

# Clinical Case Illustration of Modified Wumei Pill in the Treatment of Cholinergic Urticaria

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**Abstract:** Cholinergic urticaria is a condition triggered by factors such as physical activity, emotional fluctuations, or dietary influences, which lead to an increase or decrease in core body temperature and subsequently cause 1-3 mm non-follicular lesions on the trunk and upper limbs. The disease course is often prolonged, with severe cases lasting for years and significantly affecting patients' daily lives. This paper analyzes the principles, methods, prescriptions, and medicinals involved in a clinical case observed under mentorship, to elucidate the therapeutic mechanism and clinical experience of using Wumei Pill in the treatment of cholinergic urticaria.

**Keywords:** Cholinergic urticaria, Wheals, Wumei Pill, Jueyin syndrome.

## 1. Introduction

Urticaria is a localized edema reaction caused by mast cell-mediated dilation of small blood vessels in the skin and mucous membranes and increased permeability. Clinical manifestations include wheals of varying sizes accompanied by itching, and about 20% of patients have angioedema [1-2]. The global incidence of urticaria is 4.4% [3], and the incidence of urticaria in my country is 2.6% to 4.2%, which is much higher than that in developed Western countries and neighboring countries [4]. The course of acute urticaria does not exceed 6 weeks, and it is chronic if it exceeds this. Acute urticaria may have a more specific cause, such as food, drugs or viral infection. The cause of chronic urticaria is often difficult to determine. Up to 20% of people will experience acute urticaria in their lifetime [5], while the prevalence of chronic urticaria is about 0.05% to 3% [5]. About 50% of patients with chronic urticaria will resolve on their own within 1 year, and 80% will resolve within 5 years [6]. Western medicine believes that the pathological process may be that when factors such as emotions stimulate the heat regulation center and parasympathetic nerves, the nerve synapses abnormally release acetylcholine, which binds to mast cells, causing mast cell degranulation and the release of histamine, which increases capillary permeability, thereby producing wheals on the skin surface and causing itching and discomfort [7]. Related studies have shown that skin mast cell activation and degranulation are the key to its pathogenesis [8]. Type I allergic reactions caused by the binding of allergen-specific immunoglobulin E to its high-affinity receptors, type IIb autoimmunity mediated by immunoglobulin G autoantibodies, and type I autoimmunity mediated by immunoglobulin E autoantibodies can all cause the disease; in addition, inflammation, food, nonsteroidal anti-inflammatory drugs, coagulation, etc. also have a certain influence [8]. When the disease occurs, degranulated substances such as histamine and cytokines can activate sensory nerves, leading to vasodilation, plasma extravasation, and immune cell infiltration, inducing symptoms such as wheals or itching [3].

The principles of Western medicine treatment for urticaria are to first identify and eliminate the cause, induce tolerance, and achieve complete symptom relief using medications with minimal adverse reactions. For acute urticaria, a

standard-dose second-generation, non-sedating H1 antihistamine is the preferred treatment. If this is ineffective, glucocorticoids or equivalent doses of dexamethasone administered intramuscularly or intravenously can be used. This is also suitable for patients in shock or with laryngeal edema, along with subcutaneous or intravenous epinephrine. For chronic urticaria, a single standard-dose second-generation, non-sedating H1 antihistamine is first-line treatment. Second-line treatment involves switching to a different second-generation, non-sedating H1 antihistamine, using a combination, or combining a first-generation H1 antihistamine at bedtime, or increasing the dose by two- to four-fold. Third-line treatment, the final step, can include tripterygium wilfordii polyglycoside tablets, cyclosporine, biologic agents, or even phototherapy. Urticaria seriously affects the patient's quality of life due to its recurrent itching, leading to impaired work and learning abilities, and placing a huge burden on the medical system and the social economy [9].

Cholinergic urticaria is a type of chronic induced urticaria, accounting for about 5%-7% of chronic urticaria. Its pathogenesis, except for the involvement of acetylcholine, sweat pore blockage, sweat allergy, and serum factors, its underlying mechanism is not clear [1]. It is more common in young male patients and is caused by emotional stress, exercise, eating hot drinks or hot baths that lead to increased body temperature in the deep body. Clinical manifestations are round papular wheals with a diameter of 1 to 3 mm that appear a few minutes after stimulation, mostly on the upper trunk and proximal extremities, accompanied by itching, burning or tingling. In severe cases, it may be accompanied by allergic reactions, angioedema and respiratory symptoms. The disease has a long course and can last for several years in severe cases. Western medicine uses H1 antihistamines as the first-line treatment, which cannot be discontinued in the short term and is prone to recurrence.

## 2. Etiology and Pathogenesis

Cholinergic urticaria is categorized as "urticaria," "wind bumps," or "wheal" in Traditional Chinese Medicine. Urticaria is characterized by the occasional appearance of wheals, accompanied by itching, in random locations, and

recurring intermittently, disappearing without leaving a trace. The Suwen states: “When wind evil invades the muscles, the muscles become weak, the true qi disperses, and the cold attacks the skin, which then spreads to the pores and opens the hairs. When the evil qi runs rampant, it causes itching.” The Jinkui Yaolue·Shuigibingpian mentions that “when wind and qi attack each other, the strong wind will cause hidden rashes and itching on the body.” It explains that wind evil leads to itching.

The Zhubingyuanhou Lun·Fengsaotizhiyoushuowuzhihuazheng states: “When evil qi invades the skin and encounters wind and cold, it causes wind-induced itching.” It explains that wind evil leads to itching. The Yizongjinjian·Shangshouxinjiue states: “This syndrome is commonly known as ghost rice lumps. It is caused by sweating and being exposed to wind, or lying in the open to cool. Wind evil often attacks people with superficial deficiency.” It explains that itching is caused by wind attacking people with weak body. Therefore, traditional Chinese medicine believes that “wind evil” is closely related to the onset of itching. Traditional Chinese medicine divides wind into external wind and internal wind. The wind evil of the six external evils can cause disease, and internal wind can also cause disease [10]. The Suwen Zhizhen Yao Da Lun states: “All wind-induced dizziness and vertigo are related to the liver,” pointing out that wind and the liver are closely related. Cholinergic urticaria is often caused by emotional stress and sweating due to heat, and the course of the disease is long, seriously affecting life. Patients are prone to anxiety and depression. Therefore, this disease is closely related to emotions and can be treated from the perspective of the liver [11]. The liver governs emotions and stores blood. It likes to be smooth and hates depression. The liver belongs to the wood element in the five elements and governs growth. Wood generates wind, and liver disease can generate wind. Wind is prone to movement and changes frequently. Wind evil stagnates in the skin and causes itching. Liver depression turns into heat and damages yin blood. Blood deficiency and wind dryness cause itching [10].

### 3. The Prescription and Syndrome Characteristics and Application of Wumei Pills

Wumei Pills are from Treatise on Febrile Diseases: Differentiation of Jueyin Disease Pulse and Symptoms and Treatment. Article 338 says: “If a patient with typhoid fever has weak pulse and coldness, and the skin becomes cold after seven or eight days, and the patient is restless and has no momentary restlessness, this is visceral coldness, not ascaris coldness. Ascaris coldness means the patient will vomit ascaris. If the patient is calm but becomes restless from time to time, this is visceral coldness. Ascaris enters the diaphragm, causing restlessness, which will stop after a while. If the patient vomits after eating and becomes restless again, the ascaris comes out when it smells the food odor, and the patient often vomits ascaris. Ascaris coldness is treated with Wumei Pills. It is also effective for long-term diarrhea.” In Treatise on Febrile Diseases, Ke Qin wrote: “Wumei Pills are the main prescription for Jueyin, not just for ascaris coldness.” Later generations of doctors used Wumei Pills for many diseases such as internal medicine, gynecology, and pediatrics, not just for ascaris [12].

Wumei Pills are mainly used to treat Jueyin disease. The Treatise on Febrile Diseases states: “Thirstiness, qi rising to the heart, pain and heat in the heart, hunger without appetite, vomiting of roundworms after eating, and diarrhea that does not stop.” This article is the outline of Jueyin disease. Jueyin is the organ of wind and wood, and wind is the change of qi. Zhang Xiju said: “The disease of Jueyin is the disease of Jueyin qi.” When Jueyin is affected by evil, it will attack the spleen and stomach. Jueyin is endowed with wind and wood and harbors the fire of the phase. The cold evil suppresses the fire of Jueyin, and the fire of the phase is extremely depressed and then erupts. The depressed fire rushes upward, so the pathological symptoms are mostly mixed with cold and heat.

The composition of Wumei Pills is: Wumei (300 pieces), Asarum (6 liang), Dried Ginger (10 liang), Coptis chinensis (16 liang), Angelica (4 liang), Aconite (6 liang), Sichuan Pepper (4 liang), Cinnamon Twig (6 liang), Ginseng (6 liang), Phellodendron (6 liang) [13]. In this formula, Wumei (*Prunus mume*) is acidic, harmonizing the liver’s wood, and its sour and sweet properties transform yin, nourishing the liver, making it the main herb. Cinnamon twig, Asarum, Aconite (roasted), Dried ginger, and Sichuan pepper are pungent and hot, dispelling cold and soothing the liver, preventing the liver from overtaking the spleen. Coptis chinensis and Phellodendron chinense are bitter and cold, clearing heat. Angelica sinensis nourishes liver blood, and ginseng replenishes yin and qi. The combined effects of these herbs transform sour and sweet into yin, pungent and sweet promote yang, while sour and bitter promote yin. This approach combines attack and supplementation, balancing firmness and flexibility, and strengthening the body and dispelling pathogenic factors. Physician Liu Youyu stated, “For all symptoms of yang deficiency below, fire excess above, and qi reversal in the middle, the appropriate treatment should be tailored to the specific symptom.” He emphasized that the key to Wumei Wan’s application is its conformity to the pathogenesis of Jueyin syndrome. Therefore, it is used to treat mixed cold and heat, and upper heat and lower cold.

### 4. Case Examples

Patient Wang, a 38-year-old male, presented to our clinic on March 5, 2021, with widespread itching and wheals for over two years. He reported developing wheals of varying sizes and severe itching over his entire body two years ago due to work-related stress and emotional tension. Since then, symptoms have flared up with stress or during exercise, but have gradually subsided after his mood calmed down. He had visited other hospitals several times and was diagnosed with cholinergic urticaria. He was prescribed oral antihistamines such as loratadine and cetirizine hydrochloride, but his symptoms did not improve significantly. He therefore presented to our clinic, complaining of widespread itching and wheals with stress or during exercise. These wheals gradually subsided after his mood calmed down. He reported high work pressure, late nights, and depression. He did not experience dryness or bitter taste in the mouth, had a normal appetite, and aversion to cold beverages. His bowel movements were normal. The tongue was enlarged, pale red, with a thin white coating, burrs on the edges and tips, and a stringy pulse. Western medicine diagnosed it as cholinergic urticaria, while Traditional Chinese Medicine diagnosed it as

urticaria. The syndrome differentiation was liver depression and spleen deficiency, with upper heat and lower cold. Treatment was to soothe the liver and relieve depression, warm the middle and strengthen the spleen, and dispel wind and clear heat. I prescribed modified Wumei Wan. Wumei Wan (20g) contains 5g Sichuan peppercorns, 10g roasted ginger, 10g scutellaria baicalensis, 20g moutan bark, 10g bupleurum root, 20g white peony root, 20g dragon bone, 20g stir-fried white atractylodes, 10g poria, 10g dried tangerine peel, 20g julibrissin flower, 10g stir-fried tribulus terrestris, and 5g liquorice root. The patient took 15 doses of the original prescription, decocted and taken orally. At the second visit, the itching symptoms were significantly alleviated, the wheals had largely disappeared, his mood improved, his appetite improved, and his sleep was normal. He continued to receive 15 doses of the original prescription. Follow-up by phone showed that the wheals had not reappeared after more than two months of discontinuation, and he was fully recovered.

Note: The patient is a young male who is under great work pressure and has depression. The liver governs emotions and likes to be relaxed and hates depression. The liver fails to release. First, in the Five Elements, the liver belongs to metal and the lungs belong to wood. Metal and wood are mutually exclusive. The liver fails to release, liver wind invades the lungs, and the lung qi fails to spread and descend properly. The lung governs the skin and fur, and the skin pores are loose. The defense system is not solid, and the nutrient and defensive systems are out of balance. External pathogens and qi and blood fight against each other and form wheals on the skin surface, causing wheals of varying sizes. Second, the liver fails to release, liver depression damages the earth, liver depression suppresses the spleen, and spleen dysfunction leads to poor appetite, spleen and stomach deficiency and coldness, and aversion to cold drinks [14]. Third, the liver fails to release, liver depression turns into fire and damages yin. In addition, the patient usually stays up late, which can also secretly consume yin blood, resulting in insufficient yin blood, blood deficiency and wind dryness, and wind dryness causes itching. The syndrome is liver depression and spleen deficiency, a mixed syndrome of cold and heat. The heat is in the meridians of the lungs and liver, and the cold is in the spleen and stomach. Black plums are sour and sweet, promoting fluid production, nourishing yin and blood, and softening and tonifying the liver. Sichuan peppercorns are pungent and warm, allowing lung metal to descend, preventing heat from rising, and dispelling cold from the spleen and stomach. "Compendium of Materia Medica" states, "Pepper is a substance that follows fire to lead to metal, causing fire to descend because of metal. When fire returns, the earth is at peace, and the cold is no longer oppressive, so it naturally retreats and retreats. Isn't this the reversal of movement into stillness? Therefore, pepper is a substance that descends." Roasted ginger is pungent, warming the middle; Scutellaria baicalensis is bitter and cold, clearing lung heat; and Cortex Moutan is pungent and cold, both to benefit the lungs and calm the liver. "Compendium of Materia Medica" states, "Cortex Moutan is pungent and cold, benefiting the lungs and calming the liver. By preventing liver qi from rising and lung qi descending, all symptoms are alleviated." Second, liver depression transforms into heat to clear heat; Bupleurum Root soothes the liver and relieves depression, White Peony Root nourishes blood and softens the liver, Dragon Bone

calms the liver and suppresses yang, Albizia Julibrissin calms the mind and relieves depression, Stir-fried Tribulus Terrestris calms the liver and relieves depression, dispels wind and relieves itching, Stir-fried Atractylodes Macrocephala, Poria, and Tangerine Peel with bran strengthen the spleen and replenish qi, and Licorice harmonizes the various herbs. The combination of these herbs, sour and sweet invigorates yin, pungent and sweet promotes yang, sour and bitter promotes yin, and cold and heat, hardness and softness are used together to treat mixed cold and heat syndromes.

## 5. Discussion

The pathogenesis of cholinergic urticaria remains unclear, and the disease course is long. Western medicine primarily treats it with antihistamines and hormones, which cannot be discontinued briefly and are prone to recurrence. The condition is often triggered by emotional tension, stress, and heat exposure during exercise, and its long course significantly impacts the patient's mood. Based on this characteristic, TCM prescriptions should target the Jueyin Liver Meridian. Wumei Pills are primarily used to treat Jueyin conditions. Chen Xiuyuan once explained that Wumei Pills align with Zhongjing's theory that "liver diseases should be treated with sour tonics, aided with bitter herbs, and benefited with sweet herbs." He proposed that Wumei Pills "have a balanced combination of sour, sweet, bitter, and bitter flavors, and a balanced nature of tonics, supplements, and benefit. By integrating the Jueyin meridian and treating it together, the earth and wood meridians can function harmoniously." The Qianzhai Medical Collection states: "The lungs have the nature of hard metal, yet their structure is weak. The liver has the nature of soft wood, yet its structure is heavy and solid. Therefore, the lungs, being delicate, are easily invaded, while the liver, relying on its toughness, often bullies them. The lungs are called delicate organs, while the liver is considered a strong organ. Often, when the liver is overactive and produces excess energy, while the lungs are weak and unable to descend, liver disease invades the lungs." The above case also supports the effectiveness of Wumei Wan in treating cholinergic urticaria. The renowned Chinese medical master Pu Fuzhou stated: "Exogenous infection that invades the Jueyin meridian, and the seven emotions that damage the Jueyin meridian, although the clinical manifestations vary, Wumei Wan can be used for all diseases if the pathogenesis is adhered to. Following the principle, different diseases can be treated with the same treatment." In clinical practice, we must continue to dialectically formulate treatments, prescribing prescriptions based on the symptoms and using the appropriate medication. We should not simply use a prescription without understanding its underlying principles. We also need to inherit and innovate, and boldly apply classical prescriptions in clinical work!

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