

# Explore the Pathogenesis of Chemotherapy - Related Nausea and Vomiting from the Perspective of “Zhongqi - Gut Microbiota - Brain - Gut Axis”

Yitong Wang, Xiaoyan Zhou\*

Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

\*Correspondence Author

**Abstract:** Chemotherapy-induced nausea and vomiting (CINV) is one of the most common adverse reactions in cancer patients during chemotherapy, which seriously affects patients' quality of life and treatment compliance. Based on the traditional Chinese medicine (TCM) theory of “Zhongqi regulation and mediation”, this article aims to systematically explore the pathogenesis of CINV by combining with modern research on gut microbiota. As an exogenous “toxic pathogen”, chemotherapeutic drugs first attack the spleen and stomach, easily causing damage to Zhongqi, dysfunction of its regulation, disturbance of Qi movement (ascending and descending), and confusion between clarity and turbidity, thus leading to nausea and vomiting. Modern studies have shown that chemotherapy can lead to disorders in the structure of gut microbiota, decreased diversity, and abnormal metabolic functions. Such dysbiosis participates in the occurrence and development of CINV through multiple pathways, such as disrupting the intestinal barrier, activating immune-inflammatory responses, and interfering with gut-brain axis communication. This article proposes that the dysfunction of “Zhongqi regulation and mediation” may be the core TCM pathogenesis of CINV, while gut microbiota dysbiosis is an important pathological basis and mediating factor of this pathogenesis at the modern biological level. These two interact with each other and together form the complex pathological network of CINV through the gut-brain axis. This study attempts to provide a theoretical basis and new research ideas for the prevention and treatment of CINV from the perspective of “regulating Zhongqi and harmonizing gut microbiota” based on the “Zhongqi - gut microbiota - gut-brain axis” framework.

**Keywords:** Chemotherapy-induced nausea and vomiting, Zhongqi Woxuan, Intestinal flora, Pathogenesis, Theoretical exploration.

## 1. Introduction

Chemotherapy-induced nausea and vomiting (CINV) refers to a clinical syndrome primarily characterized by nausea and vomiting, triggered by antineoplastic chemotherapeutic agents [1]. Epidemiological data indicate that approximately 70%-80% of patients receiving chemotherapy regimens with medium to high emetogenic risk experience varying degrees of CINV [2]. Even when acute symptoms are controlled, delayed and anticipated CINV remain prevalent, posing significant challenges in clinical management. The exact pathological mechanisms remain incompletely elucidated. Although modern antiemetic regimens based on 5-HT<sub>3</sub> and NK-1 receptor antagonists are first-line options, they are often associated with adverse effects such as constipation and headache, compromising patient adherence and quality of life [3]. Therefore, exploring novel prevention and treatment strategies along with theoretical frameworks holds urgent clinical significance.

In the theoretical framework of Traditional Chinese Medicine (TCM), chemotherapeutic agents are regarded as exogenous “toxic pathogens” characterized by their potent and direct action, which readily targets the middle jiao (the digestive center) and impairs the spleen and stomach. “Zhongqi” refers to the qi of the spleen and stomach, serving as the source of qi and blood generation and the pivot for qi movement and descent/ascension. The normal functions of the spleen and stomach—reception, transportation, transformation, and descent/ascension—all depend on the abundance of “Zhongqi” and its orderly operational mechanism. Therefore, the core pathogenesis of chemotherapy-induced vomiting and nausea (CINV) in TCM can be summarized as follows: chemotherapeutic toxins damage the spleen and stomach,

leading to deficiency of “Zhongqi” and impaired “Zhongqi” regulatory function, subsequently resulting in gastric disharmony and downward movement failure, with qi rising upward and manifesting as vomiting and nausea.

Modern research has revealed that the gut microbiota, functioning as the human body's “second brain,” not only constitutes an independent enteric nervous system but also enables bidirectional communication with the central nervous system through its metabolic products via the brain-gut axis. Multiple studies indicate that chemotherapeutic agents significantly disrupt the structure, abundance, and diversity of the gut microbiota [4,5], and the resulting microbial dysbiosis has been demonstrated to contribute to the pathogenesis of chemotherapy-induced nausea and vomiting (CINV) through the brain-gut axis [6,7]. This provides a potential biological foundation for understanding the Traditional Chinese Medicine (TCM) theory of “Zhongqi Woxuan” from a microecological perspective. Building on this, this study aims to integrate TCM holistic philosophy with modern microscopic research, identifying dysfunction of “Zhongqi Woxuan” as the core pathogenic mechanism underlying macro-level regulation and gut microbiota dysbiosis as the pivotal micro-level effector and pathological carrier. The study systematically elucidates the interactive relationships and shared mechanisms between these two factors in CINV development, seeking to offer novel theoretical perspectives and research approaches for integrated TCM-Western medicine strategies in CINV prevention and treatment.

## 2. The Theoretical Foundation of “Zhongqi Woxuan” in Traditional Chinese Medicine

### 2.1 The Theoretical Connotation and Origins of the

### “Zhongqi Woxuan” Theory

The theory of “Zhongqi Woxuan” is rooted in classical Traditional Chinese Medicine (TCM), with its core focus on elucidating the pivotal physiological function of the spleen and stomach as the central hub for qi movement. The Inner Canon first established this concept, while the *Suwen: Treatise on the True Organs of the Jade Mechanism* further states: “The spleen is an isolated organ; the central earth nourishes the periphery.” This statement laid the theoretical foundation for “central qi” as the source of blood, qi, and body fluids, emphasizing its role in irrigating all visceral organs and highlighting the nourishing effects of spleen-stomach transformation functions throughout the body. Qing Dynasty physician Huang Yuanyu profoundly summarized and expanded this theory in his work *Four Sacred Heart Sources*, explicitly defining “Zhongqi as the pivot axis governing yin-yang ascent and descent.” This definition not only elevated central qi to the central axis of systemic qi circulation but also constructed a dynamic qi transformation model characterized by “central qi as the axis and four dimensions as its wheels.” The term “regulation” precisely reflects the functional dynamics of this pivot axis, manifested through the complementary balance between “the spleen’s ascent of clear qi” and “the stomach’s descent of turbid qi.” Within this model, the spleen’s ascent ensures the upward transport and distribution of dietary nutrients, enabling the elevation of clear yang energy and proper nourishment of viscera; whereas the stomach’s descent facilitates the downward passage of turbid yin (chyme and waste products), promoting qi descent and harmonizing water-fire interactions. This ascending and descending process, akin to a rotating wheel, collectively maintains orderly qi circulation in the middle jiao and throughout the body, serving as a critical mechanism for normal life processes.

### 2.2 Pathogenesis Analysis of CINV Based on “Zhongqi Woxuan”

The symptom of vomiting, although manifested in the stomach, fundamentally stems from the disruption of qi movement in the middle jiao. The “*Huangdi*” established the term “vomiting” and elucidated its multifactorial etiology: external pathogenic factors (the six exogenous pathogens), internal dietary imbalances, emotional disturbances, or toxic effects of medications can all affect the middle jiao, impair the spleen and stomach, leading to “disruption of Zhongqi” and subsequent upward reversal of stomach qi. As summarized in the *Shengji Zonglu: Vomiting*: “Vomiting occurs when stomach qi rises instead of descending.” When the ascending and descending functions of the spleen and stomach become impaired, clear yang fails to ascend while turbid yin fails to descend; the disharmony of stomach qi results in its upward reversal, thereby inducing vomiting. The orderly functioning of spleen and stomach movement relies entirely on the robust transportation and regulation provided by the “disruptive” function of Zhongqi.

The core pathogenesis of CINV in Traditional Chinese Medicine lies in the damage to the spleen and stomach caused by the “toxicity” of external chemotherapy drugs, which depletes the “central qi” and impairs its regulatory function. Cancer patients inherently exhibit constitutional weakness;

the direct invasion of toxic pathogens into the middle jiao further exacerbates spleen and stomach deficiency, leading to impaired transportation and transformation functions, internal retention of water-dampness, and obstruction of qi movement. This pre-existing constitutional weakness, combined with the additional impact of toxic pathogens, severely disrupts food intake and transportation functions, resulting in gastric disharmony and upward reversal of turbid qi. Furthermore, emotional disturbances induced by the disease and treatment contribute to liver qi stagnation, which adversely affects the spleen, further depleting central qi and disrupting ascending and descending qi movements. The combined effects of these factors ultimately paralyze the regulatory function of the middle jiao, causing gastric qi to surge upward and trigger disease manifestations. Regardless of the etiology, all cases ultimately stem from the core dysfunction of central qi regulation. Clinically, acute-phase CINV predominantly presents as excess patterns such as phlegm-dampness obstructing the spleen or liver qi invading the stomach, whereas delayed and anticipated CINV primarily manifest as deficiency patterns like spleen-stomach cold deficiency or stomach yin insufficiency, reflecting the dynamic progression from excess to deficiency in the pathological mechanism [1].

## 3. The Central Role of Gut Microbiota and the Brain-Gut Axis in CINV

### 3.1 Physiological Functions of Gut Microbiota

The gut microbiota, as a complex microecosystem within the human body, plays multifaceted and indispensable physiological roles in maintaining host health. Its functions extend far beyond digestive assistance, deeply involving core physiological processes such as metabolism, barrier maintenance, immune regulation, and neural communication. A stable and diverse gut microbiota ecosystem serves as the cornerstone for ensuring metabolic balance, immune homeostasis, and neuroendocrine coordination. Regarding the intestinal barrier, the microbiota interacts closely with epithelial cells to form a critical biological barrier, competitively inhibiting pathogen colonization while promoting mucin secretion and tight junction protein expression, thereby reinforcing physical barrier function [8]. Among short-chain fatty acids (SCFAs), butyrate serves as a key energy source for colonic epithelial cells and is essential for maintaining intestinal mucosal integrity [9,10]. In terms of immune regulation, the gut microbiota is a pivotal factor in shaping and sustaining immune homeostasis both in the gut and systemically [11]. For instance, SCFAs not only enhance the secretion of secretory immunoglobulin A (sIgA) by the intestinal mucosa, strengthening mucosal immune defense [12], but also exert anti-inflammatory effects by modulating immune cell function and suppressing excessive production of pro-inflammatory cytokines such as interleukin-1 $\beta$  (IL-1 $\beta$ ) and tumor necrosis factor-alpha (TNF- $\alpha$ ) [13]. Additionally, the microbiota and its metabolites directly or indirectly influence various immune cells, including B cells and T cells, regulating both local and systemic adaptive and innate immune responses [9]. Notably, the gut microbiota serves as a critical link in the bidirectional communication of the “brain-gut axis.” Its metabolic products and the neuroactive substances synthesized by the gut microbiota itself can directly or indirectly influence central nervous system

function and behavior through neural, endocrine, and immune pathways [14]. Therefore, a stable and diverse gut microbiota ecosystem serves as the cornerstone for maintaining metabolic balance, immune homeostasis, and neuroendocrine coordination in the organism.

### 3.2 Chemotherapy Causes Damage to the Intestinal Microbiota

Chemotherapy drugs directly damage intestinal mucosal epithelial cells, compromising the integrity of the intestinal barrier function. This injury triggers a cascade of reactions: first, disruption of the ecological niche and loss of microbial diversity; second, imbalance in microbiota structure leading to proliferation of pathogenic bacteria. The weakened barrier function disrupts the original microecological equilibrium, allowing opportunistic pathogens such as *Enterococcus* and *Klebsiella*—which exhibit greater tolerance to harsh environments—to proliferate excessively, while beneficial bacteria like *Bifidobacterium* and *Fecalibacterium* show significant depletion [4,15]. Third, metabolic dysfunction and toxic environmental conditions arise. Microbial dysbiosis inevitably leads to abnormal metabolic functions: reduced beneficial bacteria decrease the production of short-chain fatty acids (SCFAs), which are critical for maintaining energy metabolism, proliferation, and differentiation of intestinal epithelial cells [16]; simultaneously, excessive proliferation of opportunistic pathogens accumulates harmful metabolites, further toxicating the intestinal microenvironment. Through direct cytotoxicity and indirect ecological disruption, chemotherapy severely disrupts the diversity, structural balance, and metabolic functions of the gut microbiota, thereby establishing the key pathophysiological foundation for subsequent chemorheumatic nausea and vomiting (CINV) induced via the brain-gut axis.

### 3.3 Dysbiosis Drives the Occurrence of CINV

The gut microbiota and the brain engage in bidirectional interactions through multiple pathways [14]. The occurrence of CINV (chemotherapy-induced nausea and vomiting) is closely associated with gut microbiota dysbiosis, primarily mediated through synergistic effects of neural, immune-inflammatory, and endocrine pathways. Chemotherapy disrupts the gut microbiota, subsequently activating the vomiting reflex pathway via the combined actions of these three pathways, ultimately leading to the development of CINV.

#### 3.3.1 Neural Pathways

Gut microbiota dysbiosis primarily participates in the pathogenesis of CINV by affecting the neurotransmitter systems closely associated with the vomiting reflex. The classical vomiting neural pathway originates from the gastrointestinal mucosa, where enterochromaffin cells secrete neurotransmitters such as serotonin (5-HT) and substance P. These neurotransmitters bind to 5-HT<sub>3</sub> receptors and neuropeptide-1 (NK1) receptors on vagal afferent fiber terminals, transmitting signals via the nucleus tractus solitarius (NTS) to the vomiting center (primarily the chemoreceptor trigger zone, CTZ), thereby initiating the vomiting reflex [3]. Notably, the CTZ is located outside the blood-brain barrier,

allowing chemotherapeutic agents and their metabolites to directly stimulate this region and independently induce vomiting [17,18].

#### 3.3.2 Immune-Inflammatory Pathway

Chemotherapy-induced intestinal microbiota dysbiosis constitutes another pivotal mechanism underlying CINV by inducing sustained immune-inflammatory responses. The homeostatic gut microbiota suppresses pathogens through nutrient competition and antimicrobial peptide secretion, serving as a critical factor in maintaining the integrity of the intestinal epithelial barrier [19]. Following chemotherapy, the reduction of probiotics and the increase of opportunistic pathogens disrupt this ecological balance, compromising barrier function and enhancing intestinal permeability. This facilitates the translocation of pathogen-associated molecular patterns (PAMPs), such as lipopolysaccharide (LPS) from Gram-negative bacterial cell walls, into the bloodstream. Endotoxins like LPS activate both intestinal and systemic immune systems. Among these, Toll-like receptor 4 (TLR4), the key pattern recognition receptor for LPS, activates downstream signaling pathways such as NF- $\kappa$ B, triggering the release of pro-inflammatory cytokines—including IL-6, TNF- $\alpha$ , and IL-1 $\beta$ —from immune cells, thereby inducing a systemic low-grade inflammatory state [20,21]. Pro-inflammatory cytokines such as IL-1 $\beta$  and LPS itself directly stimulate enterochromaffin cells, increasing the release of vomiting mediators like serotonin (5-HT) [22]. Additionally, these cytokines can cross the blood-brain barrier or act on periventricular organs lacking a complete blood-brain barrier, directly elevating the excitability of vomiting central neurons and lowering their activation threshold, thereby amplifying and sustaining nausea and vomiting responses.

#### 3.3.3 Endocrine Pathway

The gut microbiota participates in the regulation of CINV at the endocrine level by modulating the secretion and function of gastrointestinal hormones. Gut microbiota and their metabolites directly influence the function of intestinal endocrine cells, exerting significant regulatory effects on the secretion of hormones such as glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) [23,24]. Post-chemotherapy gut microbiota dysbiosis disrupts the balance of key gastrointestinal hormones like PYY and ghrelin, contributing to the endocrine mechanism underlying CINV through both peripheral motility inhibition and central appetite-vomiting regulation. This provides a potential modern biological explanation for the TCM pathogenesis of “impaired spleen-stomach ascending and descending functions.”

## 4. Existing Research Linking Macro Theories with Micro-Ecosystems

Numerous studies have provided empirical evidence supporting the correlation between the TCM syndrome of spleen deficiency (often manifested as insufficient Zhongqi) and intestinal microbiota dysbiosis. Multiple studies indicate a significant association between spleen and stomach weakness with reduced microbial diversity and structural imbalance in the gut [25,26]. Clinical intervention studies

further elucidate the regulatory effects of “spleen-strengthening” therapies on microbiota: for example, warm acupuncture improves microbial diversity in patients with spleen-stomach deficiency-type irritable bowel syndrome [27]; spleen-strengthening herbal formulations such as Jianpi Yangzheng Xiaozheng Formula regulate microbial composition and increase beneficial bacterial abundance in gastric cancer patients post-chemotherapy [28]; the classical Zhi Shu Wan restores microbial balance and promotes the synthesis and secretion of short-chain fatty acids (SCFAs) and serotonin (5-HT) [29]; while Shenling Baizhu San corrects microbiota dysbiosis and enhances the proportion of beneficial bacteria in patients with spleen deficiency and dampness stagnation syndrome [30].

These findings preliminarily establish a conceptual bridge for the “spleen-intestine-bacteria” axis, demonstrating that spleen-tonifying therapies not only enhance spleen and stomach functions at the macroscopic level but also exert regulatory effects on intestinal microecology at the microscopic level.

## 5. Development of the “Central Qi-Microbiota-Brain-Gut Axis” Theory

Based on the aforementioned theories of traditional Chinese and Western medicine, this paper proposes an integrative theory: intestinal microbiota homeostasis serves as the critical material foundation and functional manifestation of the “Zhongqi mediation” physiological function at the microscopic level. The two components form a bidirectionally regulated and dynamically balanced organic whole through the brain-gut axis. This theory aims to elucidate the intrinsic unity between macroscopic qi movement and micro-level ecological equilibrium.

### 5.1 Positive Regulation

The gut microbiota of a healthy human body is predominantly composed of the Bacteroidetes and Firmicutes phyla [31]. These microorganisms establish a stable symbiotic relationship with the host intestinal mucosa, supporting overall health through various physiological functions. From the perspective of Traditional Chinese Medicine (TCM), the gut microbiota serves as the “micro-level executor” of the large intestine’s transformative functions, and its homeostasis essentially reflects the orderly mediation of central qi at the intestinal level. Li Dongyuan stated in *Treatise on the Spleen and Stomach*: “When the qi of the spleen and stomach is impaired, and primordial qi cannot be replenished, this becomes the root cause of various diseases.” This elucidates that robust central qi is the foundation for normal systemic function—a macroscopic physiological state that corresponds microscopically to the homeostasis of the gut microbiota. At the metabolic level, the gut microbiota ferment undigested dietary fiber, producing short-chain fatty acids (primarily butyric acid) to supply energy to intestinal epithelial cells, while also synthesizing essential nutrients such as vitamin K and B-complex vitamins. At the defense level, a stable microbiota directly maintains the intestinal mucosal barrier function through mechanisms like colonization resistance and secretion of antimicrobial substances, effectively preventing pathogen invasion [31]. In terms of immune regulation, the

microbiota and its metabolites play a critical role in maintaining local and systemic immune homeostasis [32]. From a TCM perspective, a vigorous spleen-stomach transportation and transformation process ensures: first, adequate production of dietary nutrients provides optimal substrates for beneficial gut microbiota, fostering a symbiotic relationship where “the spleen transforms nutrients to nourish the microbiota,” thereby supporting intestinal epithelial cell function and reinforcing the intestinal barrier; second, through the qi dynamics of spleen ascending and stomach descending, it maintains an “orderly transit and descent” microenvironment in the intestine, inhibiting excessive proliferation of harmful bacteria and preserving microbial structural balance.

The short-chain fatty acids, vitamins, and other substances produced by microbial metabolism are classified in Traditional Chinese Medicine (TCM) as “secondary metabolites derived from dietary nutrients.” Their role in nourishing intestinal epithelial cells and reinforcing the intestinal barrier directly embodies the TCM principle that “abundant Zhongqi ensures proper protection of the intestinal tract.” Furthermore, the regulation of gastrointestinal motility and sensory functions by gut microbiota through the brain-gut axis fundamentally represents the concrete manifestation of Zhongqi-mediated systemic regulation via the “intestine-brain” qi pathway. The unimpeded flow of spleen-stomach Zhongqi facilitates both intestinal nutrient transport and the delivery of qi, blood, and body fluids to the central nervous system, thereby maintaining coordinated qi dynamics between the “intestinal tract and central nervous system.” This mechanism aligns with how microbiota regulate the central nervous system through neural and metabolic pathways, providing a shared interpretative framework bridging TCM’s macroscopic perspective and Western medicine’s microscopic mechanisms.

### 5.2 Reverse Regulation

Traditional Chinese Medicine (TCM) posits that “deficiency of Zhongqi” constitutes the core pathological state underlying dysfunction of the spleen and stomach. The pathological progression of Zhongqi deficiency primarily affects the intestinal tract, leading to deterioration of the intestinal microenvironment and direct disruption of gut microbiota structure and ecological balance—a precise correspondence with the concept of “Zhongqi dysfunction causing intestinal microbial disorder.” The *Jingui Yaolue: Zangfu and Meridian Pathologies and Symptoms\** states: “If the spleen is not susceptible to pathogenic factors throughout the four seasons, supplementation should be avoided; if the spleen is weak and exposed to pathogens year-round, treatment is ineffective.” This emphasizes that spleen deficiency (insufficient Zhongqi) reduces the body’s defensive capacity, aligning with the pathological process where disrupted gut microbiota stability diminishes colonization resistance and facilitates pathogen invasion. Deficiency of Zhongqi impairs spleen-stomach transportation and transformation functions, yielding the primary pathological outcomes of “dampness-turbidity” and “food stagnation.” The *Jingyue Quanshu: Miscellaneous Syndromes\** notes: “Spleen deficiency prevents proper digestion of food; impaired digestion generates dampness, which internalizes and obstructs qi movement.” An internally

accumulated dampness-turbid environment in the intestines provides a “pathological substrate” for pathogenic bacterial proliferation, resulting in microbial dysbiosis—a critical link in TCM’s theory of how “macroscopic pathological manifestations induce microscopic ecological imbalance.” The three major pathological pathways triggered by microbial dysbiosis can all be elucidated through the pathogenic theory of Traditional Chinese Medicine (TCM): First, damage to the intestinal mucosal barrier and endotoxin translocation—from a TCM perspective, this corresponds to the progression of “dampness turbidity transforming into toxins, impairment of intestinal collaterals, and internal invasion of pathogenic toxins.” Prolonged stagnation of dampness turbidity can generate heat and toxins, compromising the integrity of the intestinal “collateral networks,” allowing pathogenic toxins to enter the bloodstream and induce systemic dysfunction. Second, dysregulated microbiota and their metabolites activate the intestinal immune system, triggering massive release of pro-inflammatory cytokines such as IFN- $\gamma$  and TNF- $\alpha$ , thereby initiating and sustaining a systemic state of low-grade inflammation [33]. This aligns with the TCM pathological concept of “pathogenic toxins penetrating deep into tissues, disruption of qi-blood harmony, and conflict between healthy qi and pathogens.” The systemic effects of these inflammatory factors represent further manifestations of “pathogenic toxin dissemination and depletion of Zhongqi.” Third, disturbances in neuroendocrine signaling lead to abnormalities in neurotransmitters (e.g., GABA and 5-HT) and gastrointestinal hormones synthesized and metabolized by the gut microbiota. These dysregulated signals are transmitted to the central nervous system via multiple pathways, including vagus nerve afferent fibers and the bloodstream [6,23], resonating with the TCM pathogenesis of “disruption of qi movement and mental disturbance” —where disruption of spleen-stomach Zhongqi, according to the TCM principle that “the brain is the residence of primordial spirit,” affects the central nervous system’s regulation of qi movement.

From a pathological perspective, the aforementioned micro-level dysregulation converges along the brain-gut axis to induce central regulatory dysfunction, which macroscopically manifests as “the cessation of the Zhongqi’s regulatory function.” Traditional Chinese Medicine (TCM) posits that “the stomach achieves harmony through descent,” and deficiency of Zhongqi impairs gastric descent, allowing turbid qi to ascend—a mechanism highly consistent with the nausea and vomiting symptoms of CINV. The toxin-induced pathogenic factors, inflammation, and abnormal neural signaling mediated by microbial dysbiosis ultimately transform into clinically observable gastrointestinal symptoms via the TCM pathogenesis of “Zhongqi disorder and upward surge of stomach qi,” forming an integrated TCM-Western medical pathological chain: “Zhongqi deficiency  $\rightarrow$  internal retention of dampness-turbidity  $\rightarrow$  microbial dysbiosis  $\rightarrow$  toxin invasion  $\rightarrow$  qi movement disorder  $\rightarrow$  CINV.”

### 5.3 Bidirectional Feedback Loop

The bidirectional feedback between Zhongqi deficiency and intestinal microbiota dysbiosis essentially represents a microscopic extension of the TCM pathological closed-loop

concept of “spleen deficiency generating dampness, which in turn obstructs the spleen.” Its core lies in the mutual interaction between “Zhongqi” and “dampness-turbidity,” with the microbiota serving as the key mediator of this loop. As stated in *\*Treatise on Spleen and Stomach: On the Prosperity and Decline of Spleen and Stomach\**: “Spleen and stomach insufficiency all manifest as blood disorders; this results from insufficient yang qi and excessive yin qi, leading to obstruction of the nine orifices.” Clearly, spleen deficiency leads to inadequate qi and blood production, exacerbating qi stagnation and intensifying endogenous dampness-turbidity. This macroscopic pathological cycle synchronously interacts with the microscopic mechanisms of microbiota disruption. On one hand, weakened spleen and stomach function impair digestion, resulting in undigested food transforming into dampness-turbidity. This internal accumulation not only alters the intestinal microenvironment, promoting the proliferation and abnormal colonization of pathogenic bacteria, but also impedes nutrient supply to beneficial bacteria, worsening microbiota imbalance—representing the positive pathological progression of “spleen deficiency generating dampness  $\rightarrow$  dampness-turbidity disrupting bacteria  $\rightarrow$  microbiota dysbiosis,” aligning with the TCM principle that “insufficient healthy qi allows pathogenic factors to prevail.” On the other hand, endotoxins and abnormal neurotransmitters produced by microbiota dysbiosis fall under the TCM category of “turbid toxins.” These stimulate intestinal mucosal inflammation, further depleting spleen and stomach Zhongqi: inflammatory factors entering the bloodstream can obstruct qi movement in the middle jiao, aggravating spleen ascension and stomach descent dysfunction, thereby increasing the burden on digestive functions and creating a reverse pathological reinforcement cycle of “microbiota dysbiosis  $\rightarrow$  turbid toxins damaging the spleen  $\rightarrow$  aggravated spleen deficiency.” Symptoms such as nausea and vomiting induced by CINV further deplete body fluids and Zhongqi, forming a vicious cycle where “symptoms exacerbate pathology, and pathology triggers symptoms.” This self-reinforcing closed-loop mechanism— “increased deficiency of Zhongqi  $\rightarrow$  growing microbial imbalance  $\rightarrow$  intensified turbid toxins  $\rightarrow$  further depletion of Zhongqi” —explains from the perspective of Traditional Chinese Medicine (TCM) the pathological essence of CINV, characterized by its protracted course, recurrent episodes, and slow recovery. It also corroborates the consistent understanding shared by both TCM and Western medicine theories regarding the chronic progression of the disease: the interplay between macroscopic qi movement disorders and microscopic ecological imbalance jointly drives disease progression.

## 6. Conclusion

This article integrates the Traditional Chinese Medicine (TCM) theory of “Zhongqi Wozhuan” with modern gut microbiome ecology to propose a “Zhongqi-Microbiota-Cerebroenteric Axis” theory for elucidating the pathogenesis of chemotherapy-induced nausea and vomiting (CINV). The core of this model lies in linking the macroscopic function of “Qi movement ascending and descending” with the microscopic state of “microbial homeostasis,” proposing that dysfunction of “Zhongqi Wozhuan” constitutes the central pathological mechanism of CINV, while intestinal microbial dysbiosis serves as its critical biological foundation and

effector hub. This framework not only provides a novel systemic perspective for understanding CINV but also offers a practical approach for modernizing classical TCM theories. Accordingly, clinical management strategies for CINV should shift from mere antiemetic measures to an integrated approach emphasizing Zhongqi support and microbial regulation. Specifically, alongside Western medical treatments, this strategy incorporates herbal formulations such as Liu Junzi Decoction and Xuanfu Daizhe Decoction—which tonify Zhongqi and harmonize stomach function to counteract upward flow—as well as prebiotics and probiotics to modulate the gut microbiota, aiming to break the pathological cycle through coordinated interventions at both macroscopic Qi dynamics and microscopic ecological levels.

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