

# *To Explore the Prevention and Treatment of Declining Ovarian Function in Contemporary Women from the Idea of "Prevention of Disease" in Traditionnal Chinese Medicine*

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**Keywords:** Prevention of Disease, Declining Ovarian Function, Preventing and Treating

**Abstract:** The prevalence of declining ovarian function among women in contemporary 5G life is increasing year by year, and with the gradual decline of ovarian function, more and more women are facing the threat of premature ovarian failure, which is extremely harmful, not only leading to the decline of female reproductive and endocrine function, but also leading to or aggravating multi-organ and multi-system dysfunction. The idea of "Prevention of disease" originates from the The Inner Canon of Huangdi, which is a representative academic thought of Chinese medicine, the essence of which lies in "preventing the untreated disease before it occurs, preventing changes after the disease has occurred, and preventing recurrence after the disease has occurred". Under the guidance of the idea of "treating the disease before it occurs", early identification and intervention of ovarian function decline is of great importance.

There are words in the Plain Question · the influence of seasons on spirit , "Therefore, the sages do not treat the sick to cure the sick, not to treat the chaos to cure the chaos, this is also called. If the disease has become a medicine after the medicine, chaos has become a cure after the cure, such as thirsty and wear well, bucket and cast cone, is not also late! ", emphasizing the importance of focusing on "treating the untreated" during the process of disease occurrence and development, in order to stop the occurrence and evolution of disease. Modern medicine divides disease prevention into three stages: primary prevention, also known as etiological prevention, which emphasizes taking measures in advance to eliminate disease-causing risk factors and improve the body's resistance to prevent the onset of disease; secondary prevention, that is, pre-clinical which focuses on taking "three early" and "five early "Tertiary prevention, also known as clinical prevention, focuses on timely treatment of patients, prevention of deterioration, and prevention of various complications[1]. "The three aspects of "prevention before illness", "prevention after illness" and "prevention after disease" are consistent with the theory of tertiary prevention advocated by preventive medicine. The three aspects of "prevention before illness", "prevention after disease" and "prevention after disease" are consistent with the theory of tertiary prevention advocated by

preventive medicine. Evidence-based medical evidence shows that Chinese medicine has important application value in disease prevention and control, which is the concrete practice of the idea of "treating the disease before it occurs".

Declining ovarian reserve (DOR) is a gynecologic disease in which the number of ovarian follicles retained in the ovaries decreases before the age of 40, the ovarian capacity to produce eggs decreases, the quality of oocytes decreases, and the secretory function of the ovaries decreases, ultimately leading to a decrease in female fertility, reflecting the reproductive endocrine function and fertility potential of women, so the main clinical manifestations are menstrual abnormalities and reproductive disorders[2]. DOR is a pre-disease warning state, if not actively prevented, early detection and timely treatment, ovarian function will further decline and eventually lead to premature ovarian failure (POF). In today's 5G era, driven by women's life status and certain concepts, the incidence of DOR is also increasing, with some literature reporting about 10% [3], but there is no effective clinical treatment for the time being, which seriously affects women's physical and mental health. The evolution from DOR to POF is a gradual and dynamic process, and some scholars have suggested that this process takes about 1-6 years [4], which provides a theoretical and practical basis for the prevention and treatment of DOR. DOR can be considered as the "prevention" stage of POF, if timely and effective prevention and treatment can prevent its transformation into POF, thus reducing the incidence of POF and better preventing its development. If timely and effective prevention and treatment can prevent the transformation to POF and thus reduce the incidence of POF, the advantages and characteristics of Traditional Chinese Medicine in preventing and treating gynecological diseases can be better utilized.

## **1. Contemporary Causative Factors of Ovarian Insufficiency in Women**

### **1.1 Emotional and Spiritual Factors - The Seven Emotions are Too Much, Resulting in the Internal Organs of Energy and Blood Malfunction, Affecting the Punch**

Modern women are driven by the effort to play multiple roles, work and life stress, easy to produce tension, anxiety, sadness, fear and other emotions - collectively known as the seven emotions, if subjected to sudden, strong or persistent mental stimulation, can lead to the seven emotions too much, the internal organs, energy and blood malfunction, affecting the punching of any gynecological diseases. In Fu Qingzhu's Obstetrics and Gynecology, there are "blood collapse due to depression", "abortion due to excessive anger", "miscarriage due to great anger", "difficult delivery due to adverse energy". "Lack of milk flow due to depression" and "infertility due to cynicism". The chronic negative emotions can affect the hypothalamus-pituitary-ovary axis, (H-P-O ax ), which in turn directly affects ovarian function. pal et al. showed that the long-term chronic mental and social stressors are harmful to ovarian reserve. Animal experiments have also confirmed the effect of different chronic stressors, resulting in a significant reduction in the number of sinus follicles and even in menopausal changes in rats[5]. The specific mechanism of action of stress on ovarian function is focused on H-P-O. Under the effect of prolonged negative emotions, the hypothalamus secretes more adrenal hormone-releasing hormone, which leads to an increase in  $\beta$ -endorphin, and  $\beta$ -endorphin receptors located on the neurons of GnRH ( gonadotropin-releasing hormone, GnRH) are depleted. depletion, which weakens the inhibitory effect on GnRH neuronal activity and causes a highly agonist state, thereby inhibiting ovarian function[6].

## **1.2 Life Factors-Diet and Behavioral Disorders, Resulting in Irregularities of Energy and Blood in the Viscera, Affecting the Punching Point**

### **1.2.1 Dietary Indiscretion**

Some contemporary women have two extremes of eating behavior, part of which is over-eating, spicy, hot, fatty, sweet and thick flavors hurt the stomach vitality, the spleen does not transport the stagnation in the middle burner is born Plain Question · arthralgia recorded “The stomach and intestines are injured when the diet is doubled”. Contemporary women over-interpret bony beauty, resulting in excessive weight loss and dieting for the sake of beauty, resulting in damage to the spleen and stomach, loss of nourishment to the kidneys, lack of kidney essence, lack of fullness of heavenly sap, and loss of nourishment to the ovaries. The lack of nourishment for the kidneys, the lack of the natural essence, the lack of the natural sap, the loss of nourishment for the spleen and the ovarian function. Excessive weight loss leads to ovarian dysfunction as a result of a combination of a hypothalamus-pituitary dysfunction and weight loss. The central nervous system is extremely sensitive to weight loss, and a weight loss of about 10% in 1 year can lead to apoplexy even if the weight is in the normal range[7]. In studies of nutrients and age at menopause, it was shown that high fat and high cholesterol diets and vegans can advance the age at menopause[8], thus suggesting that all of these behaviors affect ovarian function.

### **1.2.2 Unrestrained Behavior**

Contemporary women consider hair coloring as a fashionable beauty, but long-term exposure to chemicals such as hair dyes can disrupt ovarian function. Some literature suggests that tetraethylene cyclohexene, an antioxidant metabolite in hair dyes, can cause ovarian failure[9]. It has also been reported that the incidence of POF in hairdressers is more than five times that of non-hairdressers[10]. Tobacco and alcohol are used by modern women as a tool to relieve stress and release emotions, unaware that smoking, secondhand smoke and alcohol consumption are the most common influencing factors in daily life that reduce ovarian function. Smoking can decrease ovarian reserve of an anti-mullerian hormone, (AMH)[11]. Chemicals in tobacco reduce the number of initiating and growing follicles and weaken ovarian quality by mechanisms related to pathways that promote apoptosis, increase oxidative stress and activate adaptive eating in the ovary[12]. Compared to women with little or no alcohol consumption, women who drink regularly have a nearly 26% decrease in AMH , and excessive ethanol can not only directly damage the gonads triggering ovarian atrophy, but can indirectly affect pituitary hormone secretion and affect ovarian function by accelerating brain damage[13].

### **1.2.3 Contraceptive Methods are not Abstinent**

With the progress of society and economic development, people are influenced by western culture, on the one hand, the phenomenon of unmarried cohabitation and premarital sex among contemporary women is increasing, on the other hand, due to the change of ideology, the pressure of competition in the workplace and the limitation of economic conditions, the age of unwanted pregnancy among contemporary women is being pushed back, and furthermore, due to the lack of relevant knowledge of reproductive health protection, the incidence of unwanted pregnancy The incidence of unwanted pregnancy remains high, and some people even use early pregnancy abortion as a contraceptive birth control measure, as shown in the Post-Abortion Contraceptive Service Specifications (2018 Edition) formulated by the National Health and Wellness Commission, which indicates that there are about 9 million abortions in China every year [14]. It was found that both patients with negative pressure aspiration and medication abortion showed a decrease in ovarian

function after the procedure, and the older the woman and the more abortions she had, the greater the impact [15].

Abortion is an artificial interruption of pregnancy, which causes a sharp drop in hormone levels in the body, resulting in disturbance of the hypothalamic-pituitary-ovarian axis, and repeated abortions, which repeatedly affects the endocrine system in the body and then causes gradual decrease in ovarian function. According to Chinese medicine, repeated abortions not only damage the essence of the kidneys, which is the essence of the first heaven, but also the qi and blood of the spleen, which is the essence of the second heaven, disrupting the balance and function of the kidney-Menstruation-Chong and Ren Channels-uterus axis.

### **1.3 Environmental Factors-Thief Energy Causes Disease, Injures the Internal Organs, and Affects the Punching Point**

With the development of society, urbanization and industrialization have affected the natural environment, and the pollution of air, water and soil by chemical emissions has brought about environmental problems that endanger human health. Environmental pollution has become a modern pathogenic factor. Certain chemicals in contemporary women's living environment, such as pesticides, dyes, plastic products, food additives, etc. , have effects similar to hormones in the body or hormones within antibodies. These substances can enter the animal or human body through food or the food chain and interfere with endocrine function and affect the reserve function of the ovaries[16]. These substances, known as "Environmental endocrine disturbances factors ", can also interfere with the formation of the primordial pool and accelerate the recruitment of the primordial follicular pool, leading to the onset of ovarian aging [17]. In Chinese medicine, it is believed that the toxicity of air pollution first affects the lungs, which leads to the malfunction of the lungs, which in turn injures the five viscera and damages the ramifications, resulting in the malfunction of the kidney-Menstruation-Chong and Ren Channels-uterus axis, which affects ovarian function.

### **1.4 Physical Factors- Insufficient congenital Endowment, Inadequate Kidney Essence, and Lack of Consolidation of the Flush**

Record in Fu Qingzhu's Obstetrics and Gynecology, "The menstrual water out of the kidneys. The meridian originates from the kidneys". There are some words in the Plain Question ·Ancient Innocence Theory , "women seven years old, the kidney is strong, the teeth more hair long; two seven, the day of sebum to, the Ren vein through, the Taichong vein is strong, menstruation to time, so there are children . . . . . Deficiency of the Ren pulse at age 49, the Taichong vein decay less, the day of sebum, the ground is not accessible, so the form is bad childless. "The kidney collects essence, the essence of the innate, the spleen is the main transport, the spleen unifies blood, the liver collects blood, it can be seen that the ovarian function is closely related to the kidney, liver, spleen, the Ren line, and the main responsibility for the kidney - the innate essence. Modern medicine believes that the age of menopause and even early-onset ovarian insufficiency (POI) in women are closely related to genetics. Genetic studies of POI have shown that the X chromosome [18] and autosomes [19] are associated with the occurrence of POI from quantitative and structural abnormalities to point mutations [20] and epigenetic inheritance[21], thus showing that the age of menopause and even POI in women are closely related to congenital endowment.

Contemporary causative factors of decreased ovarian function in women still include medical factors, mainly including surgery, damage from radiotherapy treatment taken for malignant tumors, and infectious factors such as bacteria and viruses are also one of them, in addition to other causative factors. The etiology of the vast majority of patients with decreased ovarian function is unclear, and given the importance and danger of ovarian hypofunction, its mechanisms need to be

further investigated.

## **2. Prevention and Treatment of Declining Ovarian Function in Contemporary Women**

Further progression of ovarian function decline will eventually lead to failure, with immediate effects on women in terms of decreased or lost fertility, abnormal uterine bleeding, and distressing perimenopausal symptoms, and long-term effects in terms of neurological effects, osteoporosis, and cardiovascular and cerebrovascular diseases, which seriously affect women's quality of life and survival. It is well documented that early menopause can increase the risk of cardiovascular and cerebrovascular morbidity and mortality from myocardial infarction and angina pectoris has been shown to be associated with the menopause [22]. Therefore, the early identification and intervention of ovarian function decline is of great importance under the guidance of the idea of "treating the disease before it occurs".

### **2.1 Preventing Diseases Before they Happen - Primary Prevention**

#### **2.1.1 Prevent it from being born yet**

The occurrence of disease is often the result of the interaction between positive and negative aspects, as stated in The Inner Canon of Huangdi, "If positive energy exists within, evil cannot dry up" and "Where evil comes together, its energy must be weak". Therefore, Chinese medicine believes that while the human body is in a "disease-free" state, it is also necessary to regulate the vital energy at all times to nourish the body and maintain its normal function. At the same time, we should always be careful of the invasion of external evil, so as to "avoid the evil of deficiency and thieves wind, sometimes". First of all, to protect the body's vital energy. It is to respond to the natural climate change, to "eat in moderation, live in moderation, do not make delusional work", avoid smoking, alcohol, high-fat and high-protein food, less exercise and other bad lifestyles. Mentally, pay attention to the regulation of emotions. The emotional factor is one of the reasons for the development of many diseases in today's society, and declining ovarian function is no exception. Therefore, it is important to restrain your emotions, to "live in peace with happiness and anger, to regulate yin and yang, and to regulate rigidity and flexibility". Actively learn about reproductive health, scientific planning of childbirth, independent and efficient scientific contraception, and reduce the damage to women from frequent abortions. Second, to prevent the invasion of evil. We should "follow the four seasons and adapt to the cold and summer", to avoid the four seasons of evil damage to the human body. In short, before the onset of disease, Chinese medicine attaches particular importance to the maintenance of the body's positive energy. We should regulate our emotions, work and rest, eat well, be careful about our living, and do appropriate outdoor activities, and at the same time strengthen the popularization of health concepts and general knowledge of life, and promote a healthy and relaxed lifestyle, so as to improve people's awareness of health, and thus prevent it before it starts.

#### **2.1.2 Preventing it from becoming a reality**

Decreased ovarian reserve function is age-related and can also be caused by pathological factors [23]. Tests of ovarian reserve function are often used clinically to assess the number and even the quality of remaining oocytes in the ovaries of people at potential risk and to predict their fertility. The Society of Obstetrics and Gynecological of Canada (SOGC) 2011 clinical practice guidelines state that people who are suitable for ovarian reserve function assessment tests are those aged  $\geq 35$  years or those who are  $< 35$  years old but have the following risk factors for reduced ovarian function: (1) unilateral ovary. (2) History of previous ovarian surgery. (3) Low response to follicle

stimulating hormone (FSH). (4) History of chemotherapy or radiation therapy. (5) Unexplained infertility [24]. The most commonly used screening tests for ovarian reserve are: measurement of basal sex hormones: follicle-stimulating hormone (FSH): the pituitary gland releases FSH in response to stimulation by Gonadal hormone -releasing hormone (GnRH), which is regulated by negative feedback from estradiol (E2) and serum inhibitory hormone B (INH-B). For physicians, the most practical clinical index to assess ovarian reserve function is serum basal FSH, which can reflect the degree of DOR. bFSH correlates well with ovarian reserve function, and usually bFSH >10 IU/L indicates reduced ovarian reserve function, but there are individual differences[25]. The World Health Organization's Second International Standards Conference stipulated: normal bFSH <10 IU/L; moderately elevated bFSH >11. 4 IU/L; high bFSH >16. 7 IU/L [26]. Estradiol (E2): generally below 50 pg/mL in the early follicular phase and elevated in the early follicular phase (60-80 pg/mL) suggests early follicular recruitment, because E2 is susceptible to other factors and fluctuates widely and needs to be combined with other indicators to comprehensively assess ovarian function [27], but elevated bE2 (>60-80 ng/L) should also be considered for decreased ovarian reserve function [28]. Anti-mullerian hormone (AMH): a glycoprotein secreted mainly by granulosa cells of primary follicles, antral follicles, and sinus follicles, which reflects the reserve of the primordial follicular pool [29]. As a marker for predicting ovarian response independent of the menstrual cycle, AMH is clinically more convenient than other ovarian reserve markers and is not affected by hormonal drugs [30], and can predict ovarian responsiveness to gonadotropins, with low levels of AMH predicting poor ovarian response [31]. The decrease in AMH levels with age can reflect ovarian reserve and the decrease in AMH, which precedes the increase in FSH, has a better predictive value [32]. (2) Ultrasound: sinus follicle count (AFC): The number of follicles with a diameter of 2-10 mm can be counted visually under transvaginal ultrasound on the second to fifth day of menstruation. The number of sinus follicles reflects the ovarian reserve, and a bilateral AFC between 3 and 6 is indicative of a low rate of egg production [33]. The clinical use of AFC to predict ovarian reserve has the advantages of high accuracy, low cost and practicality, and is the best single indicator to assess ovarian reserve function. It is recommended that it can be used as the preferred index of ovarian reserve [34]. Ovarian volume: the formula is  $0.52 \times \text{length} \times \text{width} \times \text{height}$ , which is the value of the three diameters of the ovary in different cross-sectional angles [35]. As follicular reserve decreases, ovarian volume decreases. Although ovarian volume predicts ovarian reserve and responsiveness, it does not predict egg quality. Eggs are a non-renewable resource and once depleted they are irreversible. Therefore, the flexible use of various tests to correctly assess ovarian reserve function is essential for fertility prediction, clinical management and prognostic assessment.

## 2.2 Prevention of Disease and Change - Secondary Prevention

### 2.2.1 Prevention of Patients

The decrease in the number of sinus follicles or the quality of oocytes in the ovary and the imbalance of sex hormones in the body (10 IU/L <basal follicle stimulating hormone (FSH) <40 IU/L) occur before the age of 40 years, resulting in a series of clinical symptoms of perimenopause such as low menstrual flow, amenorrhea, reduced fertility, baking heat and sweating, insomnia and irritability, and loss of libido, which will gradually evolve into In the absence of early intervention, premature ovarian failure will gradually develop[36]. In December 2015, the European Society of Human Reproduction and Embryology proposed the concept of premature ovarian insufficiency (POI), which clearly requires at least 4 months of menstrual sparseness or amenorrhea with 2 measurements of FSH > 25 IU/ml at 4-week intervals [37]. The FSH diagnostic value is shifted forward, reflecting the characteristic of "treating the disease before it happens" in Traditional

Chinese Medicine. Western medicine estrogen and progestin sequential therapy (HRT) is a common clinical treatment for the decline of ovarian reserve function, that is, to improve ovarian function by cyclic supplementation of exogenous estrogen and progestin, the commonly used protocols are Estradiol Valerate tablets with progesterone or Climen cycle sequential method. Studies have shown that fentanyl can significantly improve clinical symptoms and adjust serum sex hormone levels in patients, and is simpler and more convenient to administer than HRT[38]. This method is easy to take, fast-acting, but also has significant side effects, and long-term hormone use may increase the risk of endometrial hyperplasia, endometrial cancer, breast cancer, and thrombophilia. Women with advanced DOR who need to get pregnant can use medication to promote ovulation and assisted reproduction techniques. Chinese medicine treatment is based on evidence-based and personalized treatment, incorporating the idea of "treating the disease before it happens" and holistic regulation, mostly focusing on tonifying the kidney and taking into account the pathology of the liver, spleen, heart and other internal organs. Combined with western medicine treatment, it can also reduce the toxic side effects of western medicine, strengthen the efficacy and improve the cure rate. Patients should be actively treated at this stage to prevent the gradual decline of ovarian function leading to premature ovarian failure, resulting in the decline of female reproductive and endocrine functions and aggravating multi-organ and multi-system dysfunction.

### **2.2.2 Physicians' Defense**

Most women have positive attitudes toward DOR prevention and treatment, but knowledge about DOR is poor. This leads to poor prevention-related sexual behavior. Health education is an important part of the disease prevention and control system and is a basic function of public health services. Therefore, on the one hand, we doctors should do a good job of scientific education in our outpatient work, so that more women are aware of the early warning status of declining ovarian function and can be alerted themselves. On the other hand, we need to improve our ability to identify patients with potential risks, detect, intervene and treat them early, in order to reduce the prevalence of premature ovarian failure in contemporary women, protect women's reproductive health and physical and mental health, and thus improve the quality of life and well-being of contemporary women.

### **2.3 Prevention of Recurrence after Disease-Tertiary Prevention**

The medical book Shibu Zhai records, "The sickness is more than a small cure, so the caution after the illness should be ten times greater than before." Clinically, after the decline in ovarian function is relieved by treatment, the function of the internal organs is coordinated, and the Yin and Yang of the body are in balance, consolidation treatment is still needed. In addition, declining ovarian function is a disease that requires long-term comprehensive management. During the recovery period, we cannot rely solely on medication, but also on pharmacotherapy, food therapy, emotional therapy and behavioral therapy. The progressive development of ovarian function decline with age cannot be prevented, but it can be alleviated through regular monitoring and early prevention. Although the decline cannot be prevented, it can be slowed down by regular monitoring and early prevention. Although the symptoms are reduced and ovarian function is restored with treatment, the inevitable decline of ovarian function cannot be avoided. However, after the improvement of the disease, continuing the integrated treatment with Chinese and Western medicine can not only improve the menstrual condition, but also increase the probability of pregnancy, improve ovarian function and prevent long-term complications.

As mentioned above, the prevalence of DOR in contemporary women is increasing year on year, and the risk of DOR is progressive, and once it has developed into premature ovarian failure it is

often too late to treat it. Therefore, timely prevention is the key to reducing the risk of developing the disease. The concept of "treating the disease before it happens" in Chinese medicine has been applied in the treatment of many clinical diseases and has achieved significant clinical results. In this article, we introduce how to apply the Chinese medicine concept of "treating the disease before it occurs" to guide prevention and treatment, and Prevention of recurrence after disease, with a view to benefiting the treatment of declining ovarian function. However, research in Chinese and Western medicine has not yet fully elucidated the causes and mechanisms of the disease, and there are still many questions that need to be addressed.

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