

Research Progress in Traditional Chinese Medicine Diagnosis and Treatment of Refractory Cough

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Abstract: Refractory cough, defined as chronic cough persisting for over 8 weeks with ineffective conventional treatment, involves mechanisms such as airway hyperresponsiveness, abnormal neural sensitivity, and immune imbalance. Modern medical therapies face limitations in efficacy and significant side effects. Traditional Chinese medicine (TCM), guided by the principles of “holistic concept” and “treatment based on syndrome differentiation”, demonstrates unique advantages through regulating visceral functions and improving airway microenvironment. This paper systematically summarizes theoretical characteristics and therapeutic strategies proposed by TCM practitioners for refractory cough over the past decade, integrates clinical applications and cutting-edge technologies, and explores future development directions to provide references for clinical practice and research.

Keywords: Refractory cough, TCM practitioners, Etiology and pathogenesis, Treatment methods and formulae.

1. Introduction

Refractory Cough: A Challenging Respiratory Disorder with Advances in Traditional Chinese Medicine. Refractory cough, a common complex respiratory disorder affecting 5%-10% of the global population, arises from heterogeneous etiologies such as cough variant asthma (CVA), gastroesophageal reflux-related cough (GERC), and post-infectious cough (PIC) [1]. Conventional therapies, including glucocorticoids and neuromodulators, are limited by drug resistance and adverse effects (e.g., dizziness, somnolence) [2]. In Traditional Chinese Medicine (TCM), this condition is categorized as “protracted cough” or “stubborn cough,” attributed to pathological factors such as *wind*, *phlegm*, *blood stasis*, and *deficiency*, with therapeutic principles emphasizing “eliminating pathogens, reinforcing healthy qi, and harmonizing viscera” [3]. Recent theoretical and clinical innovations by TCM scholars are summarized below.

2. Qi Movement Harmonization Theory

Prof. DING Taoying and colleagues, guided by the Yellow Emperor’s Inner Classic axiom “all viscera may induce cough,” identify “respiratory dysfunction” as the core pathogenesis. While impaired diffusion and descent of lung qi manifest superficially, the root lies in systemic dysregulation of qi movement [4] [5]. Pathomechanisms are stratified into: Excess patterns: Characterized by stagnation of body fluids in exterior-interior compartments. Deficiency patterns: Driven by insufficient qi propulsion.

Therapeutic strategies integrate: Holistic regulation: Unblocking the Shaoyang meridian, regulating triple energizer qi movement; purging heat via bowel clearance to pacify rebellious lung qi; resolving fluid retention to address the “fluid deficiency with water excess” paradox. Balanced reinforcement and elimination: Expelling pathogens while preserving healthy qi. Stratified syndrome differentiation: Deconstructing complex patterns into exterior-interior, cold-heat, and deficiency-excess layers for targeted intervention. Precision medication: High-dose single herbs (e.g., Mulberry Bark [*Sangbaipi*, *Mori Cortex*] 60g) and

simplified classical formulae (e.g., the two-ingredient Mulberry Wine Formula). Dynamic therapeutic adjustments: Tailoring treatments to pathological evolution (e.g., exogenous triggers, therapeutic complications), epitomizing ZHANG Zhongjing’s principle: “Observe the pulse and symptoms, discern pathological changes, and treat accordingly.” This paradigm offers a “dual pathogen elimination-healthy qi reinforcement, integrated local-systemic regulation” framework for modern refractory cough (e.g., chronic bronchitis, tumor-associated cough), exemplifying TCM’s scientific adaptability.

3. Wind Pathogen and Throat Theory

XUE Xiaoming and FENG Changhan et al. propose wind pathogen as the central etiology, emphasizing the “exogenous wind triggering endogenous wind” mechanism with throat involvement [6] [7] [8]: Exogenous wind: Invasion of lung-defense systems by wind-cold, wind-heat, or wind-dryness due to qi deficiency, disrupting lung qi diffusion. Endogenous wind: Arises from liver qi stagnation, yin deficiency with yang hyperactivity, or chronic blood stasis-phlegm turbidity binding in lung collaterals. Therapeutic approaches: Exogenous wind: Light diffusion of lung qi with phlegm-resolving agents (“treat the upper energizer as lightly as feathers”). Endogenous wind: Liver regulation and wind extinguishing (“still the wind to silence the bell’s resonance”). Cold-heat differentiation: Cold patterns: Warming lung-dispersing formulae (e.g., self-designed Wenfei Sanhan Zhike Tang) to resolve cold-phlegm. Heat patterns: Lung-clearing formulae (e.g., Qingfei Zhike Huatan Fang) with Rhubarb [*Dahuang*, *Rhei Radix et Rhizoma*] to purge intestinal heat (lung-intestine exterior-interior synergy). Throat regulation: Itching: Indian Trumpet Flower Seed [*Muhudie*, *Oroxylum Indicum*] and Belamcanda [*Shegan*, *Belamcandae Rhizoma*]. Congestion: Scrophularia [*Xuanshen*, *Scrophulariae Radix*] and Golden Buckwheat [*Jingiaomai*, *Fagopyri Dibotryis Rhizoma*]. Dryness: Ophiopogon [*Maidong*, *Ophiopogonis Radix*] and Trichosanthes Root [*Tianhuafen*, *Trichosanthis Radix*]. Blood activation: Applying the axiom “protracted

cough inevitably involves stasis” with Salvia [*Danshen*, *Salviae Miltiorrhizae Radix*] and Moutan Bark [*Mudanpi*, *Moutan Cortex*] to enhance wind elimination (“blood circulation extinguishes wind”).

Emphasizing “Visceral Interconnections,” the treatment protocol frequently incorporates Minor Bupleurum Decoction (Xiaochaihu Tang) to regulate the liver and harmonize the stomach, reflecting the “liver-regulating and lung-calibrating” therapeutic strategy. This approach synergizes with modern pharmacological insights: Zhisou San (Cough-Stopping Powder): Modulates inflammatory pathways (e.g., NF-kB, TNF- α) to suppress airway hyperresponsiveness. Insect-derived medicinals (e.g., Centipede [*Wugong*, *Scolopendra*], Earthworm [*Dilong*, *Pheretima*]): Alleviate bronchospasm via calcium channel blockade and smooth muscle relaxation, as elucidated through electrophysiological studies. This integrative framework bridges classical TCM theories (e.g., visceral synergy, qi-blood harmonization) with contemporary biomedical mechanisms, offering a systematic solution for refractory cough through multi-target modulation.

4. Confluence of Exogenous and Endogenous Pathogens Theory

Prof. FU Yi, inheriting YU Jiayan’s theory of “confluence of exogenous and endogenous pathogens,” posits that refractory cough primarily arises from “exogenous pathogens invading a pre-existing internal injury,” forming a synergistic pathogenic state [9]. Etiopathology Exogenous pathogens: Wind, cold, fire, dryness, influenza viruses, and environmental pollutants. Endogenous pathogens: Stem from constitutional imbalances or chronic conditions, generating internal phlegm, dampness, and blood stasis. Pathogenic synergy: Constitution-pathogen resonance (e.g., yang-deficient individuals predisposed to cold pathogen convergence; yin-deficient individuals prone to heat transformation). Seasonal influences align with Yellow Emperor’s Inner Classic viscera-season correspondences (e.g., spring wind injuring the liver, autumn dryness assaulting the lung), emphasizing season-constitution interactions.

Therapeutic Strategies: Exogenous pathogen management: Wind-cold: Ephedra Velutina (processed Ephedra herb, Mahuangrong, Ephedrae Herba Processing Product) for mild lung diffusion (suitable for debilitated patients). Wind-heat. Honeysuckle (Jinyinhua, Lonicerae Japonicae Flos) to expel pathogens. External cold with internal fluid retention: Minor Green Dragon Decoction (Xiaoqinglong Tang) to warm and resolve cold-fluid. External dryness injuring fluids: Mulberry and Apricot Kernel Decoction (Sangxing Tang) for lung moistening. Endogenous pathogen regulation (constitution-based): Qi deficiency. Astragalus (Huangqi, Astragali Radix) to fortify exterior defense. Yang deficiency. Mugwort Leaf (Aiye, Artemisiae Argyi Folium) to warm yang and resolve fluids. Phlegm-dampness obstructing the lung: Inula Flower (Xuanfuhua, Inulae Flos) to descend qi and transform phlegm. Blood stasis in lung collaterals: Salvia (Danshen, Salviae Miltiorrhizae Radix) to activate blood circulation. Herbal Synergy Core combination: Ephedra Velutina-Mugwort Leaf-Inula Flower Ephedra Velutina: Mildly diffuses lung qi. Mugwort Leaf. Warms yang, disperses cold, and exerts anti-inflammatory effects. Inula

Flower. Descends rebellious qi and resolves phlegm. Mechanism: Coordinates qi movement dynamics (ascending - descending regulation), simultaneously eliminating pathogens and reinforcing healthy qi. Diagnostic Principles: Clinical focus: Identifying cardinal symptoms and differentiating yin-yang patterns. Constitutional analysis: Tailored syndrome differentiation to “pacify internal imbalances and expel external pathogens” (an-nei rang-wai, addressing both root and branch.)

5. Warming Principles in Lung Treatment and Integrated Acupuncture-Herbal Therapy

Director XIONG Yan asserts that while “adverse rising of lung qi” (fei qi shangni) constitutes the immediate pathogenesis of refractory cough, therapeutic interventions should adhere to the principle of “treating the lung with warming methods” (zhi-fei bu-yuan wen) [10]. The disease mechanism primarily involves exogenous pathogens activating latent internal injuries or triggering recurrence of dormant pathogens. As stated in Suwen, “all viscera may induce cough,” indicating that systemic visceral dysfunction—such as liver qi stagnation, spleen deficiency generating phlegm, kidney failing to grasp qi, or heart fire disturbing the lung—can disrupt lung qi diffusion and descent. Concurrently, six-bowel obstructions may ascend to impair the lung, resulting in “concurrent exterior-interior pathology. Therapeutic Framework 1. Qi Regulation as Foundation: Integrated acupuncture and herbal therapy. Combines pharmacotherapy with acupuncture to achieve dual internal-external regulation [11] [12] [13] [14]. Clinical strategy. “Acute phases prioritize acupuncture for symptomatic relief; chronic phases employ herbs to consolidate root health.” 2. Acupuncture Interventions: Hegu (LI4) and Chize (LU5): Disperse wind and diffuse lung qi. Thunder-fire moxibustion: Resolves cold-phlegm through thermal stimulation. 3. Herbal Protocols: San’ao Decoction (Three-Unbinding Decoction) + Zhisou San (Cough-Stopping Powder): Releases exterior cold. Adjuvant herbs: Codonopsis (Dangshen, Codonopsis Radix) and Ledebouriella (Fangfeng, Saposhnikovia Radix) to reinforce healthy qi and expel pathogens. Mechanistic Rationale Synergistic action: Acupuncture regulates visceral functions and unblocks qi pathways, while herbs stabilize systemic balance. Core philosophy: “Harmonization of qi movement ensures spontaneous cough resolution” (qi-ji tiaochang ze ke zi ping). “

6. Liver-Lung Qi Disharmony Theory

Prof. SUN Jianguang and XU Jingshi established a unique therapeutic system for refractory cough centered on “liver-lung qi disharmony,” advocating liver-oriented treatment strategies [15] [16]. Pathomechanism The core etiology involves liver-lung disharmony and wind-fire interaction: 1) Anatomical-Physiological Interconnection: Liver and lung meridians interconnect (liver channel traverses the diaphragm into the lung). Five-phase theory: Excessive liver qi (wood) overacts on the lung (metal), impairing lung qi descent and causing paroxysmal cough. 2) Liver Wind Agitating Lung Collaterals: As the “wind-wood organ,” the liver generates endogenous wind that synergizes with exogenous wind, triggering airway spasm (manifesting as

throat itch-induced cough or stimulus hypersensitivity) mirroring cough variant asthma's airway hyperresponsiveness.

3) Liver Fire Injuring the Lung: Liver stagnation transforming into fire scorches the lung (dry cough, hypochondriac pain, irritability, bitter taste). Chronic cough depletes yin, inducing lung dryness and liver hyperactivity, forming a "yin deficiency-wind stirring-qi rebellion" vicious cycle.

Therapeutic Principles: Liver Regulation First: Integrate soothing, extinguishing, clearing, and tonifying methods. Liver-Lung Harmonization: Main formulae: Sini San (Frigid Extremities Powder: Bupleurum [*Chaihu*, *Bupleuri Radix*] and Immature Bitter Orange [*Zhishi*, *Aurantii Fructus Immaturus*] regulate liver qi ascent-descent. Xuanfu Daizhe Tang (Inula and Hematite Decoction) descends lung qi and resolves phlegm Adjuvant pairing: Platycodon [*Jiegeng*, *Platycodonis Radix*] and Great Burdock Achene [*Niubangzi*, *Arctii Fructus*] coordinate qi diffusion and descent. Wind Extinguishing and Spasm Relief: Insect-derived medicinals: Cicada Molting [*Chantui*, *Cicadae Periostracum*] and Silkworm [*Jiangcan*, *Bombyx Batryticatus*] (containing quercetin for antitussive effects). Earthworm [*Dilong*, *Pheretima*] relaxes bronchial smooth muscle. Exterior-wind elimination: Schizonepeta [*Jingjie*, *Schizonepetae Herba*] and Ledebouriella [*Fangfeng*, *Saposhnikovia Radix*]. Fire-Clearing Strategies: Liver fire assailing the lung. Shengjiang San (Upbearing and Downbearing Powder: Silkworm + Cicada Molting elevate clear qi; Rhubarb [*Dahuang*, *Rhei Radix et Rhizoma*] + Turmeric [*Jianghuang*, *Curcumae Longae Rhizoma*] descend turbid qi), paired with Loquat Leaf [*Pipaye*, *Eriobotryae Folium*] and Mulberry Bark [*Sangbaipi*, *Mori Cortex*] for lung heat clearance, and Sichuan Chinaberry [*Chuanlianzi*, *Toosendan Fructus*] for liver regulation - emphasizing diffusing stagnant fire over pure purgation. Yin Tonification: Yin deficiency with wind stirring. Zengye Tang (Fluid-Increasing Decoction: Rehmannia [*Shengdihuang*, *Rehmanniae Radix*], Scrophularia [*Xuanshen*, *Scrophulariae Radix*], Ophiopogon [*Maidong*, *Ophiopogonis Radix*]) nourishes water to anchor wood. Adjuncts: Aster [*Ziwan*, *Asteris Radix*] and Stemona [*Baibu*, *Stemona Radix*] moisten the lung; Chinese Angelica [*Danggui*, *Angelicae Sinensis Radix*] and Peach Kernel [*Taoren*, *Persicae Semen*] resolve stasis; Pinellia [*Banxia*, *Pinelliae Rhizoma*] eliminates phlegm while moderating harsh properties. Mechanistic Integration This protocol balances pathogen elimination and healthy qi reinforcement through multitarget modulation of qi dynamics, phlegm-stasis resolution, and viscera harmonization.

7. Western Medicine Diagnosis and Chinese Medicine Treatment

Professor Qiu Xiaotang has developed distinctive diagnostic and therapeutic strategies for chronic refractory cough by integrating TCM theory with modern medicine [17]. His approach prioritizes prevention of misdiagnosis and mistreatment, initially differentiating Western medical etiologies. This involves excluding organic diseases (e.g., pulmonary neoplasms, tuberculosis) and confirming chronic cough diagnoses (e.g., gastroesophageal reflux, postnasal drip syndrome) before initiating treatment [18]. Pathogenetically,

he attributes refractory cough primarily to mismanagement of external wind-cold invasion [19]. Initial exterior syndrome may progress to lung qi constraint through inappropriate antibiotic use or excessive cold-natured herbs (TCM "bitter-cold medicinals"), resulting in residual pathogens lodging in the lung. This leads to impaired dispersion-depuration functions and rebellious qi-induced coughing. The characteristic presentation of "throat itch triggering cough, cold/external irritant exacerbation" aligns with wind pathogen's ascending nature, while persistent "dry cough with scanty sputum" reflects cold-induced fluid congelation and phlegm-qi interaction. These mechanisms correspond to modern concepts of airway hyperresponsiveness in chronic cough conditions (e.g., cough-variant asthma, atopic cough). Emphasizing cold/heat and deficiency excess pattern differentiation, he cautions against indiscriminate use of heat-clearing medicinals or antibiotics that may consume qi-yin and drive pathogen inward. Therapeutically, he maintains wind-cold treatment principles unless clear heat manifestations emerge (e.g., yellow sputum, red tongue). His core protocol employs "wind-cold dispersion and lung qi rectification", exemplified by the modified Xing Su San formula: Principal herbs: lung qi downbearing, Perillae Folium (wind-cold expulsion), wind convulsion relief, Adjunct components: Saposhnikovia Radix (exterior resolution), Scrophulariae Radix (pharynx moistening), Asteris Radix (phlegm transformation), Poria + Pinelliae Rhizoma (spleen fortification), Platycodonis Radix-Eriobotryae Folium (qi dynamic regulation), Glycyrrhizae Radix (harmonization). This formula synergizes warming - moistening actions with simultaneous exterior-interior treatment. Modifications include: Spasmodic cough: kidney consolidation This systematic approach provides a TCM therapeutic framework for refractory cough that integrates classical theory with contemporary medical understanding.

8. Phlegm-Stasis Theory in Cough Pathogenesis

Scholars including Bai Zhengping, Zheng Xiaowei, and Li Peifu propose that refractory cough arises from "phlegm-stasis obstructing the lung with counterflow qi failing to descend" [20] [21] [22]. External pathogens (wind-cold, wind-heat, wind-dryness) invading the lung-defense phase, if mismanaged, may transform into heat, condense fluids into phlegm, and induce qi stagnation-blood stasis over time. This results in phlegm-stasis intermingling and obstructing lung collaterals ("chronic disease entering collaterals"). Concurrent internal organ dysfunction (spleen deficiency generating dampness, liver constraint transforming fire, kidney failing to grasp qi) disrupts qi dynamics, exacerbating phlegm-stasis formation and establishing a "qi deficiency → phlegm-stasis → qi counterflow" vicious cycle. Therapeutic Principles: 1. Dual Resolution of Phlegm-Stasis: Prioritize phlegm/stasis predominance, assess coexisting pathogens, and evaluate visceral deficiency/excess while addressing local-systemic interactions. 2. Empirical Formula: Core components: Mori Cortex (phlegm-heat clearance), Trichosanthis Pericarpium (heat-phlegm resolution), Platycodonis Radix (lung qi diffusion), Peucedani Radix (lung qi downbearing), Stemona Radix (antitussive), Curcumae Radix (blood activation), Pheretima (collateral unblocking). Phlegm-heat: Throat itch: Oroxyli Semen +

Belamcandae Rhizoma Severe stasis: Hirudo + Persicae Semen Liver fire: Moutan Cortex + Gardeniae Fructus Constipation: Visceral Regulation Strategies Spleen reinforcement: Citri Reticulatae Pericarpium + Poria (dampness transformation) Liver constraint: qi moisturizing Kidney consolidation: Psoraleae Fructus + Schisandrae Fructus Sign-Guided Interventions Pharyngeal follicular hyperplasia (wind-phlegm-stasis): Cicadae Periostracum (wind convulsion relief) Sublingual stasis spots (collateral obstruction): Salviae Miltiorrhizae Radix (blood activation) This framework provides novel insights into refractory cough management through synergistic phlegm-stasis resolution and systemic viscera modulation.

9. Summary

Refractory cough, characterized by its prolonged clinical course and multifactorial etiology, presents therapeutic challenges in conventional Western pharmacotherapy. Against this backdrop, TCM practitioners have achieved notable clinical efficacy through syndrome-differentiated interventions, simultaneously advancing TCM theoretical frameworks and expanding clinical applications. These developments not only provide novel therapeutic strategies but also contribute to symptom alleviation and enhanced quality of life for affected individuals, thereby demonstrating TCM's unique value in comprehensive cough management [23].

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