

# *The Etiology and Pathogenesis of Follicular Maldevelopment and Progress of Research on TCM Therapy*

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**Abstract:** Follicular maldevelopment is one of the most common causes of infertility and recurrent spontaneous abortions in women, and the complexity of the mechanisms involved in follicular maldevelopment makes the treatment of this condition difficult. In recent years, traditional Chinese medicine has accumulated a wealth of experience in the treatment of follicular maldevelopment, and has unique advantages and characteristics in treatment. Traditional Chinese medicine believes that the etiology of follicular maldevelopment is mainly in the kidneys, and is closely related to the liver, spleen and meridians, with pathological factors such as phlegm-dampness and blood stasis. Traditional Chinese medicine treatment is mainly carried out from syndrome differentiation and treatment, acupuncture and moxibustion therapy, Chinese medicine cycle therapy, Point application therapy and Point catgut-embedding therapy. By combing and summarizing the research literature on traditional Chinese medicine for follicular maldevelopment, this article discusses the etiology and mechanism of traditional Chinese medicine for follicular maldevelopment and its current research status, in the hope of providing a useful reference for more in-depth research in the future.

## 1. Introduction

Follicular maldevelopment (FM) is a condition in which the follicles do not reach the size and function of mature follicles in the later stages of follicular development, or the follicles do not develop to achieve ovulation, which subsequently leads to infertility and recurrent miscarriage, as shown in Figures 1, 2 and 3 below. A study [1] monitored follicular development by transvaginal ultrasound and suggested that there is a direct correlation between pregnancy and endometrial thickness and follicular diameter. In addition, a survey [2] showed that the prevalence of follicular maldevelopment was as high as 79.2% in patients with recurrent spontaneous abortions. Therefore, the treatment of follicular maldevelopment has a direct impact on the prevention and treatment of infertility and spontaneous abortion. The current treatment in Western medicine is based on

ovulation-promoting therapy with drugs such as clomiphene, letrozole, and urotensin, but the high ovulation rate, low pregnancy rate, and obvious adverse effects have resulted in poor patient acceptance. In recent years, traditional Chinese medicine (TCM) has accumulated rich experience in the treatment of follicular maldevelopment, highlighting the unique therapeutic features and advantages of traditional Chinese medicine. With the deeper understanding of follicular maldevelopment, the mechanism of action and clinical efficacy of traditional Chinese medicine in the treatment of this disease has been widely recognized, but at the same time there are also many controversies. The purpose of this paper is to discuss the etiology and mechanism of TCM in treating follicular maldevelopment and its current research status, in the hope of providing a useful reference basis for more in-depth research in the future.

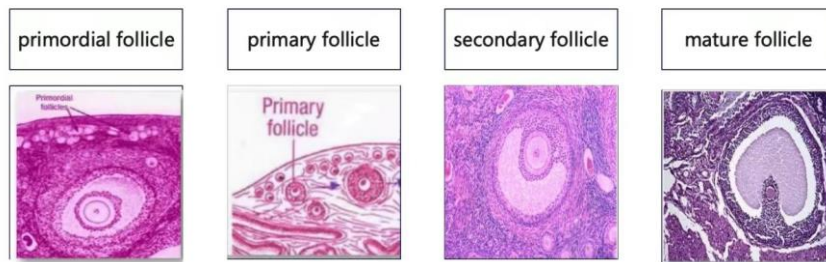


Figure 1: Four stages of follicular development

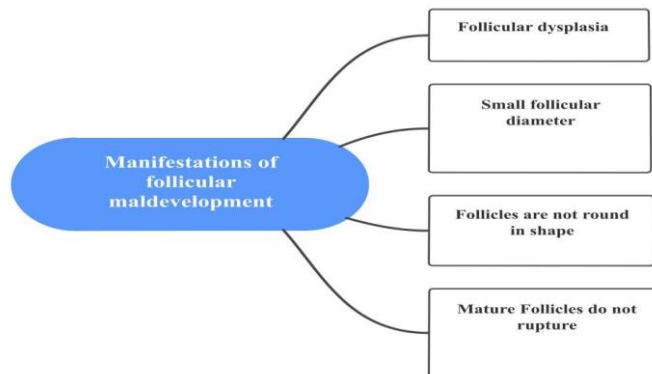


Figure 2: Signs of follicular maldevelopment



Figure 3: Six Characteristics of a Normal Dominant Follicle

## 2. Disease Causes and Pathogenesis in Traditional Chinese Medicine

There is no direct record of follicular maldevelopment in TCM. However, according to its clinical manifestations, it is categorized as "menstrual disorder", "miscarriage", "childlessness", and "breakage". The etiology of follicular maldevelopment is complex, with different schools of thought, but it is mostly attributed to the kidneys, and is closely related to the liver, spleen, and meridians and collaterals, as well as phlegm dampness, blood stasis, and other pathologic factors.

### 2.1. Kidney Qi Deficiency

The kidney is one of the five zang - organs, functions to store essence, receive qi, and govern water and fluid, serving as the innate foundation of life. One of the physiological functions of the kidney is to store and keep essence in the human body. The idea that the kidney governs innateness means that the essence stored in the kidney is responsible for the conception of the embryo as well as reproduction and development. "Fu Qingzhu Nuke" said: "The fundamental reason why a woman can get pregnant is that her kidney qi is abundant, and it is only when her kidney qi is abundant that she can take in kidney essence". Essence is stored in the kidney and relies on the action of kidney qi to fulfill its physiological function of mastering reproduction. The egg is the essence of reproduction, so the first thing to blame for poor follicular development is the malfunction of the kidneys. The kidney is the source of the "tiangui" and the origin of the thoroughfare and conception vessels. Only when the kidney qi is abundant, the "tiangui" is normal, the conception vessel is smooth, and the thoroughfare vessel is full of conditions, the woman can have regular ovulation, and the menstruation will be in time to conceive and bear children. In addition, blood is the material basis of menstruation, and qi and blood generate and utilize each other. Kidney qi deficiency will lead to qi and blood disharmony, affecting the menstrual cycle and follicle development and maturation.

### 2.2. Liver Depression

"The liver is the precursor of the woman". The liver, located above the diaphragm and inside the right hypochondrium, is responsible for storing blood, coursing and diffusion. The idea that the liver governs the activities of coursing and diffusion indicates that the liver regulates the activities of qi and propels the flow of blood, fluid, and humor in the whole body. The fact that the liver stores blood means that the liver stores a certain amount of blood to regulate the volume of blood in the body. Liver Blood enters the thoroughfare vessel and manages the regular saving and overflowing of the Blood Sea; the liver communicates with the uterus through the meridian and collateral channels, so that the uterus stores and drains blood in an orderly manner; liver and kidney have the same origin, kidney water nourishes liver wood, kidney essence and liver blood nourish each other. Therefore, the influence of the liver in the pathogenesis of follicular maldevelopment should not be overlooked. "Synopsis Golden Chamber" said: "Women's diseases are caused by deficiency, accumulation of coldly, and accumulation of qi", which lists "accumulation of qi" as one of the three major causes of women's diseases. It is evident that women are susceptible to emotional influences, and that internal injuries to the seven emotions can easily lead to live dysfunction and qi-blood imbalance, which can cause a variety of illnesses, including infertility caused by the failure of follicles to mature and be discharged as scheduled.

### 2.3. Spleen Deficiency

The spleen serves as an acquired foundation, the source of qi and blood biochemistry, functions

to transport and transform food and water nutrients, elevating lucid substances and commanding blood circulation. Spleen qi is healthy transportation, blood follows the normal way, blood and menstrual regulation; if the spleen is not healthy, insufficient qi and blood will affect, the functioning of the thoroughfare vessel and the conception vessel, and the follicles will lose nutrients and develop poorly; when the spleen yang is inadequate and there is a failure in the transportation of water and fluid, then dampness will gather and become phlegm, and phlegm and dampness will block the meridian and collateral, the uterus, and the operation of qi and blood will be impeded, leading to obstacles in follicle development and discharge, and even producing organic lesions in a long period of time. In addition, when the spleen pairs with the stomach, spleen deficiency will affect the function of the stomach. "The thoroughfare vessel is subordinate to the Yangming ", spleen and stomach disorders will affect the operation of the thoroughfare vessel, menstrual cycle, and follicle development and maturation.

#### 2.4. Phlegm-dampness

Dampness leads to diseases with heavy and turbid, sticky, and stagnant characteristics, easy to block qi leading to abnormal elevation and lowering of qi, and block the meridians and collateral leading to impassable operation of the meridian and collateral. When dampness gathers into phlegm, it is phlegm dampness, which is characterized by a lingering course of the disease that is difficult to cure over a long period of time. "Complete Works of Jingyue" said: The transformation of phlegm is invariably in the spleen, and the origin of phlegm is invariably in the kidneys." Therefore, the production of phlegm and dampness is mainly attributed to the spleen and kidney. Ancient books say: "The kidney is a water organ, the main fluid." The metabolism of fluid distribution is inseparable from the warmth of the kidney yang transpiration and kidney yin cool and moist role. In addition to the lungs and kidneys, cooperate with each other to promote the clear and turbid in the process of maintaining the metabolism of fluid distribution also has important significance. If the kidney yang is weak, the water cannot be evaporated, then the water is stagnant and gathered as phlegm, injected into the uterus, affecting the uterus, which in turn leads to a series of gynecological diseases. "The spleen is the central earth to irrigate the four sides." If the spleen is not healthy, fluid metabolism is not normal, then the water and fluid will stop gathering, and the dampness will gather into the phlegm. Day long blockage of qi, qi, and blood run poorly produces blood stasis, phlegm and blood stasis in the uterus, affecting follicular development, cannot start "Yinyun" timing, so it is difficult to conceive. Some people like to consume greasy food, which leads to the production of phlegm dampness in the body itself, high body fat, and fat obscuring the uterus, making it difficult for sperm and eggs to unite.

#### 2.5. Static Blood

Static blood is a pathological product of the malfunctioning of the blood. The Western Jin Dynasty's "The Systematic Classic of Acupuncture and Moxibustion - Miscellaneous Diseases of Women" said, "When a woman is infertile, blood stasis does not go down inside." This literature was the first to propose the mechanism of stasis resulting in infertility. Therefore, static blood is both a pathological product and a pathogenic factor. After the formation of blood stasis, it stagnates in the body and does not dissipate, not only losing the moistening effect of blood, but also triggering new lesions. According to the theory of "the blood is the mother of qi", poor local blood circulation will definitely aggravate local qi stagnation. Blood stasis for a long time, or seriously affect the operation of qi and blood, viscera and internal organs are not moistened, affecting the follicle development and maturity; or it may form lumps, blocking the thoroughfare vessel, conception vessel and the uterus, affecting menstruation and triggering infertility. As stated in "Zhu

Bing Yuan Hou Lun”: “Having sex before menstruation is over can lead to irregular menstrual cycles and the development of lumps and nodules in the uterus, leading to infertility.”

## 2.6. Injuries to the Thoroughfare Vessel, Conception Vessel, Governor Vessel and Belt Vessel

The development of gynecological diseases is closely related to injuries to the thoroughfare vessel, the conception vessel, the governor vessel, and the belt vessel. As early as in the "Nei Jing", it has been discussed that damage to the conception vessel and the governor vessel can lead to gynecological diseases such as "gynecologic abdominal lumps" and "infertility". Both the thoroughfare vessel and the conception vessel originate in the uterus and surround the lips and mouth. "The thoroughfare vessel is the sea of blood" and "the sea of the twelve meridians", regulating the qi and blood of the twelve meridians. "The conception vessel is the main fertility vessel" and is the sea of yin meridians, with the function of regulating the yin meridians of the body. The influence of the "tiangui" on the growth, development, and reproductive functions of the human body is mainly carried out through the thoroughfare vessels and conception vessels. Therefore, their damage inevitably leads to gynecological diseases. The Belt Vessel encircles the waist and connects to the longitudinal thoroughfare vessels, the conception vessel, and governor vessel and downward to the uterus. Malfunction of the Belt Vessel can lead to miscarriage and other diseases.

## 3. TCM Syndrome Differentiation and Treatment

According to traditional Chinese medicine theory, the mechanism of ovulation is mainly regulated by the reproductive axis of "Kidney- Tiangui -thoroughfare vessel and conception vessel - Uterus"(as shown in Figure 4), and the kidney, liver and spleen play a joint role. The kidney governs innateness, is the source of reproduction, and the nurturing of yin and yang. The development and growth of the follicle and its maturation and discharge depends on the formation of yin and yang in the kidney, so the promotion of follicular development and maturation mainly start with the kidney.

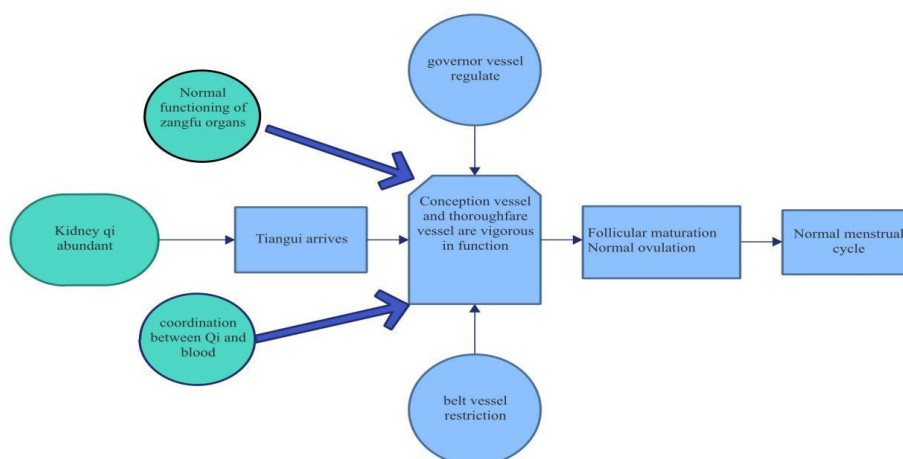


Figure 4: Female Reproductive Axis in TCM

### 3.1. Therapy for Tonifying the Kidney and Invigorating Blood

Zhang Limei [3] found that kidney tonifying and blood activating herbal formula combined with clomiphene in the treatment of follicular maldevelopment syndrome can regulate the morphology and growth rate of follicles to reach the level of normal mature follicles. At the same time, it can

significantly reduce the side effects of clomiphene, improve the tolerance of the endometrium, increase the success rate of fertilized egg implantation, and thus improve the pregnancy rate. Wu Quansheng [4] believes that "kidney deficiency and blood stasis" is the fundamental pathogenesis of infertility due to follicular maldevelopment. The treatment is based on tonifying the kidney, combining tonifying the kidney with removing blood stasis, to treat both the symptoms and the root cause. Meanwhile, letrozole combined with this method can increase the diameter of the dominant follicle and the thickness of the endometrium in the ovulation period, increase the serum estrogen level and AMH level, and thus improve the clinical pregnancy rate. Huan Chufeng [5] found that with the rapid development of the social environment, environmental factors such as environmental pollutants, radiation, and light pollution may be associated with follicular maldevelopment. The mechanism of improving follicular development and ovulation by tonifying the kidney and activating blood may be related to regulating the expression of melatonin receptors, hormones, and cytokines. Yin Yiting [6] used the method of tonifying the kidney and activating blood to treat follicular maldevelopment of kidney deficiency and blood stasis type, and the total effective rate of treatment reached 86.67%, and follicle size, endothelial thickness, and egg quality was significantly improved after treatment compared to before treatment. Li Yawen [7] replicated an animal model of follicular developmental disorders by tripterygium glycoside gavage, and found that the expression of the transcription factor FOXO3a was elevated in the ovarian tissues of rats in this model, and the expression of HIF-1a and IGF-1R was decreased. After the application of Compound Xinjiaguisheng Pill, a traditional Chinese medicine for tonifying the kidney and activating blood circulation, the level of IGF-1R was increased in the ovarian tissues of the model rats, which could inhibit follicular atresia and promote the normal growth and development of follicles by up-regulating the expression of HIF-1a and down-regulating the expression of FOXO3a.

### 3.2. Kidney and Spleen Tonifying Therapy

Lan Yujun [8] and others found that clinical treatment in the process of promoting follicular development, the addition of a formula for tonifying the kidneys and strengthening the spleen on the basis of purely Western medicine treatment was beneficial to the synchronized thickening of the endometrium, increased luteinizing hormone levels, stimulated follicular rupture and corpus luteum formation, and promoted ovulation to improve the efficacy of the treatment. Zhao Binzhu [9] used the method of tonifying the kidney and strengthening the spleen to treat patients with small follicle ovulation, which was dialectically recognized as spleen and kidney deficiency in traditional Chinese medicine, by staging the treatment before and after menstruation. The clinical symptoms and menstrual flow of these patients improved significantly after treatment, and their follicular development and follicular quality were better. Follicular maldevelopment is one of the main clinical causes of recurrent miscarriage. Based on the theory of "the kidney serving as the innate foundation of life and the spleen serves as an acquired foundation", Jiang Lijuan [10] concluded that follicular maldevelopment is closely related to the spleen and kidney. Aiming at the pathological characteristics of "spleen and kidney deficiency" of this kind of patients, the treatment warms kidney yang, strengthens spleen qi, and at the same time cooperates with the external treatment of traditional Chinese medicine to dredge the meridians and harmonize the qi and blood, and ultimately achieve a better therapeutic effect. Wang Guohua [11] was guided by the mediated "Zhongzhou" method, which tonifies the kidney and strengthens the spleen and balances yin and yang, and this method showed significant improvement in follicular development, ovulation rate, and endometrial tolerance. Zhang Zipei [12] treated postponed menstrual cycles due to follicular maldevelopment with a self-prepared herbal formula based on the method of strengthening the spleen and tonifying the kidney with an overall effective rate of 93.40%, which was clinically

effective. Zhao Xiuping [13] and others data mining Chinese medicine for the treatment of follicular maldevelopment medication pattern, found that it is mainly tonifying the kidney class of drugs, while the analysis found that tonifying the kidney and spleen formula for the ovulation obstacle of the rat model can improve the morphology of its ovarian tissue, promote the development of follicles, and improve the level of serum hormones, and effectively improve the reserve function of the ovary.

### **3.3. Kidney Tonic Combined with Liver- Clearing Therapy**

Menbo [14] believes that "the liver and kidney have the same origin", and although kidney deficiency is the main cause of patients with small follicle ovulation, we cannot ignore the important pathogenic factor of liver qi stagnation. Women use blood as their foundation and qi as their use, and the interaction between qi and blood is closely linked to the liver. Therefore, treatment should emphasize tonifying the kidneys and liver clearing at the same time, so that qi and blood can be abundant and harmonized, providing good preconditions for conceiving and nurturing the fetus. Lin Na [15] added liver-sparing herbs to the basic formula of Nourishing Essence and planted Jade Soup to treat patients with kidney deficiency and liver depression type of follicular maldevelopment, which can effectively promote follicular development and reduce the rate of small follicle ovulation and thus improve the pregnancy rate. In addition, some studies have shown [16] that tonifying the kidney and sparing liver therapy can enhance the responsiveness of the ovary and pituitary gland, promote the H-P-O-A secretion of hormone levels in the patient's body, promote the maturation of follicle development and improve the function of the corpus luteum. Liu Yongmei [17] observed the clinical efficacy of tonifying the kidney, sparing the liver, and strengthening the spleen in the treatment of infertility due to follicular maldevelopment. The treatment group was treated with traditional Chinese medicine based on tonifying the kidney and sparing the liver, while the control group was given clomiphene, and the total effective rate of the treatment group was 95.2%, which was significantly higher than the total effective rate of the control group, which was 83.3%. Wang Cai'e [18] showed that "Zuogui Shugan Tang" combined with clomiphene citrate tablets could optimize the local environment of the ovary and improve the diameter of dominant follicles to a certain extent, thus increasing the ovulation rate and conception rate. Huang Dan [19] analyzed the frequency of Chinese herbal medicines used in the treatment of follicular maldevelopment infertility in recent years, and found that the meridians of the high-frequency medicines were dominated by the liver and kidneys, and both groups of Chinese herbal formulas derived from the cluster analysis had the main efficacy of tonifying the liver and kidneys.

### **3.4. Kidney Nourishing and Resolving Phlegm Therapy**

Liu Jijuan [20] randomly divided 84 patients suffering from polycystic ovary syndrome, ovulation disorder, infertility, and at the same time dialectic is the type of kidney deficiency and blood stasis into two groups. Patients in the observation group were treated with the method of tonifying the kidney, Resolving Phlegm, and activating blood stasis combined with clomi-phenecitrate (CC), while patients in the control group were treated with CC. After treatment, the number of small follicles in the observation group was less than that in the control group, and the diameter of dominant follicles was longer, and the symptoms of obesity and hirsuteness caused by polycystic ovary syndrome could be improved at the same time. Hong Yanli [21] treated patients with polycystic ovary syndrome who was assisted in conception by in vitro fertilization, and concluded that their embryonic development potential, and clinical pregnancy rate were negatively correlated with the BMI of this patient, and that with the increase of BMI, their early spontaneous miscarriage rate was significantly higher. After the patients were pretreated with the Chinese herbal

formula for tonifying the kidney and Resolving Phlegm 3 months before IVF treatment, the patients' blastocyst formation rate and clinical pregnancy rate were significantly increased, and the early spontaneous abortion rate was significantly decreased ( $P < 0.05$ ). Hongyan Zhang [22] showed that the addition of kidney tonifying Resolving Phlegm herbs to conventional ovulation-promoting drugs can regulate hormone levels in the body, improve the endocrine environment, enhance the ability of the endometrium to accept embryos, and subsequently increase the pregnancy rate. In addition [23], studies have shown that Chinese herbal medicine tonifying the kidney and Resolving Phlegm therapy combined with "Metformin" and "Yasmin" has better efficacy than Western medicine alone in the treatment of polycystic ovary syndrome with insulin resistance, which is mainly manifested in the improvement of clinical symptoms, correction of disorders of glucose and lipid metabolism, regulation of hormone levels, and promotion of follicle development and ovulation, and other aspects. The study of Chen Jinting [24] showed a limited therapeutic effect of treating kidney deficiency phlegm-dampness polycystic ovary syndrome with kidney tonifying and phlegm-reducing formula or "Diane-35" alone. The combination of Kidney Tonifying and Phlegm Resolving Formula with "Diane-35" treatment can improve the therapeutic effect.

#### **4. Acupuncture and Moxibustion Therapy**

Acupuncture and moxibustion are a common external treatment method of traditional Chinese medicine, with the efficacy of dredging meridians and collaterals, harmonizing qi and blood, and balancing yin and yang, as well as the clinical characteristics of simplicity, safety, and effectiveness, it is widely used in the treatment of various diseases. Due to the special physiological characteristics of women and the close connection between qi, blood, and meridians, the application of acupuncture to treat follicular maldevelopment syndrome is one of the current clinical research hotspots, and the advantages of this therapy such as precise clinical efficacy, low recurrence rate, and long term efficacy have all been confirmed.

##### **4.1. Acupuncture and Moxibustion Therapy**

Guan Yujie [25] compared the clinical efficacy of acupuncture and moxibustion therapy with an ovulation stimulating needle in the treatment of follicular maldevelopment. The results showed that the diameter of the largest follicle and the ovulation rate were better in the acupuncture and moxibustion group after treatment, and this group could improve the status of the endometrium. Wang Baocheng [26] believes that the thickness of the endometrium and fertilization of the egg are closely related to the yin and yang transformation movement of the menstrual cycle. If yang is insufficient, it is difficult to produce menstrual blood, and yang deficiency with little blood affects the growth of the endometrium, and the lack of material basis for fertilized egg bedding affects the pregnancy. Based on this, the use of acupuncture with "Lei Huo" Moxibustion promotes yang production and blood growth, regulates menstruation and conception of the fetus, and achieves a good clinical efficacy. Haiying Ma [27] compared the effects of acupuncture therapy and "letrozole" + HCG therapy on the number of dominant follicles, ovulation rate, and endometrial thickness under ultrasound monitoring, and the results showed that acupuncture therapy was more effective.

##### **4.2. Acupuncture and Moxibustion Combined with Drug Therapy**

Jane Zhang [28] applied percussopunctator prick to the treatment of promoting follicular development in infertility, adding percussopunctator prick to conventional ovulation-promoting western medicine, while following the characteristics of the menstrual cycle. In the follicular phase, the focus of percussion on the thoroughfare vessel and conception vessel helped the follicles to



grow and develop; in the ovulatory phase, the focus of percussion on the surface projection of the dominant follicle helped the dominant follicle to be discharged smoothly. According to Shi Shuang [29], “Gui Shao Di Huang Tang” has the efficacy of benefiting qi and nourishing blood and nourishing yin and clearing heat, and warm acupuncture and moxibustion has the efficacy of warming the meridians and regulating qi and blood, and the combination of the two can promote the balance of the female reproductive axis and help to promote the follicle growth and development and maturation. Wang Ling [30] combined the "weekly adjustment method" with electroacupuncture therapy for the treatment of follicular maldevelopment, treating it in the premenstrual period, midmenstrual period, and late menstrual period with Gongbao Tang, Ovulation Promoting Tang, and Ovulation Assisting Tang, respectively. At the same time, electroacupuncture treatment is started on the 8th day of the menstrual cycle every other day for 30 minutes each time until the dominant follicle is discharged. This treatment can promote follicle development and maturation, improve follicle quality and ovulation rate, increase the thickness of the endometrium, and effectively make up for the defects of western medicine ovulation promotion, which is "high ovulation rate and low pregnancy rate".

## 5. Cycle Therapy

"Conception must be preceded by regulation of menstruation. "Based on the theory that "menstruation originates from the kidneys", Yuan Shiliang [31] proposed the traditional Chinese medicine treatment of "nourishing kidney yin - warming kidney yang - activating qi and blood" to treat menstrual disorders based on the characteristics of the transformation of yin and yang during the menstrual cycle, as shown in figure 5. Xia Guicheng [32-33] suggested that for the treatment of follicles that fail to mature, the focus is on the treatment of menstruation, and the regulation of menstruation is one of the necessary conditions for the conception of a fetus. Combining the characteristics of yin and yang transformation and uterine storage and drainage at different stages of menstruation, different treatment focuses are proposed. During the menstrual period, the focus is on invigorating blood, and after menstruation, the focus is on tonifying yin to promote follicular development and endometrial proliferation; during the ovulation period, yin should be tonified and yang should be assisted, and qi and blood should be toned to help the dominant follicles mature and rupture; after ovulation, yin and yang should be balanced to promote the luteal function, and by regulating the menstrual cycle to form a regular ovulation to create the conditions for conception. Cai's gynecology [34] has extensive experience in treating infertility in women. The heirs of Cai's gynecology combined the characteristics of women's menstrual cycles and annual rhythms to create the Big and Little Cycle Therapy, which has distinctive clinical features and significant therapeutic advantages. Sun Junjian [35] used the method of tonifying the kidney and regulating the menstrual cycle combined with artificial insemination to aid in the treatment of infertility caused by small follicle ovulation, which could effectively improve the clinical symptoms of the patients, improve the endometrial tolerance, and promote ovulation after follicle maturation to improve the pregnancy rate. One study [36] concluded that the theory of yin and yang transformation of the menstrual cycle in Chinese medicine is similar to the changes in basal body temperature and the cyclic "rise and fall" of ovarian hormones in Western medicine. Moreover, a clinical trial showed that the combination of Chinese and Western medicine cycle therapy could compensate for the shortcomings of CC alone and increase the thickness of the endometrium. Deng Huiling [37] treated patients with follicular maldevelopment of the kidney qi deficiency by combining herbal cycle therapy with acupoint acupuncture, which had better efficacy than oral Clomifene Citrate Tablets and helped with endothelial thickening.

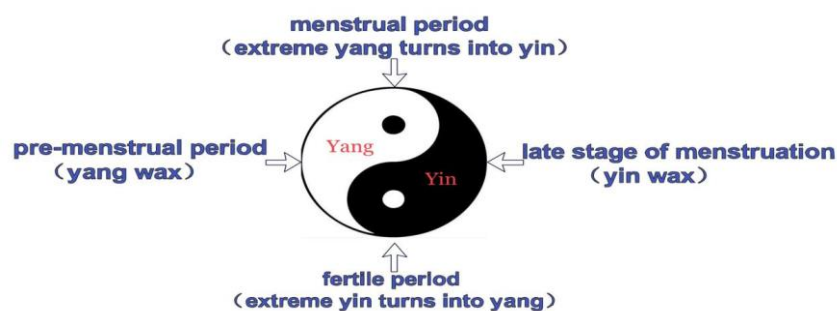


Figure 5: Yin and Yang transformations in the menstrual cycle

## 6. Other Treatments

Wen Huihua [38] found that by taking kidney tonifying and blood activating herbs orally combined with acupoint injection of compound Angelica sinensis injection, the kidney tonifying herbs could effectively help the endometrium to thicken, the blood activating drugs could help the follicles to be discharged smoothly, and the acupoint injections could be absorbed through the acupoints, and the medicine was absorbed quickly with guaranteed efficacy. This treatment is more effective when compared with clomiphene. Chen Jiaojie [39] used heat-sensitive moxibustion combined with point application therapy for the treatment of follicular maldevelopment infertility, and analyzed its effect and found that the therapy could promote follicular development and endothelial growth, improve clinical symptoms and endocrine levels, and thus improve the efficacy. Chen Ying [40] investigated the efficacy of fresh dendrobium combined with ovulation-promoting combinations in the treatment of follicular dysplasia based on the efficacy of dendrobium in replenishing deficiency and nourishing yin and found that it had an improvement in the diameter of dominant follicles, ovulation rate, endometrial thickness and pregnancy rate. Ji Lingling [41] randomly divided 60 patients with follicular dysplasia-type infertility into a treatment group and a control group, with 30 cases in each group, and gave catgut implantation at acupoints and clomiphene treatment, respectively. After 3 courses of treatment, the endometrial thickness and morphology of the treatment group were significantly better than those of the control group ( $P < 0.05$ ); and the maximum follicle diameter of the 2 groups improved significantly compared with that before treatment. It has also been shown [42] that catgut implantation at acupoints combined with oral administration of herbal formulas can improve serum sex hormone levels.

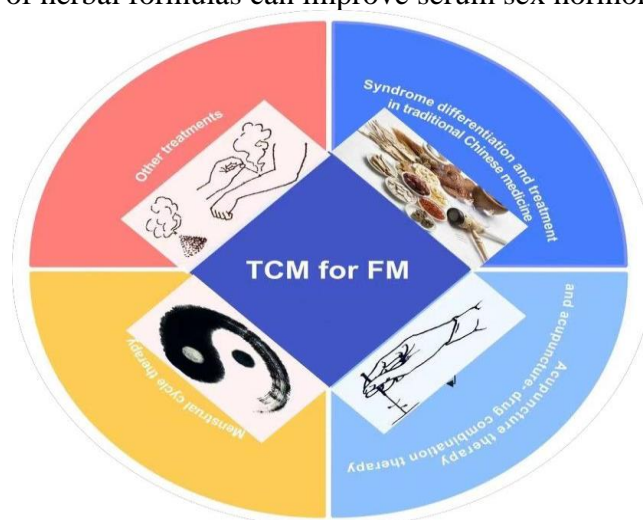


Figure 6: TCM for follicular maldevelopment

## 7. Conclusion

In summary, the current discourse and research on the treatment of follicular maldevelopment syndrome with traditional Chinese medicine has been enriching. The focus of diagnosis and treatment methods for this disease are in a state of controversy(as shown in Figure 6), but most of them are based on kidney tonic therapy, and the clinical diagnosis and treatment takes into account liver clearing, spleen strengthening, Resolving Phlegm, blood activation and so on. According to a large number of literature reports in recent years on the promotion of follicular development, induction of ovulation, and improvement of follicular quality by TCM, it can be proved that TCM treatment of follicular maldevelopment has a good clinical effect and is highly recognized by patients. In addition, a large number of scholars treating this disease combined TCM therapy with western medicine ovulation therapy, and found that the combined therapy can improve the endometrial thinness of pure western medicine ovulation, which cannot be matched with the shortcomings of the follicular development speed, and at the same time, can reduce the incidence of adverse reactions, with a high degree of safety. However, the etiology of follicular maldevelopment is complex, and the pathogenesis has not been fully clarified. At present, there is a lack of unified identification standards, efficacy standards, and a complete TCM treatment system, which requires further improvement of basic research on TCM treatment of follicular maldevelopment to provide a reference basis for clinical treatment.

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