

# ***A Spleen-Centric Therapeutic Approach for Chronic Radiation-Induced Intestinal Injury Based on the Latent Pathogen Theory***

**Jiaqi Jiang<sup>1,a</sup>, Jingtao Sha<sup>2,b,\*</sup>**

<sup>1</sup>*Shaanxi University of Chinese Medicine, Xianyang, 712046, Shaanxi, China*

<sup>2</sup>*Xi'an Affiliated Hospital of Shaanxi University of Chinese Medicine, Xi'an, 710021, Shaanxi, China*

*<sup>a</sup>535443522@qq.com, <sup>b</sup>1245328255@qq.com*

*\*Corresponding author*

**Keywords:** Chronic Radiation-Induced Intestinal Injury; Latent Pathogen Theory; Spleen-Oriented Treatment; Damp-Heat and Blood Stasis Toxin

**Abstract:** Chronic radiation-induced intestinal injury (CRII) is a common complication in patients undergoing abdominal or pelvic radiotherapy, characterized by persistent diarrhea, abdominal pain, and hematochezia. Conventional treatments often yield limited efficacy and associated side effects, underscoring the need for more effective therapeutic approaches. Based on the theory of Latent Pathogen in Traditional Chinese Medicine (TCM), this study proposes a comprehensive etiopathogenetic framework centered on spleen dysfunction. Within this model, spleen deficiency is considered the core pathological basis, which further intertwines with dampness accumulation, toxin-blood stasis interaction, and progressive yin-fluid depletion. Correspondingly, the proposed treatment strategy prioritizes: (1) strengthening the spleen and replenishing qi to address the root cause; (2) resolving dampness and detoxification; (3) activating blood circulation to resolve stasis; and (4) nourishing yin to restore fluid balance. A representative clinical case is presented, demonstrating marked symptom improvement following treatment with a customized herbal protocol tailored to these principles. This TCM-based integrative framework offers a promising translational model for synergizing with Western medicine in the holistic management of CRII.

## **1. Theoretical Foundation: Latent Pathogen Theory**

Radiation-induced intestinal injury (RIII) is a complication of abdominal, peritoneal and pelvic malignant tumor after radiotherapy, belonging to the category of radiation injury disease [1]. In recent years, radiation therapy has been widely used as an effective treatment for malignant tumors before and after operation, which also leads to the increase of the incidence of radiation intestinal injury. Chronic radiation intestinal injury is mainly manifested as recurrent diarrhea, abdominal pain, purulent blood stool, nausea, vomiting, tenesmus, etc. If progressive development can cause rectal fistula, intestinal obstruction, rectal stricture, etc. Repeated radiation intestinal injury brings serious inconvenience to patients' life and affects their quality of life. Western medicine generally takes oral anti-inflammatory drugs, formaldehyde retention enema and other symptomatic treatment,

the treatment effect is not ideal, once the drug is stopped, it is easy to occur repeatedly. Therefore, it is an important direction of intestinal radiation protection research to explore more efficient and safe prevention and treatment methods, to find effective prevention and treatment targets to reduce the incidence of radiation intestinal injury and alleviate the clinical symptoms of patients [2-3]. Therefore, from the TCM etiology and pathogenesis of radiation intestinal injury as the cut-in point, based on the theory of latent evil, the TCM syndrome differentiation treatment idea of treating chronic radiation intestinal injury from spleen is considered, in order to provide new ideas for clinical application, so as to reduce the pain of patients and improve clinical treatment effect.

The conceptual origins of Latent Pathogen Theory (Fu Xie) trace to the Qin-Han dynasties, where "latent" (Fu) denotes pathogenic concealment and "pathogen" (Xie) signifies disease-inducing factors. Foundational texts such as the Inner Canon of Huangdi describe seasonally persistent pathogens causing delayed pathology. Subsequently, Zhang Zhongjing advanced the "latent qi" concept in Treatise on Exogenous Febrile Diseases, utilizing pulse diagnosis with meridian-organ differentiation [4]. Critically, Wang Shuhe integrated these principles, proposing "latent cold transforming into warmth," thereby expanding the theory beyond acute pathogenesis. The Ming-Qing era witnessed further evolution in Treatise on Pestilential Theory, broadening "latent pathogen" to encompass Six Excesses, internal injuries, and pathological products (e.g., phlegm, blood stasis). Contemporary interpretations classify latent pathogens as any etiological agent persisting subclinically before manifestation, including pathological metabolites [5].

Modern doctors believe that latent pathogens can be divided into narrow sense and broad sense, congenital, exogenous and internal injury. In narrow sense, latent pathogens are latent temperature diseases. In broad sense, latent pathogens are latent in the body for a period of time, and the disease occurs out of date. In addition to the pathogenic factors mentioned in traditional medicine, modern medicine believes that pathological products or metabolites inside and outside the human body belong to the category of latent pathogens [6].

## **2. Pathogenesis: Spleen Deficiency as the Central Mechanism**

### **2.1 Deficiency of Healthy Qi with Pathogenic Excess: Phlegm-Dampness and Qi Stagnation**

The pathogenesis of chronic radiation-induced intestinal injury (CRIII) is fundamentally characterized by deficiency of healthy qi and excess of pathogenic factors, primarily involving the spleen as the pivotal organ and the large intestine as the target site [7]. Initially, during the conflict between healthy qi and pathogenic factors, sufficient healthy qi maintains defensive capacity, resulting in subclinical manifestations. However, prolonged exposure compromises the body's resistance, allowing latent pathogens to proliferate and inducing refractory disease. As elucidated in Essential Readings for Medical Professionals Accumulation: "Early-stage disease features robust healthy qi and superficial pathogens; chronic disease involves pathogen invasion with depleted healthy qi." Specifically, the spleen (earth element) governs physiological functions. Qi deficiency impairs its transportation capacity, exacerbated by latent pathogens directly invading spleen qi. Functionally, the spleen regulates water metabolism, supported by the lung's dispersion, kidney's fluid control, and sanjiao's coordination. Thus, the spleen serves as the hub of fluid dynamics (Jingyue Quanshu: "Water's regulation resides in the spleen"). Modern clinical studies corroborate that spleen-kidney deficiency and pervasive dampness constitute core pathological mechanisms [8-10]. Pathologically, impaired spleen transportation leads to: 1) Retention of fluids in the middle jiao; 2) Endogenous phlegm-dampness formation; 3) Dysfunctional intestinal fluid separation; 4) Incomplete digestion of water and food residues. These factors collectively result in diarrhea. Concurrently, disrupted spleen qi ascent compromises the spleen-stomach pivot mechanism for qi

movement. Consequently, abnormal qi descent induces acute abdominal pain in CRIII.

## 2.2 Intestinal Collateral Damage by Stagnant Blood

The invasion of exogenous pathogens typically exhibits progressive transmission, as described in Miraculous Pivot: "Pathogens initially penetrate through skin and striae; persistent retention leads to collateral then meridian involvement. " In contrast, radiation is characterized as a radiation-specific fiery toxin (Huo Du) that bypasses superficial defenses to directly damage viscera, particularly the spleen. This direct assault occurs through two primary mechanisms: Dose-accumulation effect: 1) Prolonged radiotherapy leads to the internal accumulation of pathogenic heat toxins, which intensify heat (as a yang pathogen) and impair the spleen's blood-generating function. This results in fluid retention and blood stasis. 2) Exacerbation of spleen deficiency: Pre-existing spleen qi deficiency further compromises blood production and circulation, promoting additional stasis formation. Pathologically, accumulated qi stagnation and blood coagulation in the large intestine manifest as abdominal pain. Moreover, intense heat scorches intestinal collaterals, causing: Local blood stasis obstruction; Collateral corrosion and erosion; Progressive tissue putrefaction → carbuncle/fistula formation [11]. At the same time, the collaterals are broken and blood overflow can be seen, and blood stasis signs such as hematochezia, dark tongue, slippery or astringent pulse, irregular menstruation of women, dark purple blood color, etc. can be seen. The specific pathogenic mechanism is shown in Figure 1.

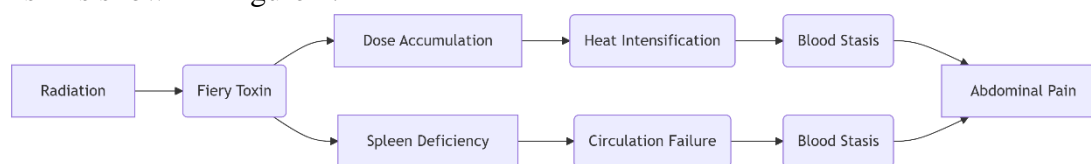


Figure 1 Pathogenic Mechanisms

## 2.3 Pathogenic Transformation into Warm-Dryness with Yin-Fluid Depletion

The established pathological triad—qi deficiency, spleen-stomach weakness, and primary phlegm-dampness—creates a milieu where latent toxins and fiery pathogens interact with blood stasis. This convergence fuels damp-heat stasis accumulation, generating endogenous fire that transforms into dryness-toxin. Critically, these elements are pathologically interdependent, collectively depleting essence-blood and body fluids. Jingyue Quanshu articulates the mechanism: "Fire-induced yang generates dryness; cold-activated yin manifests dryness." In chronic radiation intestinal injury, latent hot-turbid toxins predominantly evolve into warm-dryness (Wen Zao), which exerts triple pathogenic effects: 1) Spleen deficiency impairs maternal qi, compromising lung metal nourishment. 2) Yangming dryness transformation induces systemic malnutrition. 3) Direct nutrient yin (Ying Yin) injury [12], a self-reinforcing cycle emerges: Warm-dryness exacerbates yin deficiency, impairing fire control and amplifying pathogenic fire. Consequently, yin consumption manifests through: Local dryness: Constipation, oliguria. Systemic depletion: Weight loss, lethargy, shortness of breath.

## 3. Therapeutic Strategy: Rooted in Spleen Regulation

### 3.1 Spleen Fortification with Dampness Resolution to Elevate Middle Qi

The core therapeutic strategy for chronic radiation intestinal injury centers on spleen fortification to replenish qi, recognizing that robust spleen function is prerequisite for transforming water-grain

essence into bioavailable qi. Concurrently, adequate spleen qi sustains spleen yang abundance, generating the warm impetus required for dampness expulsion and restoring physiological dampness movement within the middle jiao. This integrated process establishes harmonious qi dynamics, as conceptualized by Huang Yuanyu's theory of spleen-stomach synergy: the spleen (Taiyin earth) governs ascent while the stomach (Yangming earth) regulates descent, their interaction forming the yin-yang pivot for qi circulation. Critically, restoring the spleen's inherent ascending property is achieved through dual spleen-tonification and dampness resolution, whereby nourished grain-respiratory qi combines with redirected dampness to alleviate sinking syndromes. Clinically, however, indiscriminate use of spleen-tonifying agents (e.g., *Atractylodis Macrocephalae Rhizoma* [Baizhu], *Dioscoreae Rhizoma* [Shanyao]) risks formula thickness impairing absorption in deficient constitutions and inducing qi stagnation; conversely, excessive damp-resolving medicinals (e.g., *Pinelliae Rhizoma* [Banxia], *Magnoliae Officinalis Cortex* [Houpo]) may provoke downward drainage exacerbating diarrhea. Therefore, balanced formulations utilizing mild sweet-warm tonics (e.g., *Glycyrrhizae Radix* [Gancao], *Astragali Radix* [Huangqi])—whose sweet nature corresponds to zang-organ deficiency patterns—alongside qi-regulating herbs are advocated to elevate qi during damp elimination while maintaining pharmacological equilibrium.

### 3.2 Integrated Detoxification and Stasis Resolution for Microcirculation Restoration

Persistent retention of latent pathogens facilitates toxic evil formation—defined as synergistic amalgamation of pathogenic qi and pathological products (e.g., phlegm, stasis)—which contributes to complex, refractory disease presentations. Specifically, long-term intestinal toxin residence induces collateral damage and blood stasis, establishing a pathogenic interaction between toxins and stasis that constitutes a core mechanism in chronic radiation-induced intestinal injury [13]. Therapeutic intervention thus necessitates combining heat-clearing detoxifiers (e.g., *Portulacae Herba* [Purslane], *Patriniae Herba* [Baijiangcao]) with blood-activating stasis-resolvers (e.g., *Curcumae Longae Rhizoma* [Turmeric], *Persicae Semen* [Taoren]) to simultaneously eliminate toxins and promote circulation. Clinically, differentiation-based herb selection is paramount: Dampness-toxin predominance warrants diuretic detoxification (*Poria* [Fuling], *Hedyotis Diffusae Herba* [Baihuasheshecao], *Achyranthis Bidentatae Radix* [Niuxi]); Heat-toxin excess requires carbuncle-resolving agents (*Hedyotis Diffusae Herba* [Baihuasheshecao], *Taraxaci Herba* [Pugongying], *Salviae Miltiorrhizae Radix* [Danshen]); Blood stasis-dominant cases demand stasis-dissipating herbs (*Corydalis Rhizoma* [Yanhusuo], *Chuanxiong Rhizoma* [Chuanxiong], *Patriniae Herba* [Baijiangcao])[14]. Notably, toxin-stasis resolution may initially manifest as increased bowel frequency—interpreted as a pathogen-elimination response requiring careful monitoring. Given the underlying healthy qi deficiency characteristic of chronic stages, vigilance against over-dispersion is imperative to prevent iatrogenic damage. Thus, toxin expulsion must be balanced with healthy qi preservation, ensuring therapeutic safety while achieving collateral repair and microcirculatory restoration.

### 3.3 Yin-Fluid Restoration with Heat Clearance for Yin-Yang Harmonization

The management of internal dryness necessitates moistening strategies categorized as: yin-nourishing dryness-moistening, heat-clearing dryness-moistening, and qi-tonifying dryness-moistening [15]. Critically, treatment must integrate yin nourishment, heat clearance, qi supplementation, and vitality promotion. This approach aligns with the Plain Question principle: "Interior dryness excess requires bitter-warm treatment assisted by sweet-acrid agents, moistened with acrid and bitter." Consequently, sweet-cold moistening medicinals are prioritized, leveraging

dual mechanisms: sweetness generates blood while coldness clears heat, collectively enriching yin fluids, replenishing essence-blood, and facilitating qi-blood-fluid distribution via lung qi dispersion [16]. In chronic radiation intestinal injury, protracted yin consumption and blood damage demand liver-nourishing and yin-tonifying herbs—including *Angelicae Sinensis Radix* (Danggui), *Paeoniae Radix Alba* (Baishao), *Rehmanniae Radix Praeparata* (Shudihuang), and *Ophiopogonis Radix* (Maidong)—to nourish intestinal tissues and stabilize blood.

## 4. Conclusion

Chronic radiation-induced intestinal injury (CRII) management is characterized by the inherent challenge of dual deficiency-excess pathogenesis, necessitating a spleen-centric therapeutic paradigm. While acute manifestations (e.g., hemorrhage, pain) require targeted interventions—including hemostasis, stasis resolution, and antidiarrheals—the spleen must be maintained as the principal therapeutic target. A validated multimodal strategy integrates: (1) spleen fortification and dampness resolution as foundational priorities; (2) concurrent detoxification and stasis elimination; and (3) complementary yin nourishment with heat clearance. This coordinated approach establishes a theoretically coherent framework grounded in Latent Pathogen Theory, providing mechanistic rationale for TCM intervention. Future multicenter clinical trials warrant rigorous validation to translate this paradigm into standardized therapeutic protocols.

## References

- [1] Moraitis, I., Guiu, J., & Rubert, J. (2023). Gut microbiota controlling radiation-induced enteritis and intestinal regeneration. *Trends in Endocrinology & Metabolism*, 34(8), 489-501.
- [2] QIU, M., GUO, Q. S., LIANG, X., et al. (2023). Chinese expert consensus on diagnosis and treatment of radiation-induced intestinal injury with integrated traditional Chinese and Western medicine. *Chinese Journal of Emergency in Traditional Chinese Medicine*, 32(10), 1693-1700+1722.
- [3] Dennis, E. P., Edwards, S. M., Jackson, R. M., et al. (2020). CRELD2 is a novel LRP1 chaperone that regulates noncanonical WNT signaling in skeletal development. *Journal of Bone and Mineral Research*, 35(8), 1452-1469.
- [4] SUN, J. Y., XIAO, J. J., LI, J. F., et al. (2023). The origin, development and clinical application of latent pathogen. *Global Traditional Chinese Medicine*, 16(02), 336-342.
- [5] WEI, S., WANG, H. J., & QIAO, M. Q. (2014). Development of Hidden-pathogen Theory—Proposition and Demonstration of Emotional Hidden-pathogen Doctrine. *World Science and Technology-Modernization of Traditional Chinese Medicine*, 16(03), 469-473.
- [6] LIU, Q. Q., & GAO, J. (2011). Exploring the origin of latent pathogens. *Journal of Traditional Chinese Medicine*, 52(02), 95-97.
- [7] JIANG, H. L., JIANG, X., YANG, M., et al. (2021). Treating Radiation Enteritis from Fire Toxin Theory. *Journal of Traditional Chinese Medicine*, 62(19), 1732-1735.
- [8] GAO, Y., WANG, Y., AN, B. P., et al. (2022). Anti-inflammatory and anti-apoptotic effects of Baitouweng decoction on mice with radioactive enteritis. *Chinese Traditional and Herbal Drugs*, 33(04), 827-830.
- [9] JIANG, L., ZHAO, C. J., JIAO, J., et al. (2022). Clinical Observation of Qingre Liangxue Jiedu Decoction Enema in the Treatment of Acute Radiation Enteritis Caused by Radiotherapy of Cervical Cancer World. *Journal of Integrated Traditional and Western Medicine*, 17(02), 311-314+318.
- [10] GENG, C. C., LI, L. Q., ZHANG, Y., et al. (2019). Modified Bazhen Decoction combined with Gegen Qinlian Decoction for 40 cases of radiation enteritis caused by cervical cancer radiotherapy with qi-blood deficiency and damp-heat accumulated in intestine pattern. *Global Traditional Chinese Medicine*, 12(03), 397-400.
- [11] XIE, Y., ZHOU, K. N., WANG, Y., et al. (2023). Discussion on the treatment of radiation injury with traditional Chinese medicine based on “conghua” theory. *Journal of Beijing University of Chinese Medicine*, 46(05), 639-643.
- [12] LI, Z. M., LI, T., WANG, F., et al. (2021). Li Tong's experience in treating acute radiation-induced skin reaction. *Journal of Hubei University of Chinese Medicine*, 23(04), 110-113.
- [13] WU, M. H., WU, Y., & LI, W. T. (2020). Discussion on Preventive and Therapeutic Principle of Radiation Injury Based on the Theory of Stasis and Heat. *Journal of Nanjing University of Chinese Medicine*, 36(03), 300-302.
- [14] LI, Z. Q., CHEN, J. G., LI, J., et al. (2022). Experience Analysis on CAO Jixun Who has Treated Radiation Proctitis by Stages with Eliminating, Supporting and Supplementing. *Chinese Journal of Gerontology*, 42(08),

1839-1842.

[15] JIA, M. Y., DENG, Y. W., ZHANG, Q. H., et al. (2021). New Progress in the Treatment of Radiation Proctitis with Traditional Chinese Medicine. *Journal of Practical Clinical Medicine*, 21(15), 157-159.

[16] DU, M. M., LUO, J., ZHOU, L., et al. (2021). Exploring etiology, pathogenesis and treatment of primary Sjögren's syndrome on basis of 'endogenous dryness' theory. *China Journal of Traditional Chinese Medicine*, 36(01), 250-252.