

# Discussion on Pathogenesis and Treatment of OHSS with TE in Special Parts Based on the Theory of “Prolonged Illness Invading the Collaterals”

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**Abstract:** *TE associated with OHSS is a rare but fatal complication, and its thrombus distribution has a significant tendency to head and neck, which is different from conventional venous thromboembolism. The study found that although the formation of OHSS thrombosis was acute attack, its root lay in the basis of “chronic disease” of “kidney essence depletion”. The core pathogenesis was “excessive yang transformation, excessive yin formation” and “liver failure to discharge”, resulting in “deficiency of body fluid and blood stasis”. The final pathological product was ascending along the liver meridian and blocking the neck-skull collaterals. The treatment should be based on “dredging collaterals” as the general principle, combined with tonic deficiency, eliminate evil, and skillfully use of drugs to guide the channel, in order to achieve accurate treatment.*

**Keywords:** Prolonged illness invading the collaterals; OHSS; TE; Collateral disease; Tcm pathogenesis.

## 1. Introduction

Ovarian hyperstimulation syndrome (OHSS) is a common iatrogenic complication in assisted reproductive technologies, and thromboembolism (TE) [1, 2] is one of its most serious complications with a high fatality rate. Both clinical observations and systematic retrospective studies have revealed that OHSS-associated thrombus exhibits a unique pattern in its anatomical distribution [1, 3-5], i.e., the involvement of the venous system of the head and neck is significantly higher than that of ordinary venous thromboembolism (VTE), except for the lower extremities. This particular phenomenon is difficult to explain by a single hemodynamic or hypercoagulable state, and a deeper theoretical explanation is urgently needed [6-9].

The theory of “long-term illness into the collateral” created by the Qing Dynasty physician Ye Tianshi revealed the development law of disease evil qi from shallow to deep and from meridians into the collateral, and pointed out that collateral blockade is the common pathogenesis of a variety of chronic and intractable diseases. This theory emphasizes the “main blood of the collaterals”, which are subtle channels for qi and blood circulation, and their lesions are lingering and difficult to heal [10]. This paper attempts to use the theory of “long-term disease into the network”, combined with the pathophysiological characteristics of OHSS, to explore the formation mechanism of special parts of thrombosis complicated by it, and to propose treatment strategies from the perspective of integrating traditional Chinese and Western medicine, in order to provide new ideas and methods for clinical practice.

## 2. Theoretical Connotation of Long-term Illness

“Luo” refers to the collateral, which was first recorded in the “Huangdi Neijing” [11]. “Suwen · The “Miao Lai Lun” states:

“The evil qi invades the body..... If it retains and does not leave, it will enter and reside in the Sun meridian, and if it resides in the collateral meridian, it will remain and not leave..... It can be seen that the collateral vessels are a huge network system, which is the channel for the circulation of qi and blood in the body, and nourishes the internal organs through branches and layers of progressive methods. “Lingshu · The Beginning and the Beginning” records: “Those who are long-suffering, evil spirit goes deep”, which first pointed out the trend of the development of long-term illness to deepen, “Jinkui Essentials · The first to describe the transmission law of meridian diseases such as “meridians are affected by evil into the internal organs”, and pointed out that attention should be paid to the role of the smooth meridian in the treatment of diseases. Ye Tianshi of the Qing Dynasty first proposed the concept of “collateral disease” on the basis of his predecessors, and founded the academic ideas of “long-term illness into the collateral” and “long-term pain into the collateral”. Ye Shi wrote in “Clinical Evidence Guide Medical Case · Accumulation Gate” proposed: “It is the initial qi stagnation in the meridians, and over time, blood damage enters the collaterals..... Qi is dull and blood stagnation, gradually bruised and paralyzed, and prolongs the pimple”, describing the process of evil qi penetrating deep into the human body, from qi to blood, and from meridians into the collaterals. As Ye said: “Yin Luo is the collateral under the organs”, while the Yang Luo (floating collateral) is located on the surface of the body, and the position is superficial. In terms of spatial structure, the disease is transmitted from the yang collateral to the meridians, the meridians are transmitted to the yin collateral (visceral collateral), and the disease develops from qi to blood in terms of the course of the disease.

## 3. Analysis of the Pathogenesis of OHSS Thrombosis from the Perspective of “Chronic Disease into the Network” Theory

### 3.1 The Basis of “chronic disease” of OHSS Thrombosis:

### Kidney Essence Depletion

The premise of the theory of “long-term illness” is “long-term illness”. Although OHSS has a rapid clinical onset, its pathological basis has the characteristics of “chronic disease”. From the perspective of traditional Chinese medicine, the process of controlled ovulation induction can be regarded as an excessive depletion of kidney essence [12, 13]. Kidney essence deficiency leads to abnormal gasification and fluid distribution disorders, resulting in water and dampness arrest, resulting in thoracic ascites, ovarian enlargement and other typical manifestations of OHSS. This process coincides with the pathological changes of increased vascular permeability and fluid extravasation in modern medicine. Therefore, kidney essence depletion is the internal root of OHSS, and it also lays the groundwork for the subsequent “entry”.

### 3.2 Evolution of Core Pathogenesis: Yang Hyperactivity and Yin Excess, Deficiency of Fluids and Blood Stasis

On the basis of kidney deficiency, ovulation induction drugs lead to abnormal increases in estrogen levels in the body [14], which the author believes is “excessive yang transformation” in traditional Chinese medicine theory. Excessive yang qi consumes yin blood on the one hand, and leads to “too much yin formation” on the other hand, blood concentration, increased viscosity, and the formation of a hypercoagulable state [7-9]. At the same time, water and dampness infiltrate, body fluid loss, and blood loss of moisture, further aggravate blood stasis, forming a pathological situation of “blood deficiency and blood stasis” or “blood and blood are the same disease”. This process is completely in line with the evolution law of collateral disease that “long-term illness will deepen evil qi, and both qi and blood will be damaged, and it will turn into stasis and condensation phlegm, mixed with meridians”.

### 3.3 The Key to the Formation of Special Parts: the Liver Meridian is Chaotic, and Evil is Uploaded Along the Meridians

Why do OHSS thrombosis occur in the head and neck? The author believes that the theory of “long-term illness into the collateral” combined with the meridian behavior provides the answer. The foot jueyin liver meridian “follows the femoral yin, passes through the genitals, reaches the lower abdomen, distributes the ribs, follows the back of the throat, goes up to the forehead, connects the eye system, goes up to the forehead, and meets the Du meridian at the top”. Its path runs through the lower jiao uterus (where the ovaries are located), abdomen, chest and flanks, throat, neck, and up to the top of the head.

OHSS disease originates from the lower jiao, and its pathological products are water dampness and blood stasis, which can be disturbed with the rebellion of the liver meridian qi under the joint action of the root of “kidney essence loss” and the pivot of “liver loss and drainage”. Patients with OHSS are often accompanied by great emotional stress [15], which can easily lead to liver qi stagnation and aggravate qi stagnation and blood stasis. When the visible evils such as blood stasis, water and dampness go upward along the “highway” of the liver meridian and block the “key” parts of the meridians, such as the neck and skull base, it leads to the formation of thrombosis in these atypical parts. The thrombus

itself, as a tangible evil blocking the veins, is a specific sign of “long-term illness entering the collaterals”, and the disease evil penetrates deep into the sun collateral and blood vessels.

## 4. Treatment Ideas Based on the Theory of “Chronic Illness into the Network”

Ye Tianshi proposed that “the network is used for communication”, and the treatment of Luo disease is nothing more than “general supplement” and “general dispersion” [10]. In view of the particularity of OHSS complicated by thrombosis, the treatment needs to be based on the general outline of “communication”, combined with the pathogenesis and location, and precise policies should be implemented.

### 4.1 General Principles: Activate Blood and Water, Clear the Circulation and Dispel Evil

For the core pathology of OHSS, blood circulation and blood stasis should be carried out throughout. In the acute stage or when evil is the main problem, it should be “clear the blood vessels, attack the strong fortifications, and be supplemented with spices”. Insect drugs [16, 17] such as leeches can be used, which have a strong ability to “search for blood stasis in the collaterals” and can loosen the root of the disease. Supplemented with spicy and fragrant qi products such as woody fragrance and fragrant attachment, taking their “running nature”, they lead various medicines deep into the blood vessels and open up depression and disperse knots. This coincides with the idea of using Guizhi Poria Pills and Wuling Powder to add and subtract in modern research, and reusing Salvia, Motherwort, Zelan, and Leeches to improve microcirculation.

### 4.2 Classification and Treatment: Both Attack and Supplement, Harmonize Yin and Yang

For those whose condition is prolonged or the righteous qi is deficient, the method of “replenishing deficiency and clearing the channel” is necessary [18]. If you see that the yang qi is deficient and the limbs are cold, then the method should be “warm yang tonification”, which can be given ginseng, astragalus, aconite, etc., so that the yang qi can pass through the collaterals and the fluids circulate blood. If you see that the yin fluid is depleted, the mouth is dry, the tongue is dry, it is advisable to “harmonize the yang and sweet cold, and promote the meridians”, you can add asparagus, dendrobium, wolfberry, etc., to clear heat and produce fluid without being greasy. According to the patient’s physique, treatment stage and the conflict between good and evil, the clinical syndrome should flexibly use strategies such as both attack and supplement, main attack and supplement, or main supplement and attack.

### 4.3 Precise Strike: Skillfully Use the Meridian to Reach the Disease

The author believes that in view of the special distribution of OHSS thrombosis, the use of meridian medicine is crucial. According to the principle of “where the meridians pass, where the disease is mastered”, on the basis of activating blood circulation and circulation, the addition of meridian inducers according to the thrombus site can significantly

improve the curative effect. If the thrombus is located in the head and neck, you can add Pueraria Pueraria and Chuanxiong to attract the drug to the head and face; located on the upper limbs, can add mulberry branches; Located on the lower limbs, you can add ox knees. This kind of targeted treatment idea is a subtle combination of the overall concept of traditional Chinese medicine and syndrome differentiation and treatment.

#### 4.4 Collaboration Between China and the West: Complementary Advantages to Ensure Safety

In clinical practice, the idea of integrating traditional Chinese and Western medicine should be adopted. Once thrombosis is diagnosed, it is necessary to strengthen the intervention of traditional Chinese medicine to “dissolve blood stasis and clear the channel” on the basis of standard anticoagulant (e.g., low molecular weight heparin) therapy in Western medicine [19]. Early intervention of traditional Chinese medicine can not only synergistically anticoagulate and improve symptoms, but may also play a unique advantage in regulating vascular endothelial function and correcting coagulation-fibrinolytic system imbalance, thereby reducing the risk of bleeding and improving the safety of treatment.

#### 5. Conclusion

In summary, Ye Tianshi’s theory of “chronic disease into the network” provides a profound and systematic theoretical framework for explaining the distribution of special sites complicated by thrombosis in OHSS. The key link lies in the rebellion of the liver meridian qi mechanism, which leads to the upward movement of evil, and eventually leads to the obstruction of the cervical-cranial collaterals. Based on this, clinical treatment should be based on “Tongluo”, organically combining blood and water activation, deficiency and circulation, and inducing meridian reporting, and synergizing with modern medical anticoagulation therapy to form a precise, safe, and effective integrated traditional Chinese and Western medicine prevention and treatment system [20], which opens up a new path for overcoming this clinical problem.

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