



# Poor ovarian reserve and high **FSH** levels

As a result of many positive studies over the past few years, the integrated treatment of infertility has become very popular. The shortcoming of Western medicine in its ability to resolve some infertility problems, in combination with the success of Chinese medicine to successfully do so, has further contributed to its popularity. This article deals with the approach to treating one of the most common problems that infertile patients present to Chinese medicine.

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## Western medicine background

Poor ovarian reserve is a condition of poor infertility characterised by low numbers of oocytes remaining in the ovaries. Other familiar terms to describe this situation are “impaired ovarian reserve”, “premature ovarian failure” or “declining ovarian reserve”. Controversy and debate still exist over the definition of ovarian quality.

The common factors for the assessment of ovarian reserve are as follows:

Age is the most consistent variable that affects ovarian potential, but quite often young women in their early 30s can also

show low ovarian potential. Passive tests, such as an isolated rise in serum FSH during the early follicular phase, may predict fertility outcome.<sup>1</sup> Along with low antral follicle count (AFC) and ovarian volume, this is considered one of the predictors of ovarian failure. Women with normal FSH levels (days two to four of the menstrual cycle –10 IU/L) behave as “normal” responders and will have an adequate number of mature oocytes available for fertilisation following standard ovarian stimulation.

On the contrary, patients with high FSH may respond poorly to standard ovarian stimulation both in terms of the number of oocytes and the outcome of treatment.<sup>2</sup> It is important to note that women can have a normal follicular phase FSH level, yet still respond poorly to ovarian stimulation and hence are considered to have poor ovarian reserve.

Serum inhibin B levels can also be used to predict ovarian reserve, including egg quality and quantity. Because inhibin B is produced directly by ovarian follicles, the levels can correlate with the number of early antral follicles. An abnormal level of inhibin B, below 45 pg/mL on cycle day three, suggests poor ovarian reserve.<sup>3</sup>

Due to the knowledge gained through

many previous studies, today FSH and AFC levels are the gold standard for diagnosing ovarian reserve. Other tests, like ones that measure inhibin B and anti mullerian hormone levels, are considered less reliable. If these test results are used clinically, the interpretation should be performed in the context of other clinical measures.

The most commonly used active test regarding oocyte quality and quantity is the Clomiphene Citrate Challenge Test (CCCT). In short, clomiphene citrate is given on days five through nine of the cycle and FSH levels are determined on days three and 10.

The value at day three is not stimulated and represents the same basal value used in the cycle day-three FSH screening. Clomiphene stimulates an increased release of FSH early in the follicular phase, which improves follicular function and when normal, the follicle would produce enough inhibin and estradiol feedback to the pituitary so as to suppress FSH production by cycle day 10. An FSH value of greater than 10 mIU/ml for either cycle days three or 10 indicates an abnormal test. However, there is little agreement about FSH values, and criteria for normal vs. abnormal results vary from study to study.<sup>4</sup>

Since FSH is an important and reliable symptom in diagnosing poor ovarian reserve, this article will try to explain the energy, function and disharmony of FSH from the point of view of traditional Chinese medicine. With this, we can then understand how TCM can be used to treat poor ovarian response.

### FSH secretion and function

FSH stimulates the growth and recruitment of immature ovarian follicles in the ovary. During the late luteal phase, estrogen and progesterone levels fall due to the degenerating corpus luteum, leading to a rise in FSH levels. This causes those antral follicles that happen to be at a more advanced stage of maturation to continue to grow. During the follicular phase, as the follicles mature they secrete estrogen and inhibin B, which leads to gradual FSH suppression via a negative feedback loop. If the follicles do not mature, FSH will

continue to be produced and rise to high levels, as seen in patients going through menopause or those with poor ovarian reserve.

### Chinese medicine theory

When trying to understand the energetic nature of FSH, we should look to the *Nei Jing* (Inner Classic) chapter one: “At the age of 14, a girl begins to have menstruation, energy in her conception meridian begins to flow, and energy in her rigorous meridian [*tai chong mai*] begins to grow in abundance. At this point, she begins to have reproductive energy, which is the reason why she is capable of pregnancy.”<sup>5</sup> Therefore follicles are related to the potential of female fertility and are part of essence. FSH is responsible for follicle maturation and growth; a fulfillment of the potential within the ovaries. Hence, FSH is related to Kidney qi energy and is considered to be yang energy.

It can be thought of as part of the Kidney-Heart *Bao mai* axis, as a pituitary-ovarian hormone that aids in the development of follicles. It should be emphasised that the energy of FSH relates to *yuan* (source) *qi* as well as Kidney qi. It is the qi that comes with the essence and influences the essence. *Yuan qi* is linked to the Kidneys and sometimes to the *ming men* (life gate), expressing a movement for regulating life in the rhythmic beating between the two kidneys.<sup>6</sup> The Kidney, Spleen, and Lung organs are very important for the production of qi and directly influence its renewal and original emanation.<sup>7</sup> Therefore, in order to support the function of FSH to stimulate the follicles, we can strengthen the *yuan qi* by supporting the Kidney, Spleen, and Lung organs.

Another way of supporting the follicles is by ensuring the harmonious distribution of the *yuan qi* throughout the *San Jiao* (triple burner). The 66<sup>th</sup> difficulty of the *Nan Jing* (Classic of Difficulties) states that the *San Jiao* carries the *yuan qi* to the source points. It is responsible for the initiation and circulation of *yuan qi* from the Kidneys to the rest of the body, and promotes the functional activities of the *zang fu* and various other tissues. By supporting the

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Yang energy is an important factor in the maturation of follicles and in transforming the potential essence into matter.

distribution of the *San Jiao*, *yuan qi* can flow into the organs and support the essence of life as well as influence folliculogenesis. The distribution of the *San Jiao* relies on the free flow of Liver qi and the *shaoyang*, therefore one should also pay attention to these systems.

The importance of the *San Jiao* in creating life might also relate to the fact that it has no form. Formlessness is the great ancestor of matter; it is transformed by *shen* to create form and life. The sense of “no form” describes the *San Jiao* as being the base of existence for the vital processes and the relation of life to *jing* (essence) and *shen* (spirit).<sup>8</sup> The *San Jiao* connects the Heart and Kidney pathways to allow the transportation of *jing* and *shen* through the body. Maintaining the Kidney (*jing* aspect) – Heart (*shen* aspect) axis can balance the ovary-pituitary axis and regulate FSH levels. In these situations, we may observe patterns of Kidney *yin* deficiency, Kidney *jing* deficiency, Heart *yin* deficiency, or *qi* obstruction.

Zhang Jing-Yue mentioned that the *San Jiao* not only regulates fluids, but that it also regulates *yang* and has a title of “Minister of Fire.”<sup>9</sup> He also stated that *jing* and *shen* reside in the *ming men*. Yang energy (*ming men*) is an important factor in the maturation of follicles and in transforming the potential essence into matter. Sometimes women with a yang deficiency constitution may show high FSH levels with few follicles and a low fertilisation percentage.

#### Summary of regulating FSH functions

■ Strengthen Kidney, Spleen and Lung organs in order to support the functions of *yuan qi*.

**Point examples:** *Taixi* KID-3, *Taibai* SP-3, *Taiyuan* LU-9.

**Herbs:** *Ren Shen* (Ginseng Radix), *Dang Shen* (Codonopsis Radix), *Huang Qi* (Astragalus Radix), *Tu Si Zi* (Cuscutae Semen).

■ Support the *San Jiao* functions of initiating and distributing *yuan qi* so as to promote folliculogenesis.

**Point examples:** *Yangchi* SJ-4, *Shimen* REN-5, *Yanglingquan* GB-34 with *Zhigou* SJ-6, or *Zulinqi* GB-41 with *Waiguan* SJ-5.

**Herbs:** *Xiang Fu* (Cyperus Rhizoma), *Chai*

*Hu* (Bupleurum Radix), *Zhi Zi* (Gardenia Fructus).

■ Support the function of the *San Jiao* to transport *jing* and *shen* (Kidney-Heart axis).

**Point examples:** *Yangchi* SJ-4, *Waiguan* SJ-5, *Zhubin* KID-9, *Lingdao* HE-4.

**Herbs:** *Dan Shen* (Salvia Miltiorrhiza, Radix), *Xiang Fu* (Cyperus Rhizoma), *He Huang Pi* (Albizia Cortex), *Niu Xi* (Achyranthis Radix).

■ Support the *ming men* as an important factor in follicle maturation, as a yang energy and as a regulator between *jing* and *shen*.

**Point examples:** *Mingmen* DU-4, *Guanyuan* REN-4.

**Herbs:** *Rou Gui* (Cinnamomum Cortex), *Tu Si Zi* (Cuscutae Semen), *Ba Ji Tian* (Morinda Radix).

Another way to understand the nature of FSH is to look at the pathological causes of its elevation:

- Genetic factors such as fragile x syndrome
- Autoimmune disorders
- Adrenal gland impairment
- Iatrogenic factors such as radiation, chemotherapy or surgery.

The above reasons relate directly or indirectly to Kidney qi and *jing* deficiency and can be treated by strengthening the Kidneys. These pathologies may appear in women over the age of 35 with high FSH levels. According to the seven-year cycles as discussed by the Yellow Emperor, this is the point of life when the body starts to decline. Therefore, by strengthening Kidney qi and *jing*, FSH levels may decrease.

**Point examples:** *Taixi* KID-3, *Guanyuan* REN-4, *Qihai* REN-6, *Shenshu* BL-23, *Gao-huangshu* BL-43.

**Herbs:** *Shu Di Huang* (Rehmannia Radix Preparata), *Shan Yao* (Dioscorea Radix), *Tu Si Zi* (Cuscutae Semen), *Gui Ban* (Testudinis Plastrum), *Lu Jiao Jiao* (Cervi Cornus Colla).

Another aspect of the nature of FSH can be understood by analysing the side effects reported by women using FSH injections during IVF and IUI treatments. By explain-

ing these side effects, we can understand the pathologies and treatments relating to high FSH levels. The side effects can be divided into three groups:

### Liver qi and blood stagnation

Headaches, dizziness, and breast tenderness. In severe cases, when ovarian hyperstimulation syndrome (OHSS) occurs, pulmonary distress and thromboembolic events may arise. Within the framework of the six levels, these symptoms correspond to *shaoyang* disharmony, and regulation of the pivot is needed.

**Point examples:** *Yanglingquan* GB-34 with *Zhigou* SJ-6, *Zulinqi* GB-41 with *Waiguan* SJ-5 (in cases with heat),<sup>10</sup> *Neiguan* P-6 with *Taichong* LIV-3.

**Herbs:** *Chai Hu* (Bupleuri Radix), *Huang Qin* (Scutellariae Radix) *Dan Shen* (Salviae Miltiorrhizae Radix), *Xiang Fu* (Cyperi Rhizoma).

### Spleen qi deficiency with accumulation of damp and fluids

Fatigue, ovarian enlargement accompanied by abdominal pain or discomfort, diarrhea, nausea, ovarian cysts and weight gain. Within the framework of the six levels, these symptoms correspond to *taiyin* disharmony.<sup>11</sup>

**Point examples:** *Yinlingquan* SP-9 with *Chize* LU-5<sup>12</sup>, *Fenglong* ST-40, *Taibai* SP-3, *Zhongwan* REN-12.

**Herbs:** *Fu Ling* (Poria), *Bai Zhu* (Atractylodis macrocephalae Rhizoma), *Shan Yao* (Dioscorea Radix), *Yi Yi Ren* (Coicis Semen).

### Kidney qi/yang deficiency causing water passage disharmony:

A dramatic increase in vascular permeability that can result in a rapid accumulation of fluid in the peritoneal cavity, thorax and potentially the pericardium. In addition, there may be thirst, scanty dark urine and ascites. These symptoms are mainly seen in OHSS.

**Point examples:** *Shuifen* REN-9, *Shuidao* ST-28, *Yinlingquan* SP-9, *Lougu* SP-7, *Fuliu* KID-7.

**Herbs:** *Ze Xie* (Alismatis Rhizoma), *Fu Ling* (Poria), *Zhu Ling* (Polyporus), *Gui Zhi* (Cinnamomi Ramulus), *Bai Zhu* (Atractylodis macrocephalae Rhizoma).

### Case 1

The patient was a 34-year-old female who had tried to conceive, without success, for three years. At the time her treatment began, her husband's semen was normal but her FSH levels had fluctuated between 27 and 50 IU/L over the previous two years. Her menstrual cycle had been irregular during the previous three years. Menstruation occurred every 24-37 days and lasted for three days. Prior to trying to conceive, she was on birth control pills for seven years. The blood amount was normal, with few clots. During recent months, pale bleeding appeared mid-cycle. Dysmenorrhea occurred on the first day but was tolerable. In addition, the patient reported hyperthyroidism, cold feet, vaginal discharge and a tendency towards urinary tract infections. She had occasional night sweats and a dry mouth, but they did not affect her sleep. Her tongue was pale with a thin white coat, swollen left side and a red tip. The pulse was deep and thin.

In 2008, the patient began IVF treatments (usually a short protocol with five ampules of Menogon and GnRH antagonist) but the response was poor with retrieval of only 1-2 follicles, and often the follicles were empty. She was told by her doctors that it would be highly unlikely that she would conceive with her own eggs.

The patient came to the clinic desperate for help, and she was frustrated and stressed by the fact she could not get pregnant with her own eggs. It was recommended that she start taking Chinese herbs and receiving acupuncture treatments on a weekly basis.

Diagnosis: Kidney qi and yang deficiency, *jing* deficiency, Liver qi stagnation, *shen* disturbance.

Treatment strategy: strengthen Kidney qi and yang, enrich *jing* and regulate Liver qi.

**Herbal formula:** *Shu Di* (Rehmanniae Radix), *Shan Yao* (Dioscorea Radix), *Shan Zhu Yu* (Corni Fructus), *Dang Gui* (Angelicae Radix), *Chuan Xiong* (Chuanxiong Rhizoma), *Tu Si Zi* (Cuscutae Semen), *Ba Ji Tian* (Morindae Radix), *Yin Yang Huo* (Epimedii Herba), *Lu Jiao Jiao* (Cervi Cornus Colla), *Dan Shen* (Salvia Miltiorrhizae Radix), *Suan Zao Ren* (Zizyphi Semen), *Ye Jiao Teng* (Polygoni Caulis).

The formula was taken as concentrated



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powder at dosage of nine grams per day. Modifications were made over time but the base formula remained the same. Omega-3 pills and barley grass were also added.

Acupuncture treatments included points such as: *Guanyuan* REN-4, *Sanyinjiao* SP-6, *Shuidao* ST-28, *Taichong* LIV-3, *Hegu* L.I-4, *Houxi* SI-3, *Shenmai* BL-62, *Taixi* KID-3.

After five months of integrated treatments, the patient underwent successful egg aspiration during which two eggs were retrieved and fertilised. Acupuncture treatments were given on days one and four after egg transfer in order to improve implantation. Shortly after, it was very exciting to hear that the pregnancy test was positive and that the couple awaits a baby boy.

### Case 2

The patient was a 37-year-old female, who had been trying to conceive for one year. The patient reported that she had done four IVF treatments and her FSH level was 16.7 IU/L. Although she was given a high amount of gonadotropins during IVF treatments, she had only one to two eggs retrieved each time. She also had a background of hypothyroidism and therefore was taking eltroxin to regulate her thyroid. She reported that her mother and sister also had fertility difficulties and early menopause. Her cycle was regular, and the amount and colour of blood and was normal. Dysmenorrhea occurred before the menses and during the first two days. Temporal headaches were common on the first day. The tongue was purple with sticky white coat in the lower *jiao* area. The pulse was deep and soft.

The patient was diagnosed with Kidney qi and *jing* deficiency, and Liver qi stagnation with damp cold. Since there was a poor response to the high amounts of gonadotropins, the patient accepted the doctor's advice to try natural cycles without any hormones, but with 20 mg/day of steroids and Evorel patches, which contain estradiol.

Points such as *Taichong* LIV-3 and *Hegu* L.I-4 or *Waiguan* SJ-5 and *Zulinqi* GB-41, *Fenglong* ST-40, *Qihai* REN-6, and *Guanyuan* REN-4 were selected. A herbal formula called "Replenish Essence" (Kan Herb company) was given during the

follicular stage. Four more IVF attempts were completed, without any result.

The continuing intake of steroids made the patient more stressed, and she had abdominal fullness and disturbed sleep. At this point the FSH level was 13.5 IU/L and a new IVF protocol of eight ampoules of Menopure was given from day three. During the follicular phase the basic formula was changed to an extracted powder containing *Zhi Zi* (Gardenia Fructus), *Chai Hu* (Bupleuri Radix), *Fu Pen Zi* (Rubi Fructus), *Tu Si Zi* (Cuscutae Semen), *Shu Di* (Rehmanniae Radix Preparata), *Xu Duan* (Dipsaci Radix), *Bai Shao* (Paeoniae Radix Alba), *Gui Ban* (Testudinis Plastrum), *Yin Yang Huo* (Epimedii Herba), *He Huan Pi* (Albiziae Cortex), *Dan Shen* (Salvia Miltiorrhiza Radix) and *Fu Shen* (Poria).

Weekly acupuncture continued with points such as *Yinjiao* REN-7, *Guanyuan* REN-4, *Shuidao* ST-28, *Taixi* KID-3 and *Taichong* LIV-3. Treatment was given one day before and five days after egg transfer. The patient was asked to take a formula after transfer that included *Shu Di* (Rehmanniae Radix Preparata), *Shan Yao* (Dioscorea Radix), *Dang Gui* (Angelicae Radix), *Chuan Xiong* (Chuanxiong, Rhizoma), *Dang Shen* (Codonopsis Pilosulae Radix), *Xu Duan* (Dipsaci Radix), *Tu Si Zi* (Cuscutae Semen).

A few months ago a healthy baby girl was born.

### Conclusion

Poor ovarian reserve and high FSH levels have become a common complaint seen in acupuncture clinics. Chinese medicine has a unique diagnostic system that can contribute to the Western approach and provide effective treatment. By analysing FSH through the lens of Chinese medicine, we can understand the treatment strategies needed to improve ovarian function, regulate hormonal secretion, and support better response to hormonal treatment. This may increase fertility outcomes.

Additional integrated studies are needed in order to determine the efficacy of Chinese medicine in the treatment of poor ovarian reserve and high FSH levels and to therefore learn more about optimal treatment for patients.

### Endnotes

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