chinese herbal formula proved superior to Clomid by improving pregnancy rate, body mass index (BMI), Ferriman-Gallwey (F-G) scoring, and reactions to the oral glucose tolerance test (OGTT). The pregnancy rate in the TCM group was 65.7% and the change in F-G scoring was reported by Song et al. (2006) to be significant. In contrast, the pregnancy rate in the Clomid group was 25.0%, and the change in F-G scoring was reported by Song et al. (2006) to not be significant.

Another study published in Chinese and reviewed by Song et al. (2006) used herbs to treat 46 PCOS patients based on the 4 phases of the menstrual cycle (He, 2004). According to Song et al. (2006) the treatment principle in the He (2004) study was to strengthen Kidney and activate blood circulation in order to remove stasis and regulate menstruation. The basic herbal formula consisted of Epimedium (Yin Yang Huo) (30 g), Curculigo Rhizome (Xian Mao) (10 g), Dodder Seed (Tu Si Zi) (30 g), Degelatinated Deerhorn (Lu Jiao Shuang) (30 g), Eclipta (Han Lian Cao) (30 g), Grossy Privet (Nu Zhen Zi) (30 g), Chinese Angelica (Dang Gui) (15 g), Chuan Xiong (10 g), Motherwort (Yi Mu Cao) (15 g), Milkvetch (Sha Yuan Ji Li) (15 g), and Licorice (Gan Cao) (6 g).

According to Song et al. (2006) the above formula was modified during cycle day (CD) 6 through 10 to nourish Kidney Yin and regulate Chong and Ren (He, 2004). At that time, the following herbs were added: Wolfberry (Gou Qi Zi) (30 g), and Solomonseal (Huang Jing) (30 g). During the pre-ovulation stage, CD 11 to 14, herbs for regulating Qi and activating blood were added, such as Red Sage Root (Dan Shen), Bugleweed (Ze Lan), and Cyperus Tuber (Xiang Fu). In the post-ovulation stage, CD 15 to 23, herbs for replenishing Kidney Yang were

added, such as Eucommia Bark (Du Zhong), Teasel Root (Xu Duan), Mulberry Mistletoe (Sang Ji Sheng), and Ass-Hide Gelatin (E Jiao). In the pre-menstrual stage, CD 24 to 28, the following herbs were added to help the menstrual blood flow more smoothly: Cyanthula Root (Chuan Niu Xi), Peach Kernel (Tao Ren), Safflower (Hong Hua), Zedoary Turmeric (E Zhu), and Burreed Tuber (San Leng). Other issues were addressed when necessary with the following modifications. If the size of the ovary expanded, herbs that soften and resolve hard masses were added, such as Prunella (Xia Ku Cao), Kelp (Kun Bu), and Pleione (Shan Ci Gu). If the period was delayed and the patient had a choppy pulse, dark purple tongue and thin, white coat, then herbs that break blood stasis were added, such as Leech (Shui Zhi), Gladfly (Meng Chong), and groundbeetle (Tu Bie Chong). The results of the study, as reported by Song et al. (2006), showed that 10 out of 46 patients got pregnant, and 30 patients had restored menstrual cycles accompanied by biphasic basal body temperature (BBT) charts, plus lowered BMI, waist-hip ratio (WHR), and testosterone levels.

One more study published in Chinese and reviewed by Song et al. (2006) is worth mentioning because it is a good example of integrative medicine (Hou, Yu, & Wei, 2000). Researchers observed 22 PCOS patients who had been unsuccessfully treated with Clomid. They separated the women into two groups in order to compare and contrast treatment with Metformin and Chinese herbs. Results reported by Song et al. (2006) showed that the herbs were better at promoting ovulation, and that Metformin was better at lowering insulin. Metformin was also shown to improve the ovaries, help follicle maturation, and reduce spontaneous abortions. The herbal formula also helped improve insulin resistance. According to Song et al. (2006), the authors concluded that the two medicines used together could improve clinical efficacy.

Treating PCOS with Acupuncture

Modern studies performed in China have shown acupuncture to have a regulatory effect on the hypothalamus-pituitary-ovarian axis. Researchers have found that acupuncture is capable of normalizing secretions of FSH, LH, E2 and P4 to improve ovulation (Song et al., 2006). One study on ovulation rate in PCOS patients that was published in Chinese and reviewed by Song et al. (2006) used 120 subjects (Yang, Hong, & Wei, 2005). Sixty women in the treatment group received acupuncture, and sixty women in the control group received Clomid and human chorionic gonadotropin (hCG). The acupuncture was started on CD 10 and lasted for five to ten consecutive days. Three groups of acupuncture points were used on alternate days. Group one consisted of SP-6, Ren-4, SP-8, and ST-28. Group two consisted of ST-29, Kid-12, Ren-2, and SP-10. Group three consisted of Ren-3, ST-28, ST-29, and SP-6. Needles were retained for 30 minutes. Points were selected based on the following explanation: TCM holds that the Yin meridians are controlled by Ren mai, and that pregnancy can only take place when the Chong and Ren Mai are harmonious and menstruation runs smoothly. Therefore, the treatment principle as reported by Song et al. (2006) was to nourish Kidney essence, regulate Liver, Chong and Ren, balance yin and yang and Qi and blood, nourish the uterus, and recover ovulatory function.

According to Song et al. (2006), ultrasounds monitored the size of the follicles beginning on CD 12 (Yang et al., 2005). When follicles reached 16 to 18 millimeters, the acupuncture was stopped and sexual intercourse was advised. In the meantime, the control group began 100 milligrams of Clomid per day for five days on CD 5. The control group patients were also

monitored by ultrasound. When follicles reached 18 millimeters, 5,000 to 10,000 units of hCG were injected to promote ovulation. Sexual intercourse was then advised. It should be noted that when patients in either group did not have regular cycles, treatment began on the tenth day of a withdrawal bleed induced by an intramuscular injection of P4. Results of the study as reported by Song et al. (2006) were as such: The treated group had an ovulation rate of 83.2% and a pregnancy rate of 60.6%. The control group had an ovulation rate of 70.5% and a pregnancy rate of 31.7%. These results, according to Song et al. (2006), suggested that the efficacy of acupuncture in treating PCOS to improve ovulation rate was significantly superior to that of the Clomid plus hCG treatment.

Dr. Elisabet Stener-Victorin is a researcher at Institute of Neuroscience and Physiology, Department of Physiology at Sahlgrenska Academy, Göteborg University in Sweden. She has worked with acupuncture research since 1991 with a focus on investigating the effect of electro-acupuncture (EA) in reproductive medicine both in clinical and experimental studies (“Acupuncture Benefits,” n.d.). One such prospective randomized controlled trial in women with PCOS investigated whether low-frequency EA would decrease hyperandrogenism and improve oligo/amenorrhea more effectively than physical exercise, or than no active intervention at all (Jedel et al., 2011). Acupuncture treatments were given twice weekly for two weeks, after that once weekly for six weeks, and then once every other week for eight weeks, for a total of 14 treatments over 16 weeks. The point protocol included those in abdominal muscles with innervations corresponding to the ovaries, such as Ren-3, Ren-6, and ST-29. Additional points on the arms and legs included SP-6, SP-9, LI-4, and PC-6. All needles were stimulated manually upon insertion. Ren-3, Ren-6, ST-29, SP-6, SP-9 were also stimulated electrically with low-

frequency EA of 2 hertz. LI-4 and PC-6 were stimulated manually by rotating the needle at least 180 degrees every ten minutes. Each treatment lasted 30 minutes. Results showed that repeated low-frequency EA was more effective than physical exercise at reducing serum testosterone and improving regularity of the menstrual cycle, and that both EA and physical exercise were more effective than no active intervention at all (Jedel et al., 2011; Stener-Victorin, Jedel, Janson, & Sverrisdottir, 2009).

Not all pearls of wisdom come from formal studies. Much wisdom is gained from ancient texts and the personal experience of seasoned practitioners. Dr. Yu Jin writes about an acupuncture strategy to induce ovulation. It involves four points: Ren-3, Ren-4, Zi Gong Xue, and SP-6. Ren-3 is a major point for regulating reproductive function. It is also a point that treats the Kidney, Liver, and Spleen, three channels that are closely related to treating reproductive dysfunction. Ren-4 is important for urogenital disorders. Zi Gong Xue treats irregular menstruation, and is a unique point for treating infertility. SP-6 is essential for gynecological disorders, because of its regulatory action on the Kidney, Liver, and Spleen channels. Acupuncture promotes the flow of Qi and blood within the channels. Studies suggest that it plays a central neuro-endocrinal function in inducing ovulation, and that 50% to 60% of anovulatory women ovulate after acupuncture (Jin, 1998).

In conclusion, this study was created to find useful information about helping infertile PCOS women achieve pregnancy and live birth. Although, it is valuable to learn from the results of a well-executed randomized controlled trial, it is also helpful to observe successful case studies and other types of systematic research. Some of the studies reviewed above were done in

China. It is difficult to know what the quality of the research was since the original articles were in Chinese. However, it is the opinion of this author that the information from these studies is important because it provides an opportunity to learn on various levels. Whether the reader chooses to draw conclusions about specific acupuncture and herbal protocols used, or whether he or she simply learns that integrative medicine is being used and studied in China, there is valuable data to be shared. Still, there remains a shortage of studies on the efficacy of Chinese medicine in the treatment of PCOS. On the other hand, PCOS has been well studied by Western medicine, with a plethora of research articles published to date and probably many more on the way. It is assumed that this study might stimulate additional research and provide useful information for the successful treatment of infertile PCOS women who want to achieve pregnancy and live birth.

It is hypothesized that an infertile woman with PCOS who is treated on a consistent basis with weekly acupuncture treatments and daily herbal intake for at least three months will conceive sooner, with fewer Western medicine fertility cycles, than a woman who undergoes similar TCM treatment for less than three months.

CHAPTER 3: METHODOLOGY

This is a qualitative research study based on the case studies of two patients. The qualitative approach allows a researcher to seek the holistic picture – a comprehensive and complete understanding of the topic they are studying. It is a descriptive approach that takes an in-depth look at the essential character or nature of something. The data gathered in this type of study describe people’s knowledge, opinions, perceptions, and the meanings they attach to activities or events. The qualitative approach endeavors to discover and explore concepts. It is a way “to uncover and understand what lies behind any phenomenon about which little is yet known” (Roberts, 2010).

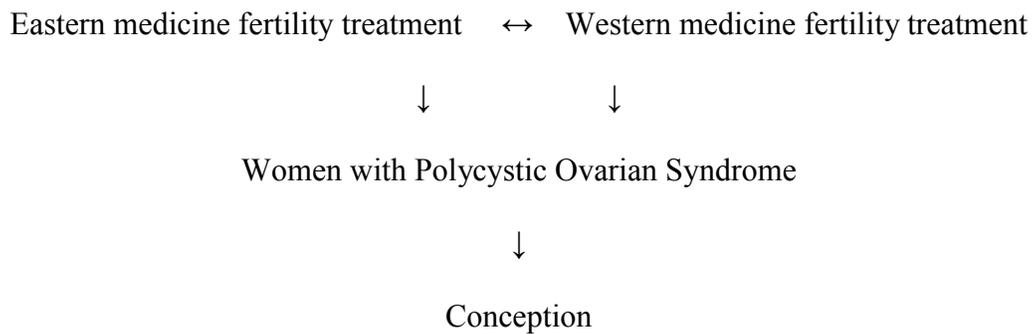
The case study format and qualitative research approach is an effective way to document the PCOS infertility to pregnancy story, because it describes and discusses many aspects of the process – from diagnosis to treatment to results. The study entailed the collection and analysis of data from two medical charts. Comparing and contrasting two cases has demonstrated a couple of ways for infertile women with PCOS to get pregnant using Western and Eastern medicine.

This is a retrospective study, as the research design was based on previously collected data (MacPherson, 2008). Non-probability, purposive sampling was applied (Roberts, 2010). One medical chart was chosen and reviewed through each office of two Los Angeles health practitioners, a reproductive endocrinologist and a Chinese medicine practitioner. Both patients were treated by a practitioner of Traditional Chinese medicine and a reproductive

endocrinologist (a different pair in each case). Charts were selected on the following predetermined inclusion and exclusion criteria. The inclusion criteria were women with PCOS diagnosed via the 2003 Rotterdam criteria, which depends on two out of three of the following: 1) Oligo- or anovulation, 2) Clinical and/or biochemical signs of hyperandrogenism, and/or 3) Polycystic ovaries diagnosed with a vaginal ultrasound, plus exclusion of other etiologies such as Cushing's syndrome, congenital adrenal hyperplasia, androgen-secreting tumors, and hyperandrogenic-insulin resistant-acanthosis nigricans syndrome (Rotterdam, 2004). Inclusion criteria also included an initial infertility diagnosis, which is defined as one year of unprotected intercourse without conception (Speroff & Fritz, 2005), and subsequent pregnancy with the help of Western and Eastern medicine resulting in a live birth. Exclusion criteria consisted of women over age 45, male factor infertility, hyperprolactinemia, fallopian tube defects, and endometrial lining abnormalities.

The theoretical/conceptual model starts with Eastern and Western fertility treatments. It's about how they work together to treat PCOS effectively enough to result in conception. (See Figure #1)

Figure #1: Theoretical/Conceptual Model



In terms of risk-to-benefit ratio, this study was set up so that the benefits would far outweigh the risks. It was assumed that this study would benefit a large community of practitioners and patients by documenting Western and Eastern medical treatment that would help infertile PCOS women conceive and deliver a baby. Patient charts were selected by two independent health practitioners based on the above inclusion and exclusion criteria. As for risks in this retrospective study, case charts and patients' names were handled with the utmost care. Precautions to minimize risks included the author of this study not being privy to either patient's real name. A fake name was given to one patient after recording details of the chart in the practitioner's office (see table #2). No chart was copied or taken out of the office. In the case of the second patient, one of the health practitioners delivered the chart details over the phone to the author. There was no physical contact with the chart or the office. The second patient was given a fake name as well (see table #2).

The data-collection instrument used for this study is entitled "Data Abstraction Chart" (see table #2). Data were reported in chart form to show differences and similarities between the two cases and their use of Western and Eastern treatments to achieve pregnancy. The chart displayed and organized the data, which helped to analyze results qualitatively as data were compared and contrasted. The chart includes age, race/ethnicity, marital status, diagnostic criteria, body mass index and height and weight, and time spent trying to conceive. The chart also includes Western medicine protocols, such as IVF and IUI dates and drugs. Information about follicles, eggs and embryos were also listed when applicable. The chart includes Chinese herbal formulas and acupuncture points for both patients. Miscarriages and other complications, plus pregnancy and live birth, were documented in the data abstraction chart as well. Data were

also abstracted into a timeline chart for each patient (see tables #3 and #4), allowing the events to be displayed with time as the variable. Data were also reported in the form of case descriptions for each patient.

The following is an explanation of the elements within the data abstraction chart (see table #2), and why they were relevant to this project. At the top of the chart is one of the most important determinants of conception, and that is age. Fertility studies have clearly stated that fertility declines with advancing age (Speroff & Fritz, 2005). As for ART and age, annual reports on “success rates in the U.S. derived from registry data collected by the Society for Assisted Reproductive Technology (SART) and the Centers for Disease Control and Prevention (CDC) since 1989 have consistently demonstrated that age is the single most important factor affecting the probability of success with ART” (Speroff & Fritz, 2005). Thus age is important whether we are dealing with PCOS, endometriosis, thyroid dysfunction, or a woman who appears to be perfectly healthy. Race and ethnicity were also important variables to explore, since PCOS affects such a large segment of the population (DeUgarte et al., 2006).

Obtaining a clear diagnosis of PCOS is not always easy, as was indicated in the literature review. However, having a proper Western medicine diagnosis was critical to this study. The 2003 Rotterdam criteria is part of the inclusion criteria, so only patients that had at least two of the three criteria were included. Space was created for other diagnostic criteria that are not part of the Rotterdam criteria but that may have been important clues to the presence of PCOS, such as acne or hirsutism. Interest in body fat, due to a high risk of obesity in PCOS (Azziz et al., 2009), explains the inclusion of height/weight and body mass index as an entry on the chart.

Since the study tracked conception success in patients receiving Western fertility treatments, the data abstraction chart was designed to include all dates for those procedures. Whether a patient did IVF, IUI, or timed intercourse, it was important to know how many cycles were done, what the timeframe was for each cycle, and how much time was between cycles. A variety of drugs were used. It was assumed that the type, dosage and frequency of these drugs would be significant in the ability to conceive and maintain a pregnancy. Therefore, the chart was used to report the many drugs that were prescribed for each patient. Drug side effects were also important to note especially since women with PCOS are prone to developing Ovarian Hyperstimulation Syndrome (OHSS) when undergoing ART (Salamalekis et al., 2004).

The number of follicles within each ovary, the eggs retrieved, and the ensuing fertilization and embryo transfer process were bound to provide data worth investigating, so these items were included in the data abstraction chart. The Chinese medicine aspect of the study necessitated a diagnosis, as well as treatment protocols. Dates for the TCM treatments, as well as specific acupuncture points, herbs, and dosages were systematically listed in the chart to help with data evaluation. Since miscarriages are a frequent occurrence in PCOS (Stone et al., 2009), it was also an important entry to have on the chart, as was live birth, part of the inclusion criteria.

CHAPTER 4: RESULTS

This retrospective study employed qualitative analytic methods, such as finding themes within the data, categorizing the variables, and finding and discussing similarities and differences. A total of two patient charts were evaluated for this study. The patients are referred to as Claire and Katie. Case descriptions of each patient are as follows:

Description of Claire's Case

The following description of Claire's case is based on her chart notes, which were partially abstracted into table 2 and table 3. Claire was a 34 year-old Caucasian, nulligravida female who presented to her RE Clinic in September 2008. Her chief complaints were irregular periods and infertility. She was married for 10 years, and had been trying to conceive for 1.5 years. Her fertility workup with the Reproductive Endocrinologist (RE) provided a diagnosis of PCOS, oligo-ovulation, and oligomenorrhea. There were no excess androgens or hirsutism.

Claire had a stressful job, and often had back pain from sitting too much. She exercised regularly and slept well, but her energy was sometimes low. She had frequent urination, increased thirst, and was prone to urinary tract infections. She had no allergies, and did not drink or smoke. She maintained a normal weight at 5'8" and 138 pounds.

Menarche was at age 13. She was on OCP for 17 years, starting at age 14. She stopped in May 2007, and it took four months to get her menses back. Whenever she was off oral

contraceptive pills (OCP), her periods were irregular and her acne flared up. The irregularity of her menstrual cycle was such that her periods came anywhere between 28 days to more than 90. It flowed between one and ten days, but most typically four days. The color was red. The first day was typically heavy. There were some clots and dysmenorrhea, for which she used over-the-counter medication. The second day was heavier, but the clots and cramps decreased. By days three and four, the flow had lightened up considerably.

Premenstrually, she was slightly moody, craved sugar, and retained water. She never detected signs or symptoms of ovulation, and did not know if or when she ovulated. She had a normal libido, good lubrication, no sexual difficulties, no abnormal pap smears, no pelvic inflammatory disease (PID), and no sexually transmitted diseases (STDs). There were no problems regarding her thyroid, skin, heart, lungs, breasts, urination, or bowel movements. Her abdomen was soft, non-tender, non-distended and without masses. Her external genitalia, vagina, cervix, uterus and ovaries were all within normal limits. There was no edema, and no fibroids.

During her first visit to the RE in September 2008, Claire had a vaginal ultrasound. The right ovary had 20 follicles, and the left had 12. Blood tests revealed a normal complete blood count (CBC). Her Thyroid Stimulating Hormone (TSH) was 1.09, FSH was 5.2, and estradiol was 51. Two weeks later, an ultrasound revealed a six millimeter lining, but no dominant/pre-ovulatory follicles were seen.

In November 2008, Claire did her first cycle of Clomid with timed intercourse. She began the Clomid on cycle day three (CD 3), and took 50 milligrams a day for five days. Later, an

ultrasound revealed no dominant follicles, which showed that she did not respond well to that dosage. So the cycle was cancelled.

A month later, in December 2008, Claire did another cycle of Clomid with timed intercourse. She began the Clomid on CD 3, with an increased dose of 100 milligrams a day for five days. An ultrasound revealed a 14 millimeter follicle on the right ovary. The couple then had intercourse, but Claire did not get pregnant.

In January 2009, she tried Clomid with timed intercourse one last time. The RE had upped the dose to 150 milligrams a day for five days. She did grow a 16 millimeter follicle on the right ovary, but there was still no pregnancy.

In February 2009, the RE suggested that Claire try gonadotropin therapy. However, she wanted to do things more naturally, so she chose Ovidrel with timed intercourse, without Clomid. On February 23rd, she had a 15 millimeter follicle on the right ovary. The lining was seven millimeters. On February 25th, that same follicle was 19 millimeters, and the lining was a 10 triple. All follicles on the left ovary were less than 10 millimeters. She took a shot of Ovidrel (6500 units) to induce ovulation and had intercourse, but no success.

In March 2009, Claire had a fluid ultrasound. Results showed the uterus and ovaries to be within normal limits without evidence of cysts, polyps, or fibroids. The tubes were patent bilaterally. The left was not open initially, but opened with increased pressure. She was still hesitant about doing shots, and wanted to try another cycle of Ovidrel and timed intercourse. On

March 26th, Claire had an 18 millimeter follicle on the left ovary, and a nine millimeter lining. She tried Ovidrel, but did not get pregnant. The RE finally convinced her to try gonadotropin therapy.

On April 8th, 2009 (CD-2), Claire began self-injecting 75 units of Gonal-F. An ultrasound on April 17th revealed that she was not responding well enough. The right ovary had 12 follicles with the largest measuring nine and ten millimeters. The left ovary had seven follicles with the largest measuring nine and eleven millimeters. The Gonal-F was increased to 112 units. Another ultrasound was done on April 20th. The right ovary had two dominant follicles measuring ten millimeters, and the left had two dominant follicles measuring ten and nine millimeters. The Gonal-F was increased to 150 units. She continued on that dose until April 24th when another ultrasound was done. Her lining was nine millimeters. The right ovary had three dominant follicles, two measuring 16 millimeters, and one measuring 11. There were no dominant follicles on the left ovary. She was instructed to stop the Gonal-F. To aid ovulation, Claire injected Ovidrel the next evening. She had an IUI on the morning of April 27th, approximately 36 hours after the Ovidrel shot. She did not get pregnant.

The May cycle was skipped because Claire had developed an ovarian cyst from the Gonal-F. She took time off to let her body heal. On May 14th, she started Metformin at 750 milligrams once a day, to be increased to twice a day in one week. The next cycle was done in July, when she no longer had the ovarian cyst. On July 15th, she started Gonal-F at 112 units. By July 23rd, her E2 was 190. She increased the Gonal-F to 150 units on July 24th. The Ovidrel shot

was scheduled for the evening of July 25th. An IUI was done 36 hours later on July 27th. She did not get pregnant.

On August 8th, 2009, Claire prepared for an IVF cycle by taking OCP for three weeks. She had been taking Metformin since May. She continued her Elite prenatal vitamins. On August 24th, she began taking 15 units of Lupron in order to control the follicles and stop them from ovulating, so that all the follicles could grow at the same rate.

At that time, Claire decided to add Chinese medicine to her protocol. She began acupuncture treatments at a TCM Clinic on August 27th. She presented with a pale tongue, a yellow greasy coat and dusky sides. Her pulses were slippery and thready. Her TCM diagnosis was damp-phlegm accumulation. Points used were Ren-10, Ren-12, ST-25, Ren-6, Ren-4, ST-28, ST-29, LI-11, LI-4, SP-9, SP-6, Liv-3, Kid-3, DU-20, and DU-24. Her herbal formula, a decoction of raw herbs that she cooked herself, was designed to resolve phlegm and drain damp. It contained the following herbs: Qing Pi (6 grams), Chen Pi (6 grams), Ban Xia (6 grams), Xiang Fu (6 grams), Mu Dan Pi (9 grams), Chuan Lian Zi (6 grams), Dang Gui (9 grams), Bai Shao (9 grams), Shen Qu (6 grams), Shan Zha (6 grams), Lai Fu Zi (6 grams), and Gan Cao (3 grams).

She got her period on August 30th. On September 4th, she decreased the Lupron to 10 units, and added 150 units of Gonal-F and 75 units of Menopur for seven days. On September 8th, her E2 was 318 and there were no follicles larger than 11 millimeters. She continued to take the Lupron, Gonal-F, and Menopur for two more days.

She had another acupuncture treatment on September 10th. Her tongue had a white coat, and her pulse was slippery and thready. She was tired, slightly bloated, and had mild hot flashes from the Lupron. She was given the same herbal formula minus Mu Dan Pi, and with the addition of Rou Gui (6 grams), Yin Yang Huo (9 grams), and Tu Si Zi (9 grams).

On September 11th, there were 13 follicles on the right ovary, with the largest being 16, 15, 13 and 13 millimeters, and 12 follicles on left ovary, with the largest being 14, 14, 13 and 13 millimeters. On September 12th, Claire's E2 was 3008, which was too high, and they almost cancelled the IVF cycle. Instead, she was instructed to inject a half dose (5,000 units) of human chorionic gonadotropin (hCG) at 8:30 p.m. to promote ovulation. A half dose (as opposed to a full dose) would decrease the chance of hyperstimulation.

Claire also had an acupuncture treatment on September 12th. She arrived feeling bloated, mildly constipated, tired, and slightly nauseous. Her herbal formula was modified to include Mu Xiang.

On September 14th at 7:30 a.m., the egg retrieval was performed with general anesthesia. The RE retrieved 16 oocytes. Four were germinal vesicle (GV), meaning they were immature. Of the 12 remaining oocytes, the RE fertilized eight with intracytoplasmic sperm injection (ICSI) and four with standard IVF. On September 15th, 100% of the eggs in the IVF group fertilized, while only 60% of the eggs in the ICSI group fertilized. Also on the 15th, Claire began taking 1cc (50 milligrams) intramuscular injections of Gestone, which is progesterone.

On September 17th, Claire arrived for her acupuncture treatment slightly bloated and mildly constipated. Her breasts were swollen. She was only slightly nauseous, and there was no shortness of breath. Her energy was fine. She had a white, thin tongue coat, and her pulses were wiry and thready. She received a new herbal formula in preparation for her upcoming embryo transfer. It was designed to tonify and slightly move Qi and contained the following herbs: Chai Hu (6 grams), Chen Pi (6 grams), Mu Xiang (6 grams), Dang Gui (9 grams), Chuan Xiong (6 grams), Bai Shao (9 grams), Gou Qi Zi (9 grams), Nu Zhen Zi (9 grams), Fu Pen Zi (9 grams), Sheng Jiang (2 pieces), Shen Qu (6 grams), Shan Zha (6 grams), and Lai Fu Zi (6 grams).

On September 18th, an ultrasound was done to rule out hyperstimulation. The right ovary measured 4.5 x 4.7 cm, and the left ovary measured 5.8 x 4.7 cm. Since both ovaries were minimally enlarged, Dostinex was prescribed at a dose of 0.5 milligrams for eight days to prevent hyperstimulation.

On September 19th, a Day-5 embryo transfer was performed without complications. In the end, seven eggs had fertilized and six had matured. Out of the six, four were grade A. Out of those four, the two best embryos were a blastocyst and an expanded blastocyst. The RE transferred those two fresh embryos. Claire continued to inject Gestone.

On September 22nd, Claire had an acupuncture treatment. She presented with abdominal bloating and slight nausea, but her risk for hyperstimulation was minimal at that point. She had incomplete dry stool, a slight low backache, and a runny nose, but her sleep was fine. Her tongue

was dusky with a yellow coat and a red tip. Her pulse was wiry and slippery. The herb formula that she received was the same as the one on September 17th, minus Chuan Xiong, which was too moving at this point, and plus Dao Zao (2 pieces).

Claire got a positive pregnancy test. On September 30th, Claire switched from Gestone to Endometrin, vaginal progesterone inserts at a dosage of 100 mg three times a day. An ultrasound taken on October 14th, confirmed the presence of a yolk sac. Her dosage of Metformin was cut back to 500 milligrams twice a day. On October 23rd, cardiac activity and adequate amniotic fluid were noted. She continued the Endometrin three times a day for three days, and then cut down to two times a day.

On November 12th, a fetus was seen with fetal cardiac activity (heart rate), and it measured 10.4 weeks. At that time, progesterone was discontinued, and Metformin was decreased to 500 milligrams once a day. Claire was referred to her obstetrician. Metformin was continued through the first trimester, tapered down and then stopped at week 13. She went on to deliver a healthy baby.

Description of Katie's Case

The following description of Katie's case is based on her chart notes, which were partially abstracted into table 2 and table 4. Katie was a 35 year-old Caucasian, nulligravida female who presented to her RE Clinic in July 2005. Her chief complaint was infertility. She had been trying to conceive for approximately a year. The RE had diagnosed her with primary

infertility, chronic anovulation and PCOS. Her husband, 32 years old and in good health, had no prior paternity. He did not smoke or take medication, and his semen analysis was normal, so male factor was not considered an issue.

Katie had a stressful job, but she was an energetic person. She worked out five to six days a week, either at the gym, or by running, hiking or biking. She suffered with neck, shoulder, and back pain, and had rib pain on occasion. She was 5'6" and her weight was 148.

Her appetite was good. She would sometimes feel bloated or heavy, and had intestinal pain or cramping on occasion. Her hands and feet were cold, yet she preferred cold drinks. Her bowel movements were normal. Her urination was frequent and urgent. She had night sweats from time to time. She was on prenatal multivitamins and probiotics.

Menarche was at age 13. However, she had a perimenarchal onset of chronic anovulation. She took OCP for five years, and had regular episodes of withdrawal bleeding. However, without the OCP, she would have only two to three spontaneous menstrual cycles per calendar year. When she did bleed, there were no clots or pain. When not bleeding, her vaginal discharge was clear, meaning there was no sign of the stretchy cervical mucus that indicates ovulation.

There was no history of cervical dysplasia, IUDs, salpingitis, or surgery. She had been diagnosed with hypothyroidism and took 88 micrograms of Levothroid a day. She was gluten sensitive, but her work-up for celiac sprue proved negative.

A vaginal ultrasound showed her uterus to be slightly retroverted, but otherwise normal. The endometrial thickness was within normal limits. The left and right ovaries had classic PCOS morphology. Their longest diameters were approximately 2.8 and 2.9 centimeters respectively. An HSG showed her tubes to be patent.

Katie stated that she had normal serum prolactin levels in the past and her androgens had been tested as well. A fasting insulin and glucose level was suggested to check for hyperinsulinemia and see if an insulin-sensitizing agent was needed. She was put on Metformin for an unknown time, but she went off. Her 17-hydroxy progesterone level was also taken to exclude non-classic adrenal hyperplasia, and that test was negative.

In July 2005, Katie tried Clomid at 100 mg/day for five days, but proved to have Clomid resistant PCOS, meaning she was still anovulatory. In October 2005, she was scheduled for a ten-day protocol of Letrozole (5 milligrams) in combination with Repronex (75 units). However, she had a vigorous response to stimulation and was coasted for the last two days. An ultrasound revealed more than 10 mature follicles bilaterally. Katie was given the option of converting the cycle to IVF, but preferred to cancel it and begin a repeat stimulation using gonadotropin therapy at a later time. To minimize development of persistent corpora lutea, she was given Desogen, a low dose OCP, and advised to use barrier contraception for one week.

In December 2005, Katie began an IUI cycle. She did low-dose gonadotropin therapy with 150 units of Follistim a day for approximately ten days. However, the dose was altered as the follicles grew, which was a standard procedure for all of her subsequent cycles. This

produced two dominant follicles on the right ovary. The plan was to trigger ovulation using one milligram of Lupron. She had a number of small follicles that were 12 to 14 millimeters. She was then coasted and did not receive any more gonadotropins. Since Katie had PCOS, she had an increased risk of multiple births. The couple would not consider selective reduction in the case of high-order multiples. Therefore, the RE recommended IVF with a one or two embryo transfer, as opposed to a repeat cycle of gonadotropin therapy and IUI with its increased tendency toward multiples.

In April 2006, Katie began an IVF cycle. She injected 200 units of Follistim a day for around ten days, which was followed by a Lupron trigger of one milligram. The cycle failed, but she had eight fertilized embryos, which were frozen. In June 2006, she did another IVF cycle with the same protocol: 200 units of Follistim a day for around ten days and a Lupron trigger of one milligram. Two of her frozen embryos were thawed and transferred. That cycle failed as well.

In September 2006, Katie started another stimulation cycle, but had a sluggish rise in serum estradiol, and a significant rise in progesterone. It was thought that this imbalance of hormones might result in poor ovum quality and compromised fertilization. Some ovarian cysts had also developed. The cycle was cancelled. A progestin withdrawal was given to expedite withdrawal bleeding. She was then followed clinically until her cysts resolved. The next stimulation was to be a low dose gonadotropin therapy, incorporating LH in the early stages. However, at that point, Katie took time off from her Western fertility treatments.

In June 2007, she began Chinese medicine treatment at a TCM Clinic. Katie came in once a week for the next six months to receive acupuncture and herbs. She presented with a slightly slippery pulse. Her tongue was pale and dusky, with teeth marks and cracks. The diagnosis was Spleen Qi deficiency, Kidney Yin deficiency with mild heat, and Blood deficiency. The treatment plan was to nourish Yin and Blood, strengthen Spleen Qi, and regulate menses.

Katie began her herbal protocol right away. The herbs were decocted off-site, and placed into sealed packages for her to drink. Her customized prescription was for one bag twice a day of the following formula: Dang Gui (10 grams), Shu Di Huang (15 grams), Bai shao (18 grams), Xiang Fu (10 grams), Tu Si Zi (10 grams), Fu Ling (15 grams), Dang shen (12 grams), Shan Yao (10 grams), Ren Shen (6 grams), Yin Yang Huo (10 grams), Ze Xie (5 grams), Bai Zhu (10 grams), and Gan Cao (3 grams).

The following acupuncture points were used throughout her treatment: ST-30 to Zi Gong Xue with electro-acupuncture, two to ten hertz, with mixed frequencies; plus Ren-6, Ren-4, Ren-3, Ren-2, ST-29, ST-36, SP-6, SP-10, PC-6, DU-20, Kid-3, Liv-3 directed toward Liv-2, Ear Shen Men, and Ear Sympathetic.

In July 2007, Katie's libido started to improve, but there were still no sign of menstruation. Toward the end of July, her period came. On CD 10, she started using an OPK to see if she was ovulating. The treatment plan was to build her Yin and Blood. She also received a new herbal formula, which included the following: Dang Gui (10 grams), Shu Di Huang (15

grams), Chi Shao (10 grams), Bai shao (15 grams), Shan Yao (10 grams), Nu Zhen Zi (10 grams), Fu Ling (15 grams), Xu Duan (10 grams), Tu Si Zi (10 grams), Hong Hua (5 grams), Chuan Xiong (5 grams), and Du Zhong (10 grams).

In August 2007, she started getting headaches and hot ears. She was instructed to dilute her herbal formula. She also got a slight pink line on her OPK one morning, which was good news that she was ovulating. However, there was no discharge. The treatment plan was to induce ovulation and continue to regulate her cycle. By the end of August, she was at CD 37, and her period had not yet arrived. In September 2007, there was still no sign of her menses.

In October 2007, with her menses still absent, she went to see the RE. An ultrasound showed her ovaries in the resting state, an endometrial thickness of four millimeters, and multiple cysts, which were consistent with the PCOS type morphology. Options were discussed regarding ovulation induction with IUI versus IVF. The couple chose IUI. The RE started Katie on 150 units of Follistim a day for around 10 days to avoid developing more than two mature follicles. Katie also resumed Metformin, using a sustained release formula of 1,000 milligrams per day. A Lupron trigger of one milligram was given to induce ovulation. The IUI did not result in pregnancy.

In November 2007, she started another stimulation cycle in preparation for an IUI. Once again she injected 150 units of Follistim per day for around 10 days, and one milligram of Lupron as an ovulation trigger. On the morning of the IUI, she had many follicles and the lining

looked good. Abdominal cupping was done at the AOM Clinic to bring more Blood and Qi to the uterus and ovaries. The IUI did not result in pregnancy.

In December 2007, she began a stimulation cycle in preparation for another IVF. Again, the drug of choice was Follistim, and the dose was 200 units a day for around 10 days, to be followed by a Lupron trigger of one milligram. She received a new Chinese herbal formula to support the upcoming stimulation: Dang Gui (10 grams), Shu Di Huang (15 grams), Bai shao (15 grams), Tu Si Zi (10 grams), Fu Ling (15 grams), Xu Duan (10 grams), Du Zhong (10 grams), Dang shen (12 grams), Ren Shen (10 grams), Yin Yang Huo (20 grams), Wang Bu Liu Xing (9 grams), Xiang Fu (10 grams), Zhi Gan Cao (10 grams), Lu Jiao Jiao (5 grams). There were special instructions to salt fry the Xu Duan, and to toast the Shu Di Huang with Chen Pi, to make it more digestible.

On 12-17-07, her follicles were a good size, and they decided to do an IUI instead of an IVF. It was scheduled for later that week. In the meantime, she got a new formula to push ovulation: Dang Gui (10 grams), Shu Di Huang (15 grams), Chi Shao (10 grams), Bai shao (15 grams), Tu Si Zi (10 grams), Fu Ling (15 grams), Shan Yao (10 grams), Nu Zhen Zi (10 grams), Xu Duan (10 grams salt fried), Hong Hua (5 grams), Chuan Xiong (5 grams), Du Zhong (10 grams), Dan Shen (10 grams), Shu Di Huang (9 grams fried). Katie got pregnant with this last IUI and went on to deliver a healthy pair of twins.

Comparison of the Two PCOS Cases

A Data Abstraction Chart summarizes the results of this study (see table #2). Both patients were diagnosed with PCOS by the same Rotterdam diagnostic criteria. Meaning, they both had anovulation and polycystic ovaries. However, Katie's anovulation was diagnosed as chronic anovulation. Her bleeding cycles occurred around 120 days apart. Claire's ovulatory dysfunction was diagnosed as oligo-ovulation. Her menstrual cycle was every 28 to 90 (or more) days.

Hyperandrogenism did not occur in either case. Although Claire had slight acne, neither patient had hirsutism or significant acne. Both patients were within normal limits for weight and body mass index (BMI). Claire had a BMI of 21, and Katie's BMI was 23.9. They were of similar age. Claire was 34 when she began fertility treatment, and Katie was 35. One difference is that Katie had been diagnosed with hypothyroidism and took 88 micrograms of Levothroid every day, and Claire had no thyroid dysfunction.

Both patients had been trying to conceive for at least a year before consulting an RE. Claire had been trying to conceive for one and a half years before consulting an RE, and began her TCM treatments one year after beginning Western treatment. Katie had been trying to conceive for one year before consulting an RE, and began her TCM treatments two years after beginning Western treatment. Claire began TCM treatments 20 days *into* her last Western fertility cycle, and received acupuncture and herbs five times during a period of approximately four weeks (see table #3). Katie began TCM treatments six months *before* her last Western

fertility cycle, and received acupuncture and herbs once a week during those six months (see table #4). In terms of their total time receiving both Western and Eastern fertility treatments, Claire's was one year, and Katie's was two and a half years.

Comparison of the Western Medicine Treatment Between the Two Cases

Both women began their fertility treatment with Clomid. Claire did not respond to Clomid at 50 milligrams, but did respond to 100 milligrams by producing a 14 millimeter follicle. She later developed a 16 millimeter follicle in response to 150 milligrams of Clomid, but none of these cycles resulted in pregnancy. Katie's dose of Clomid began at 100 milligrams. With no response at all, she was declared Clomid resistant. Katie then tried Letrozole (5 milligrams a day) in combination with Repronex (75 units a day) for eight days. Her follicles were over-stimulated and she wound up canceling the cycle.

Both women began Metformin before their final cycles, but with very different timeframes and dosages. Claire began Metformin around three months before her final IVF cycle. She started with 750 milligrams once a day and increased it to 750 milligrams twice a day a week later. She continued that dose into her pregnancy. Once she was six weeks pregnant, the dose was decreased, until she tapered down and stopped completely at 13 weeks of pregnancy. Katie began Metformin in early 2005, but stopped the drug before her initial visit with the RE six months later. She resumed Metformin in October 2007. Her dose was 1000 milligrams a day with a sustained release formula, which she was still taking when she became pregnant.

Both women did many Western fertility cycles before becoming pregnant. Claire first did three cycles of timed intercourse with Clomid, and then two cycles of timed intercourse with Ovidrel. She then did two IUI cycles and one IVF cycle, in that order. Therefore, she did eight Western fertility cycles in total. Katie did one cycle of Clomid, and then one cycle of Letrozole with Repronex. She then did one IUI cycle in 2005, two IVF cycles in 2006, and three IUI cycles in 2007. Therefore, like Claire, she did eight Western fertility cycles in total.

Drugs and dosages differed between the two cases. For Claire's first IUI cycle, she used Gonal-F with an initial dose of 75 units. When the follicles did not respond to that dose, the Gonal-F was increased to 112 units. To attain larger follicles, the dose was increased to 150 units. With Claire's second IUI cycle, Gonal-F was begun at a dose of 112 units, but based on the slow growth of the follicles, was again increased to 150 units. The drug of choice for all of Katie's IUI cycles was Follistim, for which the dose may have been 150 units right from the start.

Claire's IVF cycle included oral contraceptive pills (OCP), Lupron, Gonal-F and Menopur. Lupron was started at a dose of 15 units for 11 days and then reduced to 10 units for seven days. Dosages for Gonal-F and Menopur were 150 units and 75 units, respectively. Katie was given Follistim for her IVF cycles at a dose of 200 units. The one shift in this protocol was when the RE gave her 200 units of Follistim for her last IVF cycle, which subsequently was converted to an IUI cycle.

Claire used Ovidrel at 6500 units to facilitate ovulation with each IUI cycle. For her IVF cycle, she used a half dose of hCG at 5000 units to promote ovulation. For each of Katie's cycles, she was given Lupron to trigger ovulation at a dose of one milligram.

Summarizing their final cycles, the cycle that resulted in pregnancy for Claire was an IVF that used Lupron, Gonal-F and Menopur at 15/10 units, 150 units, and 75 units, respectively, and 5000 units of hCG to trigger ovulation. Claire delivered a single baby. For Katie, the cycle that resulted in pregnancy was an IUI that used 200 units of Follistim, and one milligram of Lupron to trigger ovulation. Katie had twins.

Claire used two different forms of progesterone to support her IVF cycle. She began injecting Gestone immediately after her egg retrieval, and then switched to Endometrin after her positive pregnancy test. The Endometrin was continued through 10 weeks of her pregnancy. Due to lack of data in Katie's chart, it is unclear whether she took any progesterone.

Both women experienced side effects from the drugs. Claire developed an ovarian cyst from the Gonal-F that measured 3.6 centimeters. She had to skip a month of treatment to resolve the cyst. For Katie, the combination of Letrozole and Repronex caused her to hyperstimulate, for which coasting off the drugs was a necessary strategy.

Comparison of the Chinese Medicine Treatment Between the Two Cases

Both Claire and Katie received Chinese medical treatment along with their Western medical treatment. There were similarities and differences. Claire started her TCM treatment 20 days *into* her final Western fertility cycle, and two and a half years into her fertility treatment. Katie started her TCM treatment six months *before* her final Western fertility cycle, and three years into her fertility treatment. Even though they had the same Western diagnosis, they had different TCM diagnoses. Claire's TCM diagnosis was Damp-Phlegm accumulation. Katie's TCM diagnosis was Spleen Qi deficiency, Kidney Yin deficiency with mild heat, and Blood deficiency. Each patient received a combination of acupuncture and herbs.

Acupuncture Comparison Between the Two Cases

Both Claire and Katie received acupuncture at least once a week during their Chinese medicine treatment. Each of their charts documented only one set of acupuncture points. Katie had electro-acupuncture, and Claire did not. Many acupuncture points were different between the cases, but these seven points were used in both: SP-6, Ren-6, Ren-4, ST-29, DU-20, Kid-3, and Liv-3.

Comparing acupuncture points in both cases, four points were used on the Ren channel in each case. Both cases used three Stomach points and two Spleen points. There was only one Liver point in both cases, which was Liv-3. There was only one Kidney point in both cases, which was Kid-3. There were two DU points used in Claire's case, but only one DU point in

Katie's. There were two Large Intestine points in Claire's point protocol, but none in Katie's.

There were two ear points used in Katie's case, but none in Claire's. There was one Extra point (Zi Gong Xue) and one pericardium point (PC-6) used in Katie's case, but not in Claire's.

A comparison chart of the acupuncture points used in Claire and Katie's point protocols shows how the points influenced multiple channels (see table #5). In Claire's case, the Spleen and Stomach channels were accessed most frequently according to her point protocol, followed by the Kidney, Liver and Ren channels. In Katie's case, the Liver channel was accessed most frequently according to her point protocol, followed by the Spleen and Kidney channels.

Table #5: Comparison of Acupuncture Points and Channels Accessed according to Deadman & Al-Khafaji (2001) in the Two PCOS Cases

Acupuncture Points Used	Channels Accessed by Claire's Point Protocol	Channels Accessed by Katie's Point Protocol
Ren-10	REN, ST, SP	n/a
Ren-12	REN, ST, SP	n/a
Ren-6	REN, KID	REN, KID
Ren-4	REN, SP, LIV, KID	REN, SP, LIV, KID
Ren-3	n/a	REN, SP, LIV, KID
Ren-2	n/a	REN, LIV
SP-6	SP, LIV, KID	SP, LIV, KID
SP-9	SP	n/a
SP-10	n/a	SP
ST-25	LI, ST, SP	n/a
ST-28	ST, UB	n/a
ST-29	ST	ST
ST-30	n/a	ST, CHONG
ST-36	n/a	ST, SP
LI-11	LI	n/a
LI-4	LI	n/a
LIV-3	LIV	LIV
KID-3	KID, LU	KID, LU
DU-20	DU, UB, GB, SJ, LIV	DU, UB, GB, SJ, LIV
DU-24	DU, UB, ST	n/a
PC-6	n/a	PC, HT, SP, ST, LU, LIV

Herbal Formula Comparison Between the Two Cases

Multiple herbal formulas were given to each woman over the course of their treatment. They both drank decoctions made from raw herbs. Claire cooked the herbs herself, whereas Katie's were cooked for her through a decocting company contracted by her TCM practitioner. They were given very different formulas, but within the various formulas, the following eight herbs were used in both cases: Xiang Fu, Dang Gui, Bai Shao, Gan Cao, Tu Si Zi, Yin Yang Huo, and Nu Zhen Zi.

Katie's herbal formulas used higher dosages of the herbs across the board. For example, nine grams of Yin Yang Huo were given in Claire's formula, while twenty grams of Yin Yang Huo were used in Katie's. Another example was Bai Shao, where nine grams were given in Claire's formula, and fifteen grams were given in Katie's. There was also six grams of Xiang Fu given in Claire's case, and ten grams given in Katie's. Those differences in dosages were more significant than the others, which were only one gram apart in dosage.

Claire's herbal formulas, during her final Western fertility cycle, contained an assortment of herbs exerting various (and sometimes multiple) actions. There were five herbs that warm, supplement or stabilize the Kidneys; five that regulate Qi; four that dry Damp and/or transform Phlegm; four that move, soothe or harmonize the Liver; and three that regulate menstruation. There were three Blood movers; three Blood tonics; three that nourish Yin, three that fortify the Yang; and three that nourish, bind or secure the Essence. There were three digestives; three that

harmonize the Stomach; one that strengthens Spleen; and one that raises Spleen Yang. There were two warming herbs at one point, and two clear heat herbs at another point, plus two herbs that tonified the Qi (Bensky, 2003).

Katie's herbal formulas, leading up to her final Western fertility cycle, contained an assortment of herbs exerting various (and sometimes multiple) actions. There were seven herbs that move blood; five that regulate and unblock menstruation; five that fortify Yang; four that nourish Yin; four that tonify Blood; four that strengthen the Spleen; and four that tonify Qi. There were three herbs that harmonize and/or regulate the Liver; three that supplement the Kidneys; three that secure the Essence; and two that harmonize the Stomach. There were two herbs that clear heat, and two that calm the spirit. There was one herb that regulates Qi, one that benefits Heart Qi, and one that drains damp and transforms phlegm (Bensky, 2003).

Herbs as categorized by their TCM functions were compared between the two PCOS cases (see table #6). The formulas preceding Katie's final Western fertility cycle were mostly focused on moving Blood, regulating menstruation, and tonifying Kidney Yang. The formulas preceding Claire's final Western fertility cycle were mostly focused on regulating Qi, supplementing Kidneys, transforming Damp/Phlegm, and harmonizing the Liver.

Both women got pregnant, and both pregnancies resulted in a live birth. Claire conceived during an IVF cycle and wound up having one baby. Katie conceived during an IUI cycle and wound up having twins.

Table #6: Comparison of Herbal Categories Used in the Two PCOS Cases

Herb Categories	Claire	Katie
Warm, supplement or stabilize Kidneys	5	3
Regulate Qi	5	1
Dry Damp and/or transform Phlegm	4	1
Soothe, harmonize or regulate Liver	4	3
Regulate menstruation	3	5
Move Blood	3	7
Tonify Blood	3	4
Nourish Yin	3	4
Fortify Yang	3	5
Nourish, bind or secure the Essence	3	3
Harmonize Stomach	3	2
Strengthen Spleen	1	4
Raise Spleen Yang	1	n/a
Warm	2	n/a
Clear heat	2	2
Tonify Qi	2	4
Calm the spirit	n/a	2
Benefit Heart Qi	n/a	1
Digestives	3	n/a

It was hypothesized that an infertile woman with PCOS who is treated on a consistent basis with weekly acupuncture treatments and daily herbal intake for at least three months will conceive sooner, with fewer Western medicine fertility cycles, than a woman who undergoes similar TCM treatment for less than three months. However, the comparison of these two PCOS cases did not confirm the hypothesis. Contradictory to the hypothesis, Katie had more than three months of TCM treatment, but she took longer to conceive than Claire, who had less than three months of TCM treatment. Compared to Claire, Katie did not have fewer Western medicine fertility cycles. Both women received the same number of Western fertility cycles (eight) before they conceived.

CHAPTER 5: DISCUSSION

This study contrasts and compares two PCOS cases. A combination of Western and Eastern medicine was used in each case to bring about pregnancy and create a live birth. Both patients, Claire and Katie, went through numerous Western fertility cycles, with various drugs and procedures. They also used Chinese medicine, with a combination of acupuncture and herbs. There are a host of differences and similarities between the two cases, but in the end they achieved the same result (live birth) through different means.

It was hypothesized that an infertile woman with PCOS who is treated on a consistent basis with weekly acupuncture treatments and daily herbal intake for at least three months will conceive sooner, with fewer Western medicine fertility cycles, than a woman who undergoes similar TCM treatment for less than three months. However, the comparison of these two PCOS cases did not confirm the hypothesis. Contradictory to the hypothesis, Katie had more than three months of TCM treatment (actually six months), but she took longer to conceive than Claire, who had less than three months of TCM treatment (actually one month). Also, Katie did not have fewer Western medicine fertility cycles than Claire. The two women had an equal number (eight) of Western fertility cycles before they conceived. In addition, Katie spent two and a half years on her integrated approach of Western and Eastern fertility treatments before getting pregnant. Whereas, Claire spent one year on her combined approach before conceiving. However, as will be discussed below, Katie had a more severe form of anovulation, which may have been a factor in her delayed success.

Both patients had irregular cycles, but Katie had chronic anovulation and Claire had oligo-ovulation. The length of Katie's menstrual cycle reflects the severity of her condition. Her bleeding cycles occurred approximately every 120 days, with about two to three spontaneous bleeds per calendar year. The bleeding was dysfunctional. Anovulatory bleeding may reflect declining estrogen levels due to immature follicles fading into atresia (the breakdown of ovarian follicles), or "estrogen breakthrough bleeding due to focal breakdown of an overgrown and structurally fragile endometrium under continuous estrogen stimulation" (Speroff & Fritz, 2005). Claire's menstrual cycle occurred more often, every 28 to 90 or more days. She was diagnosed with oligomenorrhea, which is defined as a recent history of less than eight menstrual periods annually (Svendsen et al., 2010).

Another difference between the two women is that Katie had been diagnosed with hypothyroidism. Claire did not have any thyroid problems. However, Katie took thyroid medication, and her hypothyroidism was under control. The Androgen Excess and PCOS Society task force report states that the exclusion of hypothyroidism may not be mandatory to make a PCOS diagnosis if there are no signs or symptoms of thyroid dysfunction (Azziz et al., 2009).

The total time that Claire received Western and Eastern fertility treatments was one year, while Katie received two and a half years. Claire started her TCM treatment one year after beginning Western treatment, while Katie started TCM treatment two years after beginning Western treatment. However, Katie received acupuncture and herbs once a week for six months, and Claire received acupuncture and herbs only five times during a one month period. TCM

fertility treatment is a cumulative process. Although TCM practitioners can begin whenever a patient presents to the clinic, three to six months of treatment is thought to be optimal (Lyttleton, 2004). Especially with PCOS, Chinese medicine seeks to modify the entire hormonal environment that revolves around a woman's ovaries (Lewis, 2004), which takes time. However, both women arrived at their desired goal of pregnancy and live birth even though their timelines were very different, which illustrates the fact that each case is unique.

Western Medicine Treatment for Both PCOS Cases

Both women were diagnosed with polycystic ovaries. Polycystic ovaries have been defined by the presence of twelve or more follicles in each ovary, with each follicle measuring two to nine millimeters in diameter (Rotterdam, 2004). In a woman with normal ovulation, a mature follicle is around twenty millimeters in diameter before it ruptures and releases an egg. If a woman has irregular menses and develops small follicles that do not reach normal size, ovulation will not occur. Clomid can help small, immature follicles grow to maturity (Liang, 2003).

Both women were initially treated with Clomid. Clomid is not only used to induce ovulation, but it is also used to correct irregular ovulation (Lewis, 2004). Although neither of these patients conceived with Clomid, it is understandable why their doctors thought to give it a try. Clomid is an anti-estrogen regarded as the treatment of choice for ovulation induction in anovulatory women with PCOS (Thessaloniki, 2008). In early clinical trials, 80% of anovulatory women achieved ovulation, and half of those who ovulated also conceived (Macgregor, Johnson,

& Bunde, 1968). Besides the efficacy of Clomid, there are other reasons to consider it. It is inexpensive. It is given orally, and therefore patient friendly. It does not necessitate a lot of ovarian monitoring, and there is an abundance of clinical data touting its safety. Plus, there are relatively few side effects (Thessaloniki, 2008).

Claire's protocol for Clomid was fairly standard. She started with 50 milligrams a day for five days. When that did not work, it was increased to 100 milligrams the next month, and then to 150 milligrams the following month. Although Clomid helped Claire ovulate, it did not help her conceive. Katie also tried Clomid, but started her protocol at 100 milligrams a day. However, Katie proved to be Clomid resistant, meaning she was still anovulatory in response to the Clomid. It has been shown that 20% to 25% of women are resistant to Clomid and do not ovulate when given the drug (Mitwally & Casper, 2001).

In response to Katie's failed Clomid cycle, she tried a combination of Letrozole and Repronex. Letrozole is an aromatase inhibitor that is used for inducing ovulation in anovulatory women. In one study of PCOS women who did not have a positive response to Clomid, Letrozole brought success. Ovulation occurred in 75% of the Letrozole treatment cycles, and clinical pregnancy happened in 17% of those cycles (Mitwally & Casper, 2001). Additionally, compared to Clomid's long half-life of around two weeks, aromatase inhibitors have a short half-life of about 40 hours, and are therefore eliminated from the body rapidly, causing less negative effects (Mitwally & Casper, 2004).

Repronex is a human menopausal gonadotropin (hMG) used for follicular stimulation in ART protocols (Keye et al., 2004). When Katie used Repronex and Letrozole together, she had a vigorous response to the stimulation, and was coasted for 48 hours. Coasting is a way to decrease the risk of ovarian hyperstimulation syndrome (OHSS), and also reduce cancellation rates. Coasting implies the suspension of gonadotropin therapy when there are high E₂ levels (more than 3,000 pg/mL), and the follicles have not reached full maturation (Abdallah, Kligman, Davis, & Rosenwaks, 2010). However, Katie's ultrasound revealed more than ten mature follicles bilaterally. In that case, the RE chose a common coasting technique called "late coasting," which involves stopping gonadotropins when the lead follicles are mature (more than fifteen millimeters) and estradiol levels are excessively high. The reasoning here is that larger follicles are less dependent on FSH and can continue to develop without exogenous gonadotropins (Abdallah et al., 2010). Ultimately, Katie was given an option to convert the cycle to IVF, but she preferred to cancel it altogether.

Another similarity between the cases is that both patients were treated with Metformin. Studies have shown that Metformin can treat many features of PCOS, including insulin resistance, hyperandrogenism, menstrual irregularities, decreased ovulation rates, and infertility (Maciel et al., 2004). Both women began Metformin before their final cycles. Claire began Metformin three months before her final IVF cycle, and remained on 750 milligrams twice a day into pregnancy. Katie began Metformin early in her fertility quest, but stopped taking the drug. Two years later, she began Metformin again, taking it for two months before her final IUI cycle. Her dosage was 1000 milligrams a day with a sustained release formula. She was still taking it when she became pregnant.

There has been growing interest in insulin-sensitizing drugs, like Metformin, due to widespread belief that insulin resistance and hyperinsulinemia play a major role in the pathophysiology of PCOS. Between 50% and 70% of PCOS patients have varying degrees of insulin resistance and hyperinsulinism (Bayrak et al., 2007). It is also interesting to note that women with polycystic ovaries, chronic anovulation, and hyperandrogenism are more likely to have insulin resistance and hyperinsulinemia than those who have regular cycles (Franks, 2006). Both women had polycystic ovaries, but Katie also had chronic anovulation. Claire did not have insulin resistance according to her blood values. Katie's insulin status was unclear, as there was a lack of data in her chart. However, statistically speaking, it could be possible that Katie had some degree of insulin resistance associated with her chronic anovulation.

Another factor to consider is that methods used for testing insulin resistance may be questionable. In clinical practice, the most frequently used methods for testing glucose metabolism in PCOS women are fasting plasma glucose, fasting insulin, and the oral glucose tolerance test. However, these tests may not detect early changes in insulin resistance. According to some researchers, that can only be detected with the euglycemic hyperinsulinemic clamp technique, which is primarily used in research settings (Svendsen et al., 2010). With that in mind, it may be possible that more PCOS women are insulin resistant than have been diagnosed.

Metformin has been proposed as a first-line treatment in obese or overweight women with both PCOS and hyperinsulinemia. Randomized trials showed Metformin to successfully improve insulin sensitivity, body mass index, menstrual cycle patterns, and androgen levels

(Romualdi et al., 2010). Body mass index (BMI) is used as an estimate of obesity. Women are considered obese when the BMI exceeds 30 kg/m² (Maciel et al., 2004). Claire had a BMI of 21, and Katie had a BMI of 23.9, which reflects a non-obese population for this study. The effects of Metformin have been studied in both obese and non-obese women with PCOS. Most of the studies in normal weight patients showed a significant decrease in fasting insulin and androgen levels, plus a normalization of the menstrual cycle (Romualdi et al., 2010).

It appears that insulin resistance does not need to be present to benefit from Metformin. A study was done on 28 PCOS women with normal weight and normal insulin levels. They took 500 milligrams of Metformin twice a day. The majority of the patients (70%) had their menstrual cycles regulated and restored to normal after six months of treatment (Romualdi et al., 2010). Another study showed that Metformin was effective in decreasing hyperandrogenemia and increasing ovulatory frequency in non-obese PCOS women with normal markers of insulin sensitivity (Baillargeon et al., 2004). However, when comparing the effects of Clomid or Metformin, or a combination of the two, one study found Clomid to be superior to Metformin in achieving live birth in infertile women with PCOS (Legro et al., 2007).

From a TCM point of view, Clomid is considered a heating drug. Clomid has been shown to be effective in women with Kidney Yang deficiency and Phlegm-Damp. However, women diagnosed with Kidney Yin deficiency and heat must use the drug cautiously, as it can dry up the fertile mucous, thin the endometrial lining, and damage Kidney and Liver Yin (Lyttleton, 2004). It is interesting to note that Claire had a TCM diagnosis of Phlegm-Damp, and Clomid did help her ovulate, whereas Katie had a TCM diagnosis of Kidney Yin deficiency with heat, and she

was diagnosed with Clomid resistance. Metformin, on the other hand, “can seriously undermine Spleen function, causing diarrhea and nausea in susceptible women. The concurrent use of Spleen tonic formulas can increase tolerance to the drug” (Lyttleton, 2004). Neither Claire nor Katie complained of side effects from Metformin.

Both Claire and Katie went through many Western fertility cycles with various drugs and procedures before conceiving and giving birth. Claire was initially avoiding gonadotropin therapy in an effort to keep her treatments as natural as possible. She first did three cycles of timed intercourse with Clomid, followed by two cycles of timed intercourse with Ovidrel. Then she tried two IUI cycles with Gonal-F before agreeing to an IVF cycle with Menopur and Gonal-F. Therefore, she did eight Western fertility cycles in total. Claire’s final cycle of IVF resulted in the delivery of a baby.

Katie’s story was different. She and her husband were opposed to selective reduction in the case of multiple births. Katie’s RE informed her that PCOS women have an increased risk of high-order multiples. Therefore, the recommendation was to use gonadotropin therapy and IVF with the transfer of one or two embryos, as opposed to gonadotropin therapy and IUI with its increased tendency toward multiples. However, Katie preferred to try IUI and other fertility cycles before resorting to IVF, which resulted in cancelled cycles for fear of multiples. Her various cycles included one cycle of Clomid, one cycle of Letrozole with Repronex, four IUI cycles with Follistim, and two IVF cycles with Follistim. Therefore, she did eight Western fertility cycles in total. Katie’s final IUI cycle resulted in the live birth of twins. Coincidentally,

both women completed eight Western fertility cycles before reaching pregnancy, which increased the comparability of the two cases.

Ovulation induction with gonadotropin therapy is based on the concept that follicular growth may be achieved with a transient increase in FSH above a threshold dose for just enough time to generate a limited number of developing follicles. This concept is particularly important for PCOS women, because they are prone to having too many immature follicles (Baird, 1987). The conventional protocol of gonadotropin therapy for anovulation had been a starting dose of 150 units a day. However, this was considered excessive for PCOS women due to an increased risk of OHSS (Wang & Gemzell, 1980). In order to reduce the risk of OHSS, starting doses of 150 units of FSH a day were no longer recommended (Brzyski, Grow, Sims, & Seltman, 1995), and low-dose protocols starting at 37.5 to 75 units a day were prescribed instead (Hayden, Rutherford, & Balen, 1999). There are protocols such as the “step-up regimen” that allows for slow increases in FSH to determine the threshold for follicular growth. For example, in one study, infertile PCOS women were treated with low-dose FSH starting at 75 units for two weeks before stepping up the gonadotropin dose. However, it was noted that the obese PCOS women required a longer period of stimulation and a higher dose to achieve follicular maturation (Dale, Tanbo, Lunde, & Abyholm, 1993). By keeping a close watch on follicular growth via ultrasounds and blood tests (measuring E₂), dosages can be increased slowly to reduce the risk of ovarian hyper-responsiveness (Thessaloniki, 2008).

The RE who treated Claire seems to have followed the dosing recommendations above. Her first IUI cycle began with 75 units of Gonal-F. The dose was then increased based on the

growth of the follicles, working from 112 units up to 150 units. Katie's RE, on the other hand, started her at 150 units of Follistim on her first IUI. Her subsequent IVF cycles began with 200 units of Follistim. Claire's IVF cycle also started with a higher dosage: 150 units of Follistim in combination with 75 units of Menopur. Neither patient hyperstimulated on any of these drugs or dosages. That may be because the dosages used are still considered relatively low, considering that the dosing range for Follistim is 75 to 600 units (Liang, 2003). "Overall, low-dose regimens result in a monofollicular ovulation rate of 70%, a pregnancy rate of 20% and a multiple live birth rate of 5.7%" (Thessaloniki, 2008).

Gonal-F and Follistim are both recombinant FSH drugs, which act like naturally produced FSH by stimulating the development of follicles within the ovary. However they do not induce ovulation. For that to occur, FSH drugs must be followed by a single injection of 5,000 to 10,000 units of human chorionic gonadotropin (hCG) (Liang, 2003), or Ovidrel, a recombinant hCG. Claire used Ovidrel to induce ovulation with her IUI cycles, and hCG to induce ovulation with her IVF cycle. Katie's RE took a different approach to inducing ovulation with a GnRH agonist called Lupron at a trigger dose of one milligram. Lupron is a synthetic version of the naturally occurring GnRH (Liang, 2003). Because of the long-half life of hCG, some patients may develop hCG-dependent OHSS. Triggering ovulation with a GnRH agonist, such as Lupron, has been shown to avoid OHSS (Manzanares, Gomez-Palomares, Ricciarelli, & Hernandez, 2010). However, Lupron has another, more common use, which is to "produce a clean slate for the next drug-stimulated cycle" (Lewis, 2004). Lupron was used in Claire's IVF cycle along with Gonal-F and Menopur. Lupron controls the follicles and stops them from ovulating, so that all

the follicles can grow at the same rate. For this purpose, its dosage is in units, which is a much smaller dose than the milligram used to induce ovulation.

Menopur is a purified preparation of human menopausal gonadotropin (hMG) extracted from the urine of postmenopausal women (Lewis, 2004). It contains equal amounts of FSH and LH. Many studies have found that urinary FSH and recombinant FSH are equivalent in terms of clinical efficacy. One randomized, investigator-blind trial showed no difference in mean oocyte number, clinical pregnancy rate, or live birth rate between highly purified urinary FSH and recombinant FSH (Baker et al., 2009).

In fertility clinics, progesterone is given by intramuscular injection (IM) and through vaginal suppositories. It is an important hormone to prevent miscarriage (Liang, 2003). “Increased risk of miscarriage after spontaneous or assisted conception has been reported up to 50% in PCOS patients, with rates that are threefold higher than in healthy women” (Neto et al., 2011). Claire used IM progesterone (Gestone) after her egg retrieval and then switched to vaginal progesterone inserts (Endometrin) once she became pregnant. Progesterone use was not noted in Katie’s chart, but it is possible that she took some form of it as well.

Chinese Medicine Treatment for Both PCOS Cases

By regulating hormones and improving blood flow to the reproductive organs, Chinese medicine helps improve ovarian function and follicular development, and create better quality eggs and strong, healthy embryos (Liang, 2003). When Western medicine is used, acupuncture

and Chinese herbs can help the ovaries respond better to fertility drugs by producing more follicles and better quality eggs. In patients who use IVF alone (without TCM), fewer follicles are produced. Chinese medicine can help the ovaries develop at least double the number of follicles, as well as enhance the quantity and quality of the embryos (Liang, 2003).

Both Claire and Katie received Chinese medical treatment, including both acupuncture and Chinese herbs, along with their Western medical treatment. Claire's TCM diagnosis was Damp-Phlegm accumulation. Katie's TCM diagnosis was Spleen Qi deficiency, Kidney Yin deficiency with mild heat, and Blood deficiency. It is typical to see women with the same Western diagnosis of PCOS have different TCM diagnoses and different treatment plans (Lyttleton, 2004). However, with a condition such as PCOS, it is assumed that there is some element of phlegm that is very deep, although it may not produce external symptoms (Lewis, 2004). It is also assumed that there is some element of Kidney deficiency, as the Kidney dominates reproduction. Both Kidney Yin and Yang must be properly balanced for the reproductive organs to function properly. Therefore, the treatment of Kidney Yin and Yang underlies all Chinese medicine prescriptions for infertility (Lyttleton, 2004).

There are five channels that are closely related to treating reproductive dysfunction: the Kidney, Spleen, and Liver (Jin, 1998), and the Chong and Ren (Maciocia, 1989). The Kidney stores essence, and governs birth, growth, reproduction, and development (Maciocia, 1989). Kidney Qi deficiency can cause subfertility and poor embryo quality (Stone et al., 2009). The Spleen is the central organ in the production of Qi, which is the basis for the formation of Blood. The Spleen Qi holds the Blood in the vessels, and also controls the muscles. The Spleen controls

the raising of Qi, producing a lifting effect to make sure that the internal organs remain in their proper place (Maciocia, 1989). When the Spleen Qi is deficient, uterine bleeding, organ prolapse, and/or miscarriage can occur. Deficiency of the Spleen causes weak muscles and membranes that are not able to support the placenta and embryo (Stone et al., 2009). Spleen deficiency can cause damp and phlegm, and the Spleen must be treated when damp and phlegm are present (Maciocia, 1989). The Liver ensures the smooth flow of Qi, and stores the Blood. Therefore it regulates menstruation. Stagnation of Liver Qi prevents a smooth flow of Qi and Blood in the whole body. It impairs blood flow in the Ren and Chong vessels thereby affecting the uterus and ovaries. This can create irregular menstruation (Maciocia, 1989), and contribute to infertility. Liver Blood deficiency can create scanty menstruation and also contribute to fertility (Liang, 2003).

The Chong vessel has a profound influence on the supply and proper movement of blood in the Uterus and controls menstruation (Maciocia, 1998). The Ren is also closely related to the Uterus and the whole reproductive system. The Ren is more responsible for conception, fertility and pregnancy, whereas the Chong is responsible for menstruation and most of its irregularities (Maciocia, 1998). Many of the acupuncture points and herbs used to treat Claire and Katie were linked to the five channels discussed above.

Katie's Acupuncture Treatment

Katie began acupuncture treatments six months *before* her final Western fertility cycle. She presented with a slightly slippery pulse. Her tongue was pale and dusky, with teeth marks and cracks. The TCM diagnosis was Spleen Qi deficiency, Kidney Yin deficiency with mild

heat, and Blood deficiency. The following acupuncture points were used throughout her treatments: ST-30 to Zi Gong Xue with electro-acupuncture; plus Ren-6, Ren-4, Ren-3, Ren-2, ST-29, ST-36, SP-6, SP-10, PC-6, DU-20, Kid-3, Liv-3 directed toward Liv-2, Ear Shen Men, and Ear Sympathetic.

An analysis of Katie's points shows a relationship to the five channels. An important point on the Chong is ST-30, because it is where the vessel emerges from the space between the kidneys and the uterus. This point controls all the channels of the abdomen. The Liver and Spleen channels go through this point as well. In terms of gynecology, ST-30 benefits Kidney, regulates menstruation, pacifies Liver, promotes essence, regulates Blood, and promotes fertility (Maciocia, 1998). Zi Gong Xue stimulates the ovaries, produces more follicles, improves egg quality, and thickens the uterine lining to improve embryo implantation (Liang, 2003). In Katie's case, ST-30 was connected to Zi Gong Xue with electro-acupuncture. One study found that a series of electro-acupuncture treatments increased the blood supply to the uterus (Stener-Victorin, Waldenstrom, Anderson, & Wikland, 1996). Anovulatory women with PCOS have been able to restore ovulation with electro-acupuncture (Lewis, 2004).

Katie's point prescription included four points on the Ren channel: 2, 3, 4, and 6. Ren-2 regulates menstruation. Ren-3 and Ren-4 are meeting points for the Ren, Spleen, Liver and Kidney channels. Ren-3 is a genito-urinary point that regulates menstruation and treats infertility. Ren-4 treats irregular periods, plus amenorrhea and dysmenorrhea. Ren-4 also nourishes Blood and Yin, while Ren-6 strengthens Qi and Yang. Ren-6 also moves Qi, and is an effective point for regulating menstruation, treating amenorrhea and dysmenorrhea, and resolving damp

(Maciocia, 1998). Dr. Yu Jin's acupuncture strategy to induce ovulation involves four of the points in Katie's protocol: Ren-3, Ren-4, Zi Gong Xue, and SP-6. SP-6, also used in Katie's protocol, is essential for gynecological disorders, because of its regulatory action on the Kidney, Liver, and Spleen channels (Jin, 1998). In the ovulation phase, SP-6 is used to promote blood circulation and enhance the action of the Spleen as an intermediary between the Heart and Kidneys (Lyttleton, 2004).

Besides anovulation, Katie also had amenorrhea. One point that regulates Qi in the area of the ovaries is ST-29, which is used to return the menses. SP-10 helps eliminate blood stasis in the uterus and regulate menstruation (Lyttleton, 2004). Liv-3 is the primary point for promoting the free flow of Liver Qi and can resolve Liver Qi stagnation in any part of the body. Liv-3 can treat menstrual disorders such as amenorrhea and irregular menstruation (Deadman & Al-Khafaji, 2001). The Liver channel passes through the lateral abdomen, thereby promoting a better flow of Qi and blood to aid ovulation. PC-6 pacifies the Liver and calms the mind, which is also a key factor in promoting ovulation (Lyttleton, 2004). In Katie's case, Liv-3 was directed toward Liv-2, to help clear heat (Maciocia, 1998). DU-20 "stimulates the pituitary gland, thereby increasing FSH levels and stimulating the ovaries" (Liang, 2003).

Kid-3 is the primary point to benefit the Kidneys, both Kidney Yin and Kidney Yang. It is used to nourish Yin and clear deficiency heat, which can help patients with occasional night-sweats, which Katie presented with. It is used to strengthen Kidney Yang, which can help patients with frequent and urgent urination, which Katie also presented with. The Chong and Ren channels are nourished by and have their root in the Kidneys. In the *Essential Questions*, it is

said that the “vessel of the uterus connects with the Kidneys.” Therefore, Kid-3 can be used when Kidney deficiency leads to disharmony of the Chong and Ren and results in irregular menstruation (Deadman & Al-Khafaji, 2001).

Zusanli is the Chinese name for ST-36. The name translates to “leg three miles,” and is said to enable a person to walk for three extra miles even when they are exhausted. ST-36 was included by Ma Dan-yang, the great physician of the Jin dynasty, in his list of the most vital acupuncture points. Its use is widespread and includes supporting Qi, nourishing Blood, strengthening Yin, reviving Yang, and resolving Damp. It harmonizes the Stomach and fortifies the Spleen. Katie reported that she sometimes felt bloated or heavy, and had intestinal pain or cramping on occasion. ST-36 is used to treat all of those symptoms. In fact, Qin Cheng-zu of the Song dynasty declared that “all diseases can be treated” by using ST-36 (Deadman & Al-Khafaji, 2001).

Katie’s Herbal Treatment

Katie began taking Chinese herbs six months *before* her final Western fertility cycle. In early December 2007, she began another round of fertility drugs in preparation for IVF. The following herbs were given to support that stimulation cycle: Dang Gui, Shu Di Huang, Bai shao, Tu Si Zi, Fu Ling, Xu Duan, Du Zhong, Dang shen, Ren Shen, Yin Yang Huo, Wang Bu Liu Xing, Xiang Fu, Zhi Gan Cao, and Lu Jiao Jiao.

Dang Gui nourishes and moves Blood. Shu Di Huang nourishes Blood and Yin. Bai Shao nourishes Blood, harmonizes Liver, and preserves Yin. Tu Si Zi supplements Kidney, boosts Yang, enriches Yin, and secures the Essence. Fu Ling drains damp, transforms phlegm, strengthens Spleen, and calms the spirit. Xu Duan fortifies Yang and moves Blood. Du Zhong fortifies Yang. Dang shen tonifies Qi and strengthens Spleen. Ren Shen tonifies Qi, strengthens Spleen and Stomach, benefits Heart Qi and calms the spirit. Yin Yang Huo fortifies Yang. Wang Bu Liu Xing moves Blood and unblocks menstruation. Xiang Fu regulates Liver Qi and improves menstruation. Zhi Gan Cao tonifies Qi. Lu Jiao Jiao is a Yang tonic that nourishes Blood and Essence (Bensky, 2003).

Katie had amenorrhea. She did not have a period for almost six months at the point this herbal formula was given. Therefore, the formula was based on her constitutional diagnosis rather than a menstrual cycle. However, Western drugs were given to stimulate the growth of the follicles, and, in a sense, create a follicular phase. For this stage, it was important to nourish Yin and build Blood (Lyttleton, 2004), which was exactly what the formula was doing. Taking Katie's TCM diagnosis into account as well, the formula was strengthening the Kidneys and Spleen, and tonifying Qi. One herb that drains damp and transforms phlegm was also included, even though she has Yin deficiency and no apparent damp. Once again, with a condition such as PCOS, it is assumed that there is some element of phlegm that is very deep, although it may not produce external symptoms (Lewis, 2004).

In mid December, Katie's follicles were adequately enlarged, and a decision was made to do an IUI instead of an IVF. She received a new formula to encourage ovulation. The following

herbs were carried over from the last formula: Dang Gui, Shu Di Huang, Bai shao, Tu Si Zi, Fu Ling, Xu Duan, and Du Zhong. The following herbs were added: Chi Shao, Shan Yao, Nu Zhen Zi, Hong Hua, Dan Shen, and Chuan Xiong.

Chi Shao moves Blood and clears heat. Shan Yao tonifies Qi and strengthens Spleen, Stomach, and Kidneys. Nu Zhen Zi nourishes Liver and Kidney Yin. Hong Hua moves Blood and unblocks menstruation. Dan Shen moves Blood and clears heat. Chuan Xiong invigorates the Blood.

In preparing for ovulation, Yin levels grow and Yang is consumed. So it is important for Yang tonics, such as Tu Si Zi and Xu Duan, to be in the formula at this point, which they were. The ovulation phase is a critical time. It requires Qi and Blood to be active as Yin switches to Yang. Strong treatment is needed to promote ovulation, and using many blood moving herbs is one way to do it (Lyttleton, 2004).

Claire's Acupuncture Treatment

In contrast to Katie, Claire began acupuncture 20 days *into* her final Western fertility cycle. She presented with a pale tongue, yellow greasy coat and dusky sides. Her pulses were slippery and thready. The TCM diagnosis was Damp-Phlegm accumulation. The following acupuncture points were used throughout her treatments: Ren-10, Ren-12, ST-25, Ren-6, Ren-4, ST-28, ST-29, LI-11, LI-4, SP-9, SP-6, Liv-3, Kid-3, DU-20, and DU-24. Many of these points were also used in Katie's treatments. Points that were the same for both cases include: SP-6,

Ren-6, Ren-4, ST-29, DU-20, Kid-3, and Liv-3. Points that were unique to Claire's case include: SP-9, Ren-10, Ren-12, ST-28, ST-25, LI-11, LI-4, and DU-24.

Claire's diagnosis explains the use of SP-9, a premier damp resolving point. Since she tended toward low energy and damp, Spleen Qi deficiency was probably present. Spleen Qi deficiency with damp is one of the most common patterns in clinical practice. "By far the most common and pervasive symptom of Spleen Qi deficiency is tiredness: a very high proportion of patients present with this as their main complaint" (Maciocia, 1998). Ren-10, a meeting point with the Spleen channel, helps promote the transformation and transportation of the Spleen. It relieves abdominal distention and can help patients presenting with bloating issues, which Claire presented with. Ren-12 is a major point for tonifying Stomach and Spleen and resolving damp, and also helps decrease abdominal distention. Both Ren-10 and Ren-12 help descend Stomach Qi (Maciocia, 1989), and were probably used to treat Claire's nausea, which may have been caused by the fertility drugs.

Shuidao, meaning "Water Passage," is the Chinese name for ST-28 (Deadman & Al-Khafaji, 2001). ST-28 is one of the main points for treating damp (Maciocia, 1998). It is also used for difficult urination (Maciocia, 1989), which Claire tended to have in the form of frequent urination and urinary tract infections. "The great 7th century physician Sun Simiao referred to left Shuidao as *Baomen* (Gate of the Uterus) and right Shuidao as *Zihu* (Child's Door), emphasizing its action on gynaecological disorders" (Deadman & Al-Khafaji, 2001). This point is useful in clearing Qi and Blood stasis from the uterus (Deadman & Al-Khafaji, 2001).

Claire also struggled with constipation and incomplete evacuation of stool. ST-25 was probably used to address those symptoms. LI-11 may have been chosen to clear damp heat, as she first presented to the clinic with a yellow, greasy tongue coat. Both LI-4 and DU-24 soothe the mind and allay anxiety (Maciocia, 1989).

Points used by both Claire and Katie included SP-6, Ren-6, Ren-4, ST-29, DU-20, Kid-3, and Liv-3. Ren-4 is as a meeting point for the Spleen, Liver, Kidney and Ren channels, which are all channels that treat reproductive dysfunction. Ren-6 moves Qi and helps to resolve damp (Maciocia, 1998). SP-6, an essential point for gynecological disorders, exerts a regulatory action on the Kidney, Liver, and Spleen channels (Jin, 1998), and helps promote blood circulation (Lyttleton, 2004).

Although Claire's main TCM diagnosis was Phlegm-Damp accumulation, her tongue initially presented with dusky sides and her pulse was occasionally wiry, both indicating a Liver component. Liv-3 helps move Qi in the liver channel, which is a channel that passes through the lateral abdomen, thereby promoting the movement of Qi and blood in the area of the ovaries (Lyttleton, 2004). Kid-3 is an extremely important point used to strengthen the Kidneys, benefit the Essence, and regulate the function of the Uterus. DU-20 lifts the spirit and strengthens the ascending function of the Spleen (Maciocia, 1989).

Since Claire struggled with oligomenorrhea, ST-29 would have been a good point to use in order to regulate menstruation. However, since her acupuncture treatment took place solely

during her IVF cycle, ST-29 was probably used to promote a healthy flow of blood in the uterus to prepare the endometrial lining for implantation (Maciocia, 1989).

Claire's Herbal Treatment

In contrast to Katie, Claire began taking Chinese herbs 20 days *into* her final Western fertility cycle. Claire's first herbal formula consisted of the following herbs: Qing Pi, Chen Pi, Ban Xia, Xiang Fu, Mu Dan Pi, Chuan Lian Zi, Dang Gui, Bai Shao, Shen Qu, Shan Zha, Lai Fu Zi, and Gan Cao.

Within this formula, Qing Pi and Chen Pi regulate Qi, dry damp and transform phlegm. Chen Pi also improves the transportation function of the Spleen. Ban Xia dries damp, transforms phlegm, and harmonizes the Stomach. Xiang Fu regulates Liver Qi and improves menstruation. Chuan Lian Zi moves Liver Qi, and harmonizes Liver and Stomach. Mu Dan Pi clears heat, moves blood, and dispels blood stasis. Dang Gui nourishes Blood, moves Blood, and regulates menstruation. Bai Shao nourishes Blood, harmonizes Liver, regulates menstruation, and preserves Yin. Shen Qu, Shan Zha, and Lai Fu Zi are digestives used to reduce food stagnation and harmonize the Stomach. Lai Fu Zi also reduces phlegm. Gan Cao tonifies Spleen Qi, and harmonizes the other herbs in the formula (Bensky, 2003).

Overall, this formula was used to regulate Qi, strengthen Spleen, harmonize Stomach, and transform Damp-Phlegm accumulation, but it also nourished Blood, moved Blood, preserved Yin, and soothed Liver Qi. The formula was given in the follicular phase when it is necessary to

strengthen Spleen and nourish blood in order to facilitate the growth of the follicles, produce more follicles, and thicken the uterine lining (Liang, 2003).

Claire's next herbal formula was the same as the first with some modifications. Since her tongue was no longer yellow, Mu Dan Pi was eliminated since it had already done its job of clearing heat. Rou Gui, Yin Yang Huo, and Tu Si Zi were added. Rou Gui warms the Kidneys and fortifies Yang. Yin Yang Huo fortifies Kidney Yang. Tu Si Zi supplements the Kidneys, boosts Yang, enriches Yin, and secures the Essence. These herbs were appropriate for the current phase of Claire's IVF cycle. She was still on gonadotropin therapy and the follicles were getting larger. The newly added herbs were meant to facilitate the process of going from Yin (the follicular phase) to Yang (the ovulation phase). Yang tonics support ovulation. The next step of the IVF cycle was a trigger dose of hCG to promote ovulation. So there was an integrated approach to support ovulation.

Two days before the embryo transfer, Claire began the following herbal formula: Chai Hu, Dang Gui, Bai Shao, Gou Qi Zi, Chuan Xiong, Nu Zhen Zi, Fu Pen Zi, Chen Pi, Mu Xiang, Sheng Jiang, Shen Qu, Shan Zha, and Lai Fu Zi.

Chai Hu soothes Liver Qi, harmonizes Liver and Spleen, and raises Spleen Yang. Dang Gui nourishes and moves Blood. Bai Shao nourishes Blood, harmonizes Liver, and preserves Yin. Gou Qi Zi tonifies Liver and Kidney, and nourishes Blood, Yin and Essence. Chuan Xiong moves Blood. Nu Zhen Zi is a Yin tonic that nourishes the Liver and Kidneys. Fu Pen Zi stabilizes the Kidneys and binds the Essence. Sheng Jiang warms the middle jiao and harmonizes

the Stomach. Chen Pi regulates Qi, dries damp, transforms phlegm, and improves the transportation function of the Spleen. Mu Xiang regulates Qi and strengthens Spleen. Shen Qu, Shan Zha, and Lai Fu Zi aid the digestive system (Bensky, 2003).

In comparison, Dr. Lifang Liang uses a formula called Huo Jing Zhong Zi Fang before the embryo transfer. Her chosen formula also includes Chai Hu, Dang Gui, Bai Shao, as well as the following herbs: Fu Ling, Bai Zhu, Zhi Ke, Dan Shen, and Gan Cao. This formula is designed to “soothe the Liver Qi and nourish the Heart Blood in order to quiet the spirit, and to fortify the Spleen and supplement the Qi in order to hold the embryo in the uterus” (Liang, 2003).

After an embryo transfer, it is important to maintain a good circulation of blood in the uterus to preserve embryo implantation and nourish embryo growth (Liang, 2003). Claire received one more herbal formula after the embryo transfer. It was the preceding formula with the removal of Chuan Xiong, which is too moving for embryo implantation, and the addition of Dao Zao, a Qi tonic that nourishes Blood and calms the spirit.

Herbal Formula Comparison Between the Two Cases

Both patients had unique herbal formulas based on their TCM diagnoses, their menstrual cycle, and their Western fertility treatment. Claire and Katie were given very different formulas, but within the various formulas, the following eight herbs were used in both cases: Xiang Fu,

Dang Gui, Bai Shao, Gan Cao, Tu Si Zi, Yin Yang Huo, and Nu Zhen Zi. This group of herbs includes Qi tonics and Qi movers, Blood tonics and Blood movers, Yin tonics and Yang tonics.

The formulas used during Katie's final Western fertility cycle were mostly focused on moving Blood, regulating menstruation, and tonifying Kidney Yang. Since she had amenorrhea, it was important to invigorate the blood and move the Qi, especially in her reproductive organs.

The formulas used for Claire's final Western fertility cycle were mostly focused on regulating Qi, supplementing Kidneys, transforming Damp/Phlegm, and harmonizing the Liver. This strategy took her TCM diagnosis of Damp/Phlegm accumulation into account, as well as the side effects she was having from the fertility drugs, such as bloating and constipation. For this it was important to regulate the Qi. The formulas were also supplementing her Kidneys and Liver, which, as mentioned above, are two of those five important organ channels that are key to reproductive success.

Katie's herbal formulas used higher doses of herbs than Claire's formulas. For example, twenty grams of Yin Yang Huo were used in Katie's formula, while nine grams were used in Claire's. In Bensky's *Materia Medica* text, the dosage for Yin Yang Huo is stated to be six to fifteen grams. The *Materia Medica* text gives cautionary advice about toxicity in "very large doses," but does not say how large a toxic dose would be (Bensky, 2003). It is interesting to note that six months earlier, Katie's first herbal formula had only ten grams of Yin Yang Huo. Therefore, it appears that during her last IUI cycle, higher doses of both herbs and drugs were used. Katie's dose of Follistim had been 150 units for her previous IUI cycles, but in her last

cycle, scheduled to be an IVF, she was given 200 units. At the last moment, that IVF cycle was converted to an IUI cycle, so her IUI dose was higher than it had been in the past. It is possible that these higher doses helped contribute to her positive outcome.

Acupuncture Point Comparison Between the Two Cases

Acupuncture points typically have multiple actions and are often able to exert influence on more than one channel. A comparison chart of the acupuncture points used in Claire and Katie's cases (see table #5) shows how these points can affect multiple channels.

As discussed above, there are five channels that are important in the treatment of reproductive dysfunction. They are the Kidney, Spleen, Liver, Chong and Ren channels. In Claire's case, the Spleen and Stomach channels were accessed most frequently according to her acupuncture protocol, followed by the Kidney, Liver and Ren channels. Therefore, the acupuncture points used in Claire's treatment made use of four of the five channels mentioned above. Her TCM diagnosis of Damp-Phlegm accumulation would explain the predominant use of the Spleen and Stomach channels.

The acupuncture points used in Claire's treatment also accessed points on the Large Intestine and DU channels and made contact with the Urinary Bladder channel. Use of these additional channels took her symptoms into account, which included constipation, incomplete evacuation of stool and urinary issues.

In Katie's case, the Liver channel was accessed most frequently according to her acupuncture protocol, followed by the Spleen and Kidney channels. The Ren channel was also largely used. Katie's point protocol also accessed the Chong channel through one of its most important points, ST-30. From that perspective, Katie's point protocol used all five of the key channels mentioned above.

Implications for Theory and Practice

This study includes two cases, which demonstrate how women who tried many drugs and Western fertility procedures over a long period of time and added TCM to their treatment protocol conceived and gave birth.

This study showed how short-term use of Chinese medicine (one month) was as successful as long-term use (six months), when combined with Western fertility treatments. This could have significant implications for practice because more Western health practitioners might be more open to include a short-term Chinese medical adjunct into their protocols. On the other hand, Claire, who got pregnant with short-term use of Chinese medicine had also employed IVF for the first time, so it is difficult to ascertain if IVF or Chinese medicine or a combination of the two were responsible for her successful outcome. The same reasoning can be applied to Katie. She received numerous Western fertility cycles and many months of acupuncture and herbs. Therefore, it is difficult to know what caused her to finally conceive. If future studies were to look into these scenarios further, successful protocols might come to light and advance the relationship between Western and Eastern fertility medicine.

This study can also be of benefit to individual practitioners of both Eastern and Western medicine. Western practitioners might get a better impression of TCM theory and practice by learning how it can increase their chances of success in treating infertile patients with PCOS. They may come to understand how acupuncture and/or herbs can complement Western fertility treatments, and they might discover various acupuncture and herb protocols that can be used in conjunction with IUI and IVF.

TCM practitioners may gain an understanding of how reproductive endocrinologists treat women with infertility. Specifically, they can get to know the course of events that is likely to occur when their PCOS patient steps into the RE's office. They will come away with a better understanding of the drugs and dosages used by reproductive endocrinologists, as well as the pros and cons of various procedures.

Limitations of Study

The limitations of the present study include sample size. It was a small study comparing only two cases. Another limitation is that the two patients were approximately the same age (34 and 35 years old). This is a weakness because the results of the study cannot be extrapolated to other age groups, whether older or younger. In fact, women over age 45 are less likely to get pregnant with either TCM or Western fertility treatments, so the results can not be applied to that population. However, on the other hand, the two women being approximately the same age can be considered a strength because it makes the comparison between the two women more valid.

In a small, qualitative study such as this, one must even be careful about generalizing and extrapolating results to the *same* age group, because both patients had positive outcomes with very different protocols: different herbs, drugs, acupuncture points, and doctors.

The limitations of the study also include a lack of chart notes, and therefore a lack of data. Western medical information was missing from Katie's chart. Not all drugs and dosages were listed. For example, she probably took progesterone after her ART cycles, but there was no mention of that. Other limitations include a lack of progress report notes on how the patients felt after each treatment. There was also inadequate documentation of acupuncture points used, with only one set of acupuncture points listed in each chart.

With regard to the limitations listed above, the data for this study may not be externally valid. The term *trustworthiness* is often used to refer to the concept of validity. Validity is the degree to which one's instrument measures what it claims to measure (Roberts, 2010). External validity refers to whether the results of the study might be true for a larger population (MacPherson, 2008). A larger study, with both treatment and control groups, would be needed to determine whether or not data is externally valid.

Suggestions for Future Research

For future research, a retrospective study would need to use cases that had more detailed documentation than the ones available for this study. However, a study with treatment and control groups would provide the best possible scenario to investigate this subject further.

In the current study, it was hypothesized that an infertile woman with PCOS who is treated on a consistent basis with weekly acupuncture treatments and daily herbal intake for at least three months will conceive sooner, with fewer Western medicine fertility cycles, than a woman who undergoes similar TCM treatment for less than three months. However, the comparison of these two PCOS cases did not confirm the hypothesis. Contradictory to the hypothesis, Katie had more than three months of TCM treatment and took longer to conceive than Claire who had less than three months of TCM treatment. Compared to Claire, Katie did not have fewer Western medicine fertility cycles. The two women had an equal number of Western fertility cycles before they conceived.

The next logical step might be to do a retrospective case study with a larger number of cases. However based on the difficulty in finding well-documented charts for comparison needed for this study, a more advanced approach, such as a randomized controlled trial (RCT), is suggested for future research.

A RCT could test the hypothesis that infertile women diagnosed with PCOS, chronic anovulation and polycystic ovaries, who are treated on a consistent basis with weekly

acupuncture treatments and daily herbal intake for at least three months will conceive sooner, with fewer Western medicine fertility cycles, than women with the same diagnosis who undergo similar TCM treatment for less than three months.

The inclusion criteria would be infertile women between the ages of 31 and 35, with a Western diagnosis of PCOS, chronic anovulation and polycystic ovaries. The exclusion criteria would be male factor infertility, hyperprolactinemia, thyroid disorders, fallopian tube defects, and endometrial lining/uterine abnormalities.

The research design would consist of three groups, with 50 women in each group. One treatment group would receive acupuncture and herbs for three months before receiving IVF. A second treatment group would receive acupuncture and herbs for one month before receiving IVF. The third group, a control group, would receive IVF only. All study subjects would be treated within the same group practice of reproductive endocrinologists, and they would use the same fertility drugs. Both Chinese medicine treatment groups would receive acupuncture and herbs within the same group practice of acupuncturists and herbalists. The study would continue for one month after the Embryo Transfer with both Chinese medicine (acupuncture and herbs) and Western medicine (progesterone).

Conclusion

Although the outcome of pregnancy and live birth was required for the cases to be included in this comparative study, it is interesting to see how two individual PCOS cases treated by independent practitioners both led to successful outcomes despite differences in their approaches and treatments.

Western medicine and Chinese medicine complement each other well. The patient who is lucky enough to have access to both modalities is likely to get the best of both worlds. Together they can produce a more complete diagnosis and provide better treatment options.

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Table #2: Data Abstraction Chart

Variables	Patient: Claire	Patient: Katie
Age of Patient	34	35
Race/ethnicity	Caucasian	Caucasian
Marital Status	Married	Married
Age of Husband	35	32
Time spent trying to conceive before seeking Western fertility treatment	1.5 years	1 year
Time spent trying to conceive before seeking TCM fertility treatment	2.5 years	3 years
Total time spent on combined Western and Eastern fertility treatments	1 year <i>(September '08 to September '09)</i>	2.5 years <i>(July '05 to December '07)</i>
Rotterdam 2003 Diagnostic Criteria for PCOS	<ul style="list-style-type: none"> • Oligo-ovulation • Polycystic ovaries 	<ul style="list-style-type: none"> • Chronic Anovulation • Polycystic ovaries
Length of Menstrual Cycle	28 to \geq 90 days	\approx 120 days
Hyperandrogenemia	No	No
Other Diagnostic Criteria	Some acne	Unknown
Other Pathological Factors	No Thyroid issues	Thyroid disorder
Height/Weight and Body Mass Index (BMI)	5'8" & 138 lbs. BMI = 21	5'6" & 148 lbs. BMI = 23.9

Blood Work Results	<u>9-24-08:</u> FSH: 5.2 E2: 51 TSH: 1.09 <u>10-3-08</u> Insulin level: 1.3 Serum glucose: 81 <u>8-17-09:</u> TSH: 1.21	<u>October 2007:</u> FSH: unavailable E2: unavailable TSH: 4.37 T4: 5.7 T3: 55
Treatments with a Reproductive Endocrinologist	Yes	Yes
<u>Drug: Clomid</u> <i>(Selective Estrogen Receptor Modulator)</i>	<u>November 2008:</u> 50 mg/day for 5 days <u>December 2008:</u> 100 mg/day for 5 days <u>January 2009:</u> 150 mg/day for 5 days	<u>July 2005:</u> 100 mg/day for 5 days
<u>Drug: Metformin</u> <i>(Insulin-sensitizing drug)</i>	<u>5-14-09 – 5-21-09</u> 750 mg once a day <u>5-21-09 – 10-14-09</u> 750 mg twice a day <u>10-14-09 – 11-12-09</u> 500 mg twice a day <u>11-12-09 – 12-2-09</u> 500 mg once a day	<u>2007</u> 1000 mg/day <i>(Sustained Release)</i>
<u>Drug: Ovidrel</u> <i>(Recombinant Human Chorionic Gonadotropin)</i>	<u>February 2009</u> 1 shot, 6500 units <u>March 2009</u> 1 shot, 6500 units <u>April 2009</u> 1 shot, 6500 units <u>July 2009</u> 1 shot, 6500 units	n/a
<u>Drug: OCP</u> <i>(Oral contraceptive Pills)</i>	<u>8-8-09 to 8-28-09:</u> 21 days	n/a

<u>Drug: Letrozole</u> (<i>Aromatase Inhibitor</i>)	n/a	<u>October 2005:</u> 5 mg/day for 8 days
<u>Drug: Repronex</u> (<i>Human menopausal Gonadotropin: hMG, menotropins</i>)	n/a	<u>October 2005:</u> 75 units/day for 8 days
<u>Drug: Lupron</u> (<i>GnRH Agonist</i>)	<u>8-24-09 – 9-4-09:</u> 15 units/day for 11 days <u>9-4-09 – 9-10-09:</u> 10 units/day for 7 days	Ovulation trigger dose: 1 mg
<u>Drug: hCG</u> (<i>Human Chorionic Gonadotropin</i>)	<u>9-12-09:</u> Ovulation trigger dose: 5,000 units	n/a
<u>Drug: Menopur</u> (<i>Human menopausal Gonadotropin: hMG, menotropins</i>)	<u>IVF Cycle</u> <u>9-4-09 – 9-10-09:</u> 75 units/day for 7 days	n/a
<u>Drug: Follistim</u> (<i>Recombinant FSH</i>)	n/a	<u>Dec '05 IUI Cycle</u> 150 units/day for around 10 days <u>April '06 IVF Cycle</u> 200 units/day for around 10 days <u>June '06 IVF Cycle</u> 200 units/day for around 10 days <u>Oct '07 IUI Cycle</u> 150 units/day for around 10 days <u>Nov '07 IUI Cycle</u> 150 units/day for around 10 days <u>Dec '07 IVF Cycle converted to IUI</u> 200 units/day for around 10 days (Dosages altered as follicles grew)
<u>Drug: Gonal-F</u> (<i>Recombinant FSH</i>)	<u>IUI Cycle</u> 4-8-09: 75 units 4-17-09: 112 units 4-20-09: 150 units <u>IUI Cycle</u> 7-15-09: 112 units 7-24-09: 150 units <u>IVF Cycle</u> <u>9-4-09 – 9-10-09:</u> 150 units/day for 7 days	n/a

<u>Drug: Gestone</u> (<i>Progesterone: Intramuscular injections</i>)	<u>9-15-09 – 9-30-09:</u> 50 mg/day	n/a
<u>Drug: Endometrin</u> (<i>Vaginal Progesterone Inserts</i>)	<u>9-30-09 – 10-25-09:</u> 100 mg 3 times a day <u>10-26-09 – 11-12-09:</u> 100 mg 2 times a day	n/a
<u>Drug: Dostinex</u> (<i>Dopamine Receptor Agonist</i>) [Generic: Cabergoline]	<u>9-18-09 – 9-25-09:</u> 0.5 mg/day for 8 days	n/a
<u>Drug: Desogen</u> (<i>Oral contraceptive pills</i>)	No	<u>October 2005</u> Dosage Unavailable
Drug Side Effects	<u>2009:</u> 3.6 cm ovarian cyst from Gonal-F	<u>2005:</u> Hyperstimulation from Letrozole and Repronex
Timed Intercourse with Clomid	November 2008 December 2008 January 2009	n/a
Timed Intercourse with Ovidrel	February 2009 March 2009	n/a
<u>Dates: IUI</u> (<i>intrauterine insemination</i>)	4-27-09 7-27-09	December 2005 October 2007 November 2007 December 2007
<u>Dates: IVF</u> (<i>in vitro fertilization</i>)	9-8-09	April 2006 June 2006
<u>ICSI</u> (<i>Intracytoplasmic sperm injection</i>)	Yes	n/a
Number of Follicles for IVF Cycle	16	n/a

Number of Eggs retrieved	8 ICSI, 4 IVF (8 eggs were fertilized with ICSI & 4 eggs were fertilized with standard IVF procedures.)	n/a
Embryology Report	<u>Post 9-19-09:</u> <ul style="list-style-type: none"> • 7 eggs fertilized • 6 matured • 4 were grade A • 1 blastocyst • 1 expanded blastocyst 	n/a
Embryo Transfer Day 3 or Day 5	Day 5	n/a
Number of Embryos Transferred	2	n/a
Type of Embryos Transferred	1 blastocyst and 1 expanded blastocyst	
Fresh or Frozen Embryos Transferred	Fresh	n/a
Treatments with a Chinese Medicine Practitioner	Yes	Yes
TCM Diagnosis	Damp-Phlegm accumulation	Spleen Qi deficiency, Kidney Yin deficiency with mild heat, and Blood deficiency
Acupuncture	Yes	Yes
Acupuncture Points at Each Acupuncture Treatment	<u>8-27-11</u> Ren-10, Ren-12, ST-25, Ren-6, Ren-4, ST-28, ST-29, LI-11, LI-4, SP-9, SP-6, Liv-3, Kid-3, DU-20, DU-24	<u>Points used throughout treatment:</u> ST-30 to Zi Gong Xue with electro-acupuncture, 2 to 10 hertz, with mixed frequencies; plus Ren-6, Ren-4, Ren-3, Ren-2, ST-29, ST-36, SP-6, SP-10, PC-6, DU-20, Kid-3, Liv-3 directed toward Liv-2, Ear Shen Men, Ear Sympathetic

Herbs	Yes	Yes
Herbs Given by Acupuncturist at Each Treatment	<p><u>8-27-09: First formula</u> Qing Pi (6 g), Chen Pi (6 g), Ban Xia (6 g), Xiang Fu (6 g), Mu Dan Pi (9 g), Chuan Lian Zi (6 g), Dang Gui (9 g), Bai Shao (9 g), Shen Qu (6 g), Shan Zha (6 g), Lai Fu Zi (6 g), and Gan Cao (3 g)</p> <p><u>9-10-09: Modification</u> Minus Mu Dan Pi; Add Rou Gui (6 g), Yin Yang Huo (9 g), and Tu Si Zi (9 g)</p> <p><u>9-12-09: Modification</u> Add Mu Xiang</p> <p><u>9-17-09: New formula</u> Chai Hu (6 g), Chen Pi (6 g), Mu Xiang (6 g), Dang Gui (9 g), Chuan Xiong (6 g), Bai Shao (9 g), Gou Qi Zi (9 g), Nu Zhen Zi (9 g), Fu Pen Zi (9 g), Sheng Jiang (2 pcs), Shen Qu (6 g), Shan Zha (6 g), and Lai Fu Zi (6 g)</p> <p><u>9-22-09: Modification</u> Minus Chuan Xiong, plus Dao Zao (2 pcs)</p>	<p><u>June 2007</u> Dang Gui (10 g), Shu Di Huang (15 g), Bai shao (18 g), Xiang Fu (10 g), Tu Si Zi (10 g), Fu Ling (15 g), Dang shen (12 g), Shan Yao (10 g), Ren Shen (6 g), Yin Yang Huo (10 g), Ze Xie (5 g), Bai Zhu (10 g), Gan Cao (3 g)</p> <p><u>July 2007</u> Dang Gui (10 g), Shu Di Huang (15 g), Chi Shao (10 g), Bai shao (15 g), Shan Yao (10 g), Nu Zhen Zi (10 g), Fu Ling (15 g), Xu Duan (10 g), Tu Si Zi (10 g), Hong Hua (5 g), Chuan Xiong (5 g), Du Zhong (10 g)</p> <p><u>December 2007</u> Dang Gui (10 g), Shu Di Huang (15 g), Bai shao (15 g), Tu Si Zi (10 g), Fu Ling (15 g), Xu Duan (10 g salt fried), Du Zhong (10 g), Dang shen (12 g), Ren Shen (10 g), Yin Yang Huo (20 g), Wang Bu Liu Xing (9 g), Xiang Fu (10 g), Zhi Gan Cao (10 g), Lu Jiao Jiao (5 g) (Toast Shu Di Huang with Chen Pi)</p> <p><u>12-17-07</u> Dang Gui (10 g), Shu Di Huang (15 g), Chi Shao (10 g), Bai shao (15 g), Tu Si Zi (10 g), Fu Ling (15 g), Shan Yao (10 g), Nu Zhen Zi (10 g), Xu Duan (10 g salt fried), Hong Hua (5 g), Chuan Xiong (5 g), Du Zhong (10 g), Dan Shen (10 g), Shu Di Huang (9 g fried)</p>
Approximate Conception Date	September 2009	December 2007
Miscarriages	None	None
Live Birth	One baby	Twins

Table #3: Claire's Conception Timeline

<u>Time</u>	<u>Met</u> 750 mg 2x/d since May '09	<u>OCP</u>	<u>Lup</u>	<u>Acu</u>	<u>Herbs</u>	<u>Gon</u>	<u>Men</u>	<u>hCG</u>	<u>ER</u>	<u>Ges</u>	<u>Dos</u>	<u>ET</u>	<u>P</u>
8-8-09	x	For 3 weeks											
8-24-09	x	x	15 iu/d 11 days										
8-27-09	x	x	x	x	x								
8-28-09	x	Stop	x		x								
9-4-09	x		10 iu/d 9 days		x	150 iu/d 9 days	75 iu/d 9 days						
9-10-09	x		x	x	x	x	x						
9-12-09	x		Stop	x	x	Stop	Stop	5,000 iu					
9-14-09	x				x				x				
9-15-09	x				x					50 mg/d			
9-17-09	x			x	x					x			
9-18-09	x				x					x	0.5 mg/d 8 days		
9-19-09	x				x					x	x	x	
9-22-09	x			x	x					x	x		
9-25-09	x				x					x	Stop		
9-29-09	x									x			x

Key: Met = Metformin; OCP = Oral Contraceptive Pills; Lup = Lupron; Acu = Acupuncture; Gon = Gonal-F; Men = Menopur; hCG = Human Chorionic Gonadotropin; ER = Egg Retrieval; Ges = Gestone; Dos = Dostinex; ET = Embryo Transfer; P = Pregnant.

Table #4: Katie's Conception Timeline

<u>Time</u>	<u>Acupuncture</u>	<u>Herbs</u>	<u>Metformin</u>	<u>Follistim 150 units</u>	<u>Follistim 200 units</u>	<u>Lupron</u>	<u>IUI</u>	<u>P</u>
6-07	x	x						
7-07	x	x						
8-07	x	x						
9-07	x	x						
10-07	x	x	1000 mg/d sustained release	150 iu/d 10 days		1 mg trigger	x	
11-07	x	x	x	150 iu/d 10 days		1 mg trigger	x	
12-07	x	x	x		200 iu/d 10 days	1 mg trigger	x	x

Key: IUI = Intrauterine Insemination; P = Pregnant.