Acupuncture and In Vitro Fertilisation: Recent Research and Clinical Guidelines

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Abstract

The use of acupuncture to improve the outcome of in vitro fertilisation (IVF) has become widespread over the past five years. Three of four randomised controlled trials (RCT) published since 2002 have shown that acupuncture significantly increases pregnancy rates. Although the research has a number of methodological limitations, it does strongly endorse the use of acupuncture during IVF. Protocols for IVF are complex, involving multiple phases with specific physiological aims. Correspondingly, acupuncture treatments before and during IVF need to be carefully considered in relation to the biomedical aspects that are being manipulated. This article summarises recent research in this area, and provides an explanation of the IVF process and associated acupuncture treatment guidelines.

Introduction

Recent estimates suggest that 10-15% of couples in the US experience infertility, with the prevalence higher in women over age 34 (Wright et al, 2001). In vitro fertilisation (IVF) is the most successful of the infertility treatments, and for many people is the last possibility for pregnancy. In 2001 (the most recent year for which national data were published) there were 29,344 deliveries from IVF, which resulted in the birth of 40,687 infants. This represents 1% of all U.S. births in that year (Wright et al, 2001).

Three to six cycles of standard IVF can now result in over 65% of patients ultimately delivering a baby (Kovacs et al, 2001; Olivius et al, 2002). However the average delivery rate of IVF per single initiated cycle using fresh, non-donor oocytes was still only 33% (2001 Assisted Reproductive Technology Success Rates; CDC Reproductive Health; 2003). Therefore, the majority of IVF cycles do not result in pregnancy, and there is generally the need for multiple IVF cycles for pregnancy to be achieved.

Due to the relatively low success rate of IVF per cycle, as well as the high emotional and financial costs associated with IVF, many patients have turned to complementary and alternative medical (CAM) treatments to enhance the success of IVF treatment (Beal et al, 1998). Among CAM treatments acupuncture is a frequently used adjunctive therapy.

Infertility from a biomedical perspective

A growing body of research has begun to identify a number of physiological and psychological mechanisms that may underlie female infertility and explain the limited success of IVF treatments. The causes of female infertility can be broadly grouped into four major categories (Strauss et al, 2002): 1. Abnormalities in oocyte production; 2. Anatomic abnormalities leading to obstruction of transport of the sperm, oocyte, and/or embryo through the reproductive tract (i.e., tubal, uterine, cervical and peritoneal factors); 3. Abnormalities in the implantation process, including early defects in embryo development, and embryo-endometrial interaction; and 4. Numerous other factors that are probably most important in women with unexplained infertility (e.g. age, body weight, cigarette smoking, alcohol and caffeine intake, psychological and emotional factors, immunological abnormalities and borderline hormonal imbalances).

The IVF procedure can overcome many of the conditions that cause infertility by artificially modifying oocyte production, fertilising oocytes in-vitro, and ensuring delivery of one or more embryos into a hormonally stimulated endometrium. For these reasons, combined with the superior success of IVF compared to other assisted reproductive technologies, IVF is now widely used for the treatment of infertility of known and unexplained aetiology.

The IVF process

The IVF process has several phases that must all be very carefully coordinated and precisely timed. There are several different protocols, the details of which are beyond the scope of this paper, and these protocols are constantly being refined, creating some variability in procedures among different women, IVF centres and physicians. A diagram of the basic timeline is shown in Figure 1.

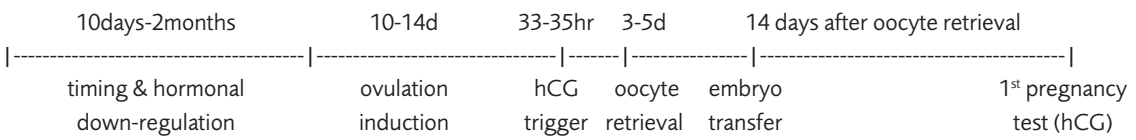

Figure 1: Timeline for IVF

Timing and hormonal down-regulation
Most commonly, the IVF protocol begins with regulation of hormones. Many clinics use the oral contraceptive pill (OCP) followed by GnRH agonist Lupron to suppress the natural cycle and inhibit ovulation, thereby allowing the ovaries to "rest" prior to stimulation. The OCP can be used for ten days to two months, in some cases to coordinate timing for a batch of women. Lupron is generally given for five to ten days.

Ovulation induction
In ovulation induction, the ovaries are stimulated to produce multiple follicles. Gonadotropin drugs such as Follistim, Gonal-F or Bravelle are begun day 2-3 of the menstrual cycle. Dosages can vary significantly depending on age and perceived ovarian function. Generally the younger the woman and the healthier the ovaries, the lower the dosage. The older the woman, or if there are other factors such as previous poor response to ovarian stimulation, the higher the dosage. In addition, Lupron or the GnRH antagonist Antagon, are used to prevent premature ovulation.

During the stimulation phase, the woman's oestrogen and LH levels are carefully monitored using blood tests, and follicular development is tracked by ultrasound, in many cases daily, so that the gonadotropin dosage can be adjusted accordingly. Often clinics aim to produce between 10-20 follicles, however in older women, five to six follicles may be considered a good response.

HCG trigger
Just before ovulation would be occurring the patient is given an injection of hCG (human chorionic gonadotropin) to help complete the final stages of maturation. The hCG trigger is given 33-35 hours before oocyte retrieval.

Oocyte retrieval
Oocyte retrieval is a surgical procedure performed under either local or general anaesthesia, in which the follicular fluid containing the eggs is collected. A long thin needle is inserted through the vagina and into the ovaries. The follicular fluid is aspirated into the lumen of the needle and withdrawn. The fluid is then transferred to a special laboratory.

Laboratory component
In the laboratory, oocytes are identified under a microscope, graded for maturity, and placed in an incubation medium in a petri dish by an embryologist. Oocytes are generally cultured for three to six hours before being exposed to sperm.

The sperm may have already undergone several procedures to help improve the quality of the sample to be utilised. In cases of poor sperm quality or low numbers, the sperm may be injected directly into the oocyte in a procedure called intracytoplasmic sperm injection or ICSI.

The sperm and oocytes are incubated overnight in an incubation medium with nutrients that allow fertilisation to occur. The next morning, the oocytes are checked for signs of fertilisation and then on the following days for development. Not all the eggs will fertilise and not all of the fertilised eggs will continue to divide. The embryos will be allowed to grow to the five to six-cell to eight-cell stage (day three) or to the blastocyst stage (day five) before being returned to the woman's uterus.

Embryo transfer
Prior to embryo transfer (ET), the embryos are graded in terms of appearance and development. The best embryos are selected and gently placed into the uterus via a catheter inserted through the cervix. Embryo transfer is an outpatient procedure, which takes only a few minutes to perform and no pain relief is required. Most programs transfer two to three embryos in patients under age 35 and three+ embryos in women over 35 to maximise the chance of success. If there are additional embryos, they can be frozen for use later if implantation and pregnancy do not occur.

Luteal phase monitoring
In order to help support the endometrium and increase the chance of success, progesterone is given in either vaginal suppositories, injections with oil, or micronised oral tablets. A pregnancy (hCG) test is given 14 days after oocyte retrieval.

Side effects of IVF
The process of IVF can be quite gruelling for the patient. It involves receiving numerous injections of drugs, with subsequent soreness and bruising, as well as getting up early to get to the IVF centre for

Author/Year	Study design	Study population	Interventions/ sample size	Acupuncture treatment	Relevant Outcomes measured	Results
1. Paulus et al, 2002	RCT	• 160 women • Age 32.5 y; range 28.5-36.5 y	• Acu (n=80) • Control: No Acu (n=80)	• MA • 25 min before and after ET Before: Neiguan P-6, Diji SP-8, Taichong LIV-3, Baihui DU-20, Guilai ST-29 After: Zusanli ST-36, Sanyinjiao SP-6, Xuehai SP-10, Hegu L.I.-4 Ear: Shenmen, Zigong (Uterus), Naodian (Brain), Neifenmi (Endocrine)	• Clinical pregnancy - presence of a foetal sac (by ultrasound) 6 wk post ET • Uterine artery pulsatility index	• Women receiving Acu had a higher clinical pregnancy rate (42.5% vs 26.3%) • No difference between the acu and no acu groups in the uterine artery pulsatility index
2. Dieterle et al, 2006	RCT	• 225 Women • Avg age 34.9 y; range 31.3-38.9 y	• Acu (n=116) • Control: placebo Acu (sham pts) (n=109)	• MA • Two txs 30 mins & 3 days after ET 30 min after ET: Guanyuan REN-4, Qihai REN-6, Guilai ST-29, Neiguan P-6, Diji SP-8, Xuehai SP-10 (+ear seeds) 3 days after ET: Hegu L.I.-4, Sanyinjiao SP-6, Zusanli ST-36, Taixi KID-3, Taichong LIV-3 (+ear seeds) Sham Pts: Sidu SJ-9, Xiaoluo SJ-12, Fengshi GB-31, Zhongdu GB-32, Yanglingquan GB-34 (+sham ear seeds)	• Clinical preg rate • Biochemical preg rate • Implantations rate • Ongoing preg rate • Miscarriages	• Acu group compared to the placebo group had sign higher clinical preg rate (33.6% vs 15.6%), biochemical preg rate (35.3% vs 16.5%), implantation rate (14.2% vs 5.9%), & ongoing preg rate (28.4% vs 13.8%) • No diff in miscarriages
3. Smith et al, 2006	RCT	• 128 Women • Avg age 36 y; range 31.2-40.9 y	• Acu (n=110) • Control: Placebo (sham pts, Streitberger) (n=118)	• MA • 3 txs: Day 9 of stimulating injections, before & after ET Ist Tx based on TCM Dx (6-14 needles) Txs before and after ET were the same as Paulus, without Zhongfeng-LIV-4 (?Taichong LIV-3) and Baihui DU-20 Sham tx used pts close to the real pts	• Clinical preg rate • Implantation • Ongoing preg • Adverse events • Health status	• No sign diffs in any outcomes • Clinical preg rate: Acu vs placebo – 34% vs 27%
4. Westergaard et al, 2006	RCT	• 273 Women • Avg age 37 y; range 24-45 y	• Acu-1 tx (n=95) • Acu -2 tx (n=91) • Control: no acu (n=87)	• MA • 25 min before & after ET (Acu-1); plus 2 days post ET (Acu-2) Before ET: Baihui DU-20, Guilai ST-29, Diji SP-8, Neiguan P-6, Taichong LIV-3 Acu 1: Zusanli ST-36, Sanyinjiao SP-6, Xuehai SP-10, Hegu L.I.-4 Acu 2: Baihui DU-20, Zhongji REN-3, Guilai ST-29, Xuehai SP-10, Sanyinjiao SP-6, Zusanli ST-36, Hegu L.I.-4	• Clinical preg • Ongoing preg	• Acu-1 group compared to control had sign higher clinical and ongoing preg rates (39% vs 26% & 36% vs 22%) • Acu-2 group not sign diff to control • Acu-2 had a higher, but not sign, early preg loss compared to Acu-1 & control (33% vs 15% vs 21%)

Abbreviations: Acu – acupuncture; Avg – average; ET – embryo transfer; MA – manual acupuncture; preg – pregnancy; RCT – randomised controlled trial; sign – significant to at least $p < 0.05$; y – year; Tx – treatment

Table 1: **Summary of RCTs Evaluating Acupuncture as an Adjunct Therapy for IVF**

blood and ultrasound monitoring, in addition to the emotional and financial pressure for it to be successful (Verhaak et al, 2007). All this is difficult to separate out from the effects of the drugs themselves. What is clear is that undergoing IVF is a highly stressful experience for most women. While some feel fine during parts of it, others feel irritable and bloated throughout.

During down-regulation, the most common side effects include hot flushes, night sweats, emotional lability, insomnia, depression, headaches, decreased libido, bloating and fatigue. In ovulation induction, patients often experience depression, irritability, headache, abdominal or pelvic pain or pressure, bloating, weight gain and fatigue. Following oocyte retrieval some women experience abdominal pain. During the luteal phase, many women experience bloating, dizziness, depression, breast tenderness, headache, abdominal pain and distention, nausea and irritability. And throughout the cycle injectible drugs are used so injection site reactions such as tenderness, infection, haematoma and swelling or bruising at the injection site are commonplace.

The most serious risk of IVF is ovarian hyperstimulation syndrome (OHSS), which is classified as mild, moderate or severe. IVF hyperstimulates the ovaries on purpose in order to produce multiple follicles, thus very mild OHSS symptoms such as bloating and lower abdominal tenderness occur routinely in many women undergoing IVF. However, a small percentage of women will produce too many

follicles, sending oestrogen to potentially dangerous levels, and causing the ovaries to become swollen and enlarged. Symptoms of severe OHSS include severe pelvic pain, swelling of the hands or legs, abdominal pain and swelling, shortness of breath, weight gain, low urine output, diarrhoea, and nausea or vomiting. Severe OHSS can be fatal so it is crucial to get prompt medical attention if an IVF patient starts experiencing these symptoms.

Research into the use of acupuncture to improve IVF outcomes

There have been several studies investigating the use of acupuncture to improve the outcome of IVF (Anderson et al, 2007). The highest quality and most conclusive studies are the four randomised controlled trials (RCT) that specifically addressed the hypothesis that acupuncture can improve the outcome of IVF (Paulus et al, 2002; Dieterle et al, 2006; Smith et al, 2006; Westergaard et al, 2006). These studies are summarised in Table 1. Of these four RCTs two had sham acupuncture controls (Dieterle et al, 2006; Smith et al, 2006). Three of the RCTs present evidence suggesting acupuncture can significantly improve the success of IVF. The first study by Paulus and colleagues (2002) included 160 women (average age 32.5 years) undergoing IVF with or without intracytoplasmic sperm injection (ICSI). Two groups were compared (n = 80 each). One group received acupuncture 25 minutes before and 25 minutes after ET, and the other underwent a standard IVF procedure without acupuncture. The clinical pregnancy rate in the non-acupuncture group was 21/80 (26.3%) compared to 34/80 (42.5%) in the acupuncture group.

The Paulus et al (2002) study provided the impetus for further studies, three of which were published in 2006 (Dieterle et al, 2006; Smith et al, 2006; Westergaard et al, 2006). Dieterle et al (2006), in a study involving 225 women (average age 34.9 years), investigated the effect of real (n = 116) and sham (n = 109) acupuncture on the outcome of IVF with and without ICSI. Sham acupuncture was performed by using points that were not appropriate for fertility-related conditions. Two manual acupuncture treatments were given 30 minutes and three days after ET. The group that received real acupuncture compared with the sham group had significantly higher implantation rates (14.2% vs 5.9%), clinical pregnancy rates (33.6% vs 15.6%), biochemical pregnancy rates (35.3% vs 16.5%), and ongoing pregnancy rates (28.4% vs 13.8%).

Smith et al (2006) compared real acupuncture to sham acupuncture. The sham intervention involved the use of non-acupuncture points and the non-insertive Streitberger needle (the shaft of the needle collapses into the needle handle), in women undergoing IVF with and without ICSI. All subjects (average age 36 years, randomised into two n = 114 groups) received three acupuncture treatments on day nine of stimulating injections, and immediately before and after ET (similar to Paulus et al mentioned above). Subjects in the real acupuncture group as compared with the sham group exhibited statistically non-significant trends towards higher pregnancy rates (31% vs 23%) and ongoing pregnancy rates at 18 weeks (28% vs 18%).

Westergaard et al (2006), in a study of women (average age 37 years) undergoing IVF with and without ICSI, compared subjects that had not received acupuncture (n = 87) with those that received acupuncture immediately before and after ET (ACU 1 group, n = 95), and with an additional acupuncture treatment two days post ET (ACU 2 group, n = 91). Clinical and ongoing pregnancy rates were significantly higher in the ACU 1 group as compared with controls (39% vs 26% and 36% vs 22%, respectively). The ACU 2 group as compared with the control group exhibited statistically non-significant trends towards higher clinical and ongoing pregnancy rates (36% and 26%).

Significance and limitations of the RCTs

These RCTs suggest that acupuncture may improve the outcome of IVF, and that it is a safe adjunctive therapy for women undergoing IVF as no adverse events associated with the acupuncture intervention were reported. However these results must be considered inconclusive and interpreted with caution for several reasons (Collins, 2006; Domar, 2006; Meyers 2006; Anderson and Rosenthal, 2007). Firstly the majority of available studies have significant design limitations. Only two of the four RCTs included sham acupuncture controls. In studies without a sham control it is difficult to distinguish the effects of acupuncture needling from placebogenic, non-specific effects associated with treatments (Kaptchuk, 2002; Birch 2003). In many studies details of procedures related to eligibility screening, randomisation, blinding and statistical analyses were often absent, as noted previously (Collins, 2006; Domar, 2006; Meyers 2006).

Secondly the majority of the acupuncture protocols employed in studies to date do not reflect clinical practice. The dosages of acupuncture employed in most of the trials were very low (two to three treatments). TCM diagnoses were only assessed in one of the RCTs (Smith et al, 2006), and even in this study were not used to determine all acupuncture treatments. In the other three RCTs treatment protocols were not tailored to address specific TCM diagnoses and the same treatment protocol was given to all subjects. This potentially creates a fixed protocol bias and reduces the likelihood that the treatment will be appropriate and effective for individual subjects (Schnyer et al, 2006).

The choice of acupuncture points was often difficult to understand and justify and without a high degree of similarity to suggested protocols in Chinese medicine texts (Maciocia, 1998; Liang, 2003; Lyttleton, 2004). Furthermore some points (Sanyinjiao SP-6 and Hegu L.I.-4) are contraindicated in pregnancy and may therefore

be unsuitable after ET. This may explain the outcome reported by Westergaard et al (2006) of a greater early pregnancy loss in the group who were given acupuncture two days after ET, as compared with those not receiving acupuncture, and those only receiving acupuncture immediately before and after ET (33% vs 21% vs 15% respectively).

Thirdly, important details of the experimental protocol were not provided. The qualifications and experience of the acupuncturists involved in the design and administration of the treatment protocols are poorly described, making it difficult to assess the validity of the intervention. Additionally many other details of the experimental protocol, as suggested by STRICTA (MacPherson et al, 2001), were not reported making the quality of the outcomes from these trials difficult to evaluate.

In summary, although methodological problems with the existing clinical research limit conclusions, there is some evidence to suggest that acupuncture may be a safe and effective adjunct therapy for women undergoing IVF. There is a definite need for more thorough and carefully designed clinical trials to evaluate the effect of acupuncture on IVF success rate.

Infertility from a Chinese medicine perspective

Chinese medical treatment of infertility began long before the advent of modern technologies like IVF. There were no blood tests to measure oestrogen or progesterone levels or ultrasounds to determine the development of follicles or presence of cysts. Instead, diagnosis and treatment were based upon detailed observation of external signs and symptoms. In modern practice, integrating medical disease diagnoses, blood tests and stages of the IVF process can help further refine TCM diagnosis and treatment, and improve clinical outcomes.

Traditional Chinese medicine texts (Maciocia, 1998; Liang, 2003; Lyttleton, 2004) say the Uterus, Heart, and Kidney form the core of reproductive activity.

Kidney

The Kidney houses reproductive essence (jing) and governs reproduction. In modern terminology, essence refers to eggs and sperm, the most primordial building blocks of reproduction. As we age, our inherited essence decreases. We can see this clearly in a woman's maturation. As a twenty week old foetus, a woman has 6-7 million eggs, the greatest number she will have in her lifetime. By birth, that number falls to 1-2 million eggs. By puberty, a scant 300,000-400,000 remains. Of these, perhaps 300-400 will be ovulated during a woman's reproductive lifetime. This perhaps reflects the use of precious essence in the incredibly energy expensive process of growing from a few cells into a foetus and from a baby into an adult.

While Kidney essence correlates to eggs and sperm, Kidney yin and yang can be thought of as the hormonal underpinnings of the reproductive system. Kidney yin, with its substantive and cooling properties, correlates to oestrogen and FSH. Kidney yang, with its warming and holding properties, correlates to progesterone and testosterone.

Heart

The Heart governs the emotions, thus explaining the impact of stress and emotions on fertility. Lyttleton (2004) says, "the Heart encompasses the mind and the activity of the hypothalamus and pituitary, which controls the whole cycle … old Chinese medicine texts describe the Heart as the master controller (Emperor) of the other organs. In the same way, Western medicine often refers to the hypothalamus and pituitary as the master controllers of the other glands in the body."

Uterus

The Uterus, or Bao Gong, includes not only the anatomical uterus, but also, according to Lyttleton (2004), all the reproductive organs in the pelvis including the ovaries and fallopian tubes. In TCM, the Uterus is connected energetically to the Heart via the Bao Mai or Uterus Vessel, and to the Kidney via the Bao Luo or Uterus Channel. In TCM it is said that the menstrual blood comes down to the Uterus from the Heart, though there is no physical structure that can be shown to do this.

Liver and Spleen

In addition to the above organs, the health of the Liver and Spleen also performs a central role in reproduction. The Liver regulates the smooth flow of qi, as well as moving and storing blood. The Spleen is of paramount importance in the generation of blood and qi.

Other organs

Though rarely spoken about in TCM texts, other organs such as the Large Intestine and Lung may also play an indirect role. If constipation is a significant issue the entire pelvic region is in a greater state of stagnation. This slow transit time can influence steroid hormone levels (Stephen et al, 1999). In cases of extreme asthma or other Lung pathologies, the Lung's contribution to the production of qi can be inhibited to the point where it becomes a fertility issue. While these are not main causes of infertility, when they become more extreme they should not be ignored.

Acupuncture through the stages of IVF

Thus far, research has only investigated the use of acupuncture in the very narrow window before and after IVF embryo transfer. There have been no clinical studies investigating the use of acupuncture in preparation for IVF or a detailed investigation of acupuncture during the stages of IVF as outlined by Liang (2003). Thus, in clinical practice, one may choose to stick to the well-documented

Acupuncture treatments

Phase 1	2	3	4	5
Tx Prep for IVF TCM Pattern Dx	Tx during down-regulation	Tx during ovulation induction	Tx before/ after embryo transfer	Tx to maintain pregnancy

Acupuncture treatment phases (Liang, 2003)

Phase 1: Tx (treatment) is according to the TCM Dx (differentiation)
Phase 2: Zusanli ST-36, Sanyinjiao SP-6, Taichong LIV-3, Hegu L.I.-4, Yintang (Modification: Xuehai SP-10, Zigongxue M-CA-18)
Phase 3: Zusanli ST-36, Sanyinjiao SP-6, Taichong LIV-3, Hegu L.I.-4, Taixi KID-3, Yintang, Baihui DU-20, Zigongxue M-CA-18
Phase 4: Before ET: Zusanli ST-36, Sanyinjiao SP-6, Taichong LIV-3, Hegu L.I.-4, Taixi KID-3, Yintang, Qixue KID-13, Baihui DU-20, Sishencong M-HN-1; Ear – Shenmen, Kidney, Liver, Spleen; After ET: Zusanli ST-36, Taixi KID-3, Yintang M-HN-3, Baihui DU-20, and Ear – Kidney, Shenmen, point halfway between Liver and Spleen
Phase 5: Up to 1st hCG: use after ET protocol
After positive hCG: Yintang, Baihui DU-20, and Ear – Kidney, Shen Men, point halfway between Liver and Spleen
In case of threatened miscarriage: Baihui DU-20, Sishencong M-CA-18, Yintang M-HN-3, Ear – Shenmen, Kidney, point halfway between Liver and Spleen

Figure 2: Timeline for acupuncture treatments during IVF

Paulus (2002) protocol and perform acupuncture only before and after embryo transfer. Or one may prepare the body for IVF by beginning acupuncture three months ahead of IVF and continuing throughout the stages of IVF. A diagram of the stages of IVF and proposed acupuncture treatments is shown in Figure 2. This adapted from Liang (2003).

1. Preparation of IVF / TCM pattern diagnosis

The TCM patterns can be informed by the patient's Western medical diagnosis as well as by the standard diagnostic tools of Chinese medicine. According to Liang (2003) the various Western medical infertility diagnoses can be viewed within the context of the various TCM patterns. TCM pattern diagnoses of Kidney yin deficiency, Kidney yang deficiency, blood deficiency and qi deficiency include the western medical diagnoses of anovulation, small or misshapen uterus, poor follicle and/or egg quality, low oestradiol, low progesterone and high FSH. TCM pattern diagnoses of qi stagnation, blood stasis and phlegm-damp obstruction include the western medical diagnoses of blocked fallopian tubes, uterine fibroids, ovarian cysts, endometriosis, adhesions and stress. The TCM pattern diagnosis of damp-heat includes the Western medical diagnoses of infections of the cervix, vagina, pelvis, urinary tract and fallopian tubes. Unexplained infertility, the most common medical diagnosis, generally presents as a combination of TCM patterns. Table 2 details the most common TCM diagnostic patterns, along with signs and symptoms and acupuncture points to treat female infertility.

A further level of refinement in the development of a more nuanced TCM pattern diagnosis and treatment strategy can be achieved by interpreting a basal body temperature chart (BBT) through a TCM lens. The interpretation of BBT charts is a powerful tool. Though it is beyond the scope of this article, we encourage readers to study it further in Lyttleton (2004). Whilst BBT data is being collected, acupuncture can be administered once or twice per week, using points determined by the patient's TCM pattern diagnosis.

2. Timing and down regulation

Once the patient begins hormonal down-regulation, the acupuncture protocol and treatment strategy is tailored to be compatible with the goals of the IVF medications. During down-regulation, the goal is to allow the ovaries to rest. Lupron can cause pronounced yin deficiency or deficiency heat signs, as well as qi stagnation. Thus, one can use acupuncture points to gently nourish yin, clear heat, and move qi. Liang recommends Zusanli ST-36, Sanyinjiao SP-6, Taichong LIV-3, Hegu L.I.-4, Yintang (M-HN-3) with Diji SP-10 and Zigongxue M-CA-18 if needed to move blood.

3. Ovulation induction

During ovulation induction, just as the gonadotropins stimulate the production of multiple follicles, so can acupuncture support the movement of blood in the pelvis, as well as tonifying Kidney yin and blood to improve the body's response to the medications and to improve circulation of blood in the pelvis. During this phase Liang recommends Zusanli ST-36, Sanyinjiao SP-6, Taichong LIV-3, Hegu L.I.-4, Taixi KID-3, Yintang (M-HN-3), Baihui DU-20 and Zigongxue M-CA-18. Some practitioners also utilise points such as Lieque LU-7, Zhaohai KID-6, Gongsun SP-4, Neiguan P-6, to open the Conception (Ren) and Penetrating (Chong) vessels, plus additional points based on the patient's pattern diagnosis. Commonly, three to four acupuncture treatments are given prior to oocyte retrieval.

4. Before and after embryo transfer

As discussed earlier, research studies looked at acupuncture delivered 25-30 minutes before and after ET. When possible, that is certainly supported

TCM Diagnosis	Diagnostic Signs and Symptoms	Acupuncture Points
Kidney jing deficiency	Developmental disorders of the reproductive organs, poor development of secondary sexual signs like breast development, under-functioning ovaries (poor response to fertility drugs) Pulse-weak (esp. 3rd position); Tongue-pale	Guanyuan REN-4, Shenshu BL-23, Mingmen DU-4
Kidney yin deficiency	Malar flush, night sweats, thirst, symptoms worse in afternoon and evening, insomnia, restlessness, irritability, weak/sore lower back and knees, hot flashes; Period-scanty or heavy bright red Pulse-rapid, fine; Tongue-red, peeled	Sanyinjiao SP- 6, Taixi KID-3, Fuliu KID-7, Shenmen HE-7, Rangu KID-2, Zhaohai KID-6, Lieque LU-7
Kidney yang deficiency	Cold sensations, weak/sore lower back and knees, frequent urination, nocturia, copious and clear urine, swollen ankles, puffiness or overweight, fatigue, low libido; Period-diarrhoea and low back pain just before or at beginning, dysmenorrhoea, clots composed of tissue Pulse-slow, deep; Tongue-swollen, pale, wet	Shenshu BL-23, Mingmen DU-4, Fuliu KID-7
Blood deficiency	Dry eyes, dry skin, pale complexion, brittle nails, dizziness, poor memory, fatigue, numbness; Period-amenorrhoea, irregular periods, long cycle length, scanty period Pulse-weak, fine, empty; Tongue-pale	Zusanli ST-36, Sanyinjiao SP-6, Ququan LIV-8, Xuehai SP-10, Geshu BL-17, Danshu BL-19
Qi deficiency	Fatigue, poor appetite, spontaneous sweating, low voice, poor digestion; Period-scanty or heavy, early or late Pulse-weak; Tongue-swollen, pale	Qihai REN-6, Zusanli ST-36, Sanyinjiao SP-6, Taiyuan LU-9
Heart qi stagnation	Palpitations, anxiety, insomnia, hysteria/neurosis, emotional stress; Period-irregular, or amenorrhoea which was preceded by emotional shock Pulse-knotted (esp. left 1st position); Tongue-red tip	Neiguan P-6, Shenmen HE-7, Ear Shenmen, Taichong LIV-3
Liver qi stagnation	Sub-costal pain, intermittent moving pain, irritability, anger, depression, sighing, PMS, breast distention, stress, headaches with blood shot eyes, endometriosis; Period-late, irregular Pulse-wiry; Tongue-normal	Hegu L.I.-4, Taichong LIV-3, Qimen LIV-14, Xingjian LIV-2

Table 2: **TCM diagnostic patterns of female infertility, associated signs and symptoms, and acupuncture points commonly used for treatment.**

by the research. However, in clinical practice this is not always possible. Many clinicians feel that treating by acupuncture 12-24 hours before and after ET is also useful, though this has not been studied. The Paulus (2002) protocol that was used as the basis for the studies is as follows: before ET: Neiguan P-6, Diji SP-8, Taichong LIV-3, Baihui DU-20 and Guilai ST-29. After ET: Zusanli ST-36, Sanyinjiao SP-6, Xuehai SP-10, Hegu L.I.-4. Ear points Shenmen, Zigong (Uterus), Naodian (Brain), Neifenmi (Endocrine) were used both before and after, with two of these points needled in each ear, and then alternated with the opposite ear after ET.

The Paulus (2002) protocol is not the only protocol that has been suggested for this purpose. Liang (2003) recommends before ET: Zusanli ST-36, Sanyinjiao SP-6, Taichong LIV-3, Hegu L.I.-4, Taixi KID-3, Yintang, Qixue KID-13, Baihui DU-20, Sishencong M-HN-1; Ear: Shenmen, Kidney, Liver, Spleen. After ET: Zusanli ST-36, Taixi KID-3, Yintang (M-HN-3), Baihui DU-20, and Ear: Kidney, Shenmen and a point halfway between Liver and Spleen. She notes that Zusanli ST-36 and Taixi KID-3 should be used only immediately after transfer and omitted after a positive pregnancy test because of their strongly stimulating properties. Other practitioners feel that these protocols are good starting points and should also be modified based on the patient's pattern diagnosis. To date, no study has compared protocols to determine which approach is most successful.

5. Luteal phase

During the luteal phase, the goal is to encourage implantation and prevent miscarriage. In natural cycles, implantation occurs approximately one week following fertilisation. In IVF, several days of development have already occurred in the laboratory, so implantation occurs only a few days after ET. In terms of acupuncture, the luteal phase corresponds to yang, so supporting yang and strengthening

its holding function is a key goal of acupuncture treatment. Liang (2003) recommends Baihui DU-20, Sishencong M-HN-1, Yintang (M-HN-3), Ear: in cases of threatened miscarriage, Shenmen, Kidney, and a point halfway between Liver and Spleen.

One research study (Westergaard et al, 2006, Table 1) investigated the use of acupuncture in the luteal phase two days post-ET with the following protocol: Baihui DU-20, Zhongji REN-3, Guilai ST-29, Xuehai SP-10, Sanyinjiao SP-6, Zusanli ST-36, Hegu L.I.-4. The inclusion of Sanyinjiao SP-6 and Hegu LI-4, points historically used to induce abortion (O'Connor and Bensky, 1981), as well as Zhongji REN-3 and Guilai ST-29 on the lower abdomen, perhaps account for the high pregnancy loss rate in this study. Therefore, based on the results of that study, we recommend avoiding points contraindicated in pregnancy as well as lower abdominal points from ET-day onward.

Conclusions

Recent research suggests that acupuncture may be a safe and effective adjunct therapy for women undergoing IVF. Probable mechanistic explanations for how acupuncture improves IVF have been explored (Anderson et al, 2007), but further research is required. Chinese medicine texts describe the aetiology and treatment of infertility, and several address the use of acupuncture and herbal medicine in conjunction with IVF (Liang, 2003; Lyttleton, 2004). However, due to the fact that IVF protocols are constantly being refined, Chinese medicine practitioners need to keep abreast of IVF protocol changes and how best to combine these with Chinese medicine treatments. This requires a thorough understanding of both the biomedical and Chinese medical aspects of this complex condition and the evolving and highly technical IVF process.

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References

Anderson, B.J., Haimovici, F., Ginsburg, E.S, Schust, D.J. & Wayne, P.W. (2007). "In vitro fertilisation and acupuncture: clinical efficacy and mechanistic basis," Alternative Therapies in Health and Medicine, 13(3), 38-48.

Anderson, B.J. & Rosenthal, L. (2007). "Acupuncture and IVF studies lack protocol analysis and external validity," Fertil Steril, 87(4), 1000.

Beal MW. (1998). "Women's use of complementary and alternative therapies in reproductive health care," J Nurse Midwifery, 43(3), 224-34.

Birch S. (2003). "Controlling for non-specific effects of acupuncture in clinical trials," Clinical Acupuncture and Oriental Medicine, 4(2-3), 59-70.

Collins J. (May 2006). "The play of chance," Fertil Steril, 85(5), 1364-7.

Dieterle S, Ying G, Hatzmann W & Neuer A. (May 2006). "Effect of acupuncture on the outcome of in vitro fertilisation and intracytoplasmic sperm injection: a randomized, prospective, controlled clinical study," Fertil Steril, 85(5), 1347-51.

Domar, AD. (2006). "Acupuncture and infertility: we need to stick to good science," Fertil Steril., 85(5):1359-61.

Kaptchuck TJ. (2002). "The placebo effect in alternative medicine: can the performance of a healing ritual have clinical significance?" Ann Intern Med 136(11), 817-25.

Kovacs GT, Maclachlan V & Brehny S. (2001). "What is the probability of conception for couples entering an IVF program?" Aust N Z J Obstet Gynaecol 41(2), 207-9.

Liang, L. (2003). *Acupuncture and IVF*. Blue Poppy Press: Boulder.

Lyttleton, J. (2004). *Treatment of Infertility with Chinese Medicine*. Churchill Livingstone: London.

Maciocia, G. (1998). *Obstetrics and Gynecology in Chinese Medicine*. Churchill Livingstone: London.

Myers ER. (2006). "Acupuncture as adjunctive therapy in assisted reproduction: remaining uncertainties," Fertil Steril. 85(5),1362-3.

MacPherson H, White A, Cummings M, Jobst K, Rose K, & Niemtzow R. (2001). "Standards for reporting interventions in controlled trials of acupuncture: the STRICTA recommendations," Complement Ther Med 9(4), 246-9.

O'Connor, J. Bensky, D. (1981). *Acupuncture, A Comprehensive Text*. Eastland Press: Washington.

Olivius K, Friden B, Lunden K, & Bergh C. (2002). "Cumulative probability of live birth after three in vitro fertilisation/intracytoplasmic sperm injection cycles," Fertil Steril, 77, 505-10.

Paulus WE, Zhang M, Strehler E, El-Danasouri I, & Sterzik K (2002). "Influence of acupuncture on the pregnancy rate in patients who undergo assisted reproduction therapy," Fertil Steril 77(4), 721-4.

Smith C, Coyle M, & Norman RJ. (2006). "Influence of acupuncture stimulation on pregnancy rates for women undergoing embryo transfer," Fertil Steril. 85(5), 1352-8.

Stephen J Lewis M.R.C.P & Kenneth W Heaton F.R.C.P. (1999). "The metabolic consequences of slow colonic transit," The American Journal of Gastroenterology. 94(8), 2010–2016.

Strauss, JF, Barbieri, RL. Yen & Jaffe (2004). *Reproductive Endocrinology: Physiology, Pathophysiology and Clinical Management*. 5th Ed. Elsevier: Philadelphia.

Schnyer RN, Wayne PM, Kaptchuk TJ, Cheng X, Zhang Z, & Stason WB. (2006). "Standardization of individualized treatments in a randomised controlled trial of acupuncture for stroke rehabilitation," J Altern Complement Med., 12(2), 106-9.

Verhaak CM, Smeenk JM, Evers AW, Kremer JA, Kraaimaat FW, & Braat DD. (2007) "Women's emotional adjustment to IVF: a systematic review of 25 years of research," Hum Reprod Update, 13(1), 27-36.

Westergaard LG, Mao Q, Krogslund M, Sandrini S, Lenz S, & Grinsted J. (2006)

"Acupuncture on the day of embryo transfer significantly improves the reproductive outcome in infertile women: a prospective, randomised trial," Fertil Steril, 85(5), 1341-6.

Wright VC, Schieve LA, Reynolds MA, Jeng G. & Kissin D. (2004). "Assisted Reproductive Technology Surveillance – United States 2001. MMWR Surveill 53, 1-20.

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