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Theoretical Basis and Mechanisms of Traditional Chinese Medicine for the Prevention and Treatment of Chronic Endometritis: An Immune Microenvironment Perspective

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Abstract: ***Chronic endometritis (CE) is an insidious inflammatory disorder characterized by focal plasma-cell infiltration of the endometrium and is closely associated with adverse reproductive outcomes, including infertility, recurrent implantation failure, and recurrent pregnancy loss. From the perspective of the immune microenvironment, this review systematically examines the pathogenesis of CE and the theoretical basis and potential pathways of traditional Chinese medicine (TCM) intervention. It first describes the composition and homeostatic features of the normal endometrial immune microenvironment and then analyzes persistent inflammation and impaired tissue repair in CE arising from pathogen recognition, plasma-cell infiltration, dysregulation of immune-cell subsets, disruption of cytokine networks, and aberrant activation of the TLR4/NF-κB/NLRP3 signaling pathway. In TCM theory, CE may be classified under such categories as leukorrheal disease, abdominal pain in women, and infertility. Its core pathogenesis involves the dynamic evolution of dampness, heat, blood stasis, and deficiency: damp-heat pathogenic factors initially invade the uterus; prolonged disease leads to qi stagnation and blood stasis; and chronicity eventually results in spleen and kidney deficiency, producing a pattern of root deficiency with branch excess and a complex mixture of deficiency and excess. Treatment should therefore follow a stage-based approach: clearing heat and draining dampness when damp-heat predominates, invigorating blood and unblocking the collaterals when stasis is prominent, warming the channels and dispelling cold when cold-dampness congeals, and supplementing qi, strengthening the spleen, and tonifying the kidney when spleen-kidney deficiency is present. TCM may exert therapeutic effects by modulating inflammatory-mediator release, improving local microcirculation, promoting endometrial repair, and restoring immune homeostasis. However, current evidence is derived mainly from symptom scores, serum biomarkers, and animal experiments, and high-quality clinical validation of local immune phenotypes in CE tissue remains lacking. This review emphasizes that TCM syndromes should not be assigned simple, fixed correspondences with specific immune pathways; such associations should be treated as research hypotheses rather than established conclusions. Integrated Chinese and Western medicine should be based on standardized diagnosis and anti-infective therapy, with TCM serving as a component of syndrome-differentiated intervention and recovery management. Validation through standardized syndrome assessment, local tissue testing, and prospective studies is needed to advance more targeted integrated diagnostic and therapeutic strategies for CE.***

Keywords: Chronic endometritis, Traditional Chinese medicine, Immune microenvironment, Inflammatory response, Syndrome differentiation and treatment.

1. Introduction

Chronic endometritis (CE) is an insidious disorder characterized by persistent localized infection or inflammation of the endometrium. Because its symptoms are nonspecific, some patients present only with abnormal uterine bleeding, lower abdominal discomfort, or adverse reproductive outcomes, making the condition easy to miss in clinical practice [1-2,6-7]. Microbial stimulation can recruit B lymphocytes to the endometrial stroma and per-glandular regions, where they differentiate into plasma cells [9,12]. Plasma-cell infiltration and associated abnormalities in inflammatory mediators may disrupt endometrial homeostasis, impair decidualization and embryo-endometrium synchrony, and are associated with adverse reproductive outcomes such as unexplained infertility, recurrent implantation failure, and recurrent pregnancy loss [1-5].

Previous treatment strategies have placed considerable emphasis on etiologic assessment and anti-infective therapy. However, a reduction in or elimination of pathogens does not necessarily lead to immediate recovery of local tissue function [3,5-7]. Persistent immune-cell infiltration, imbalance between pro- and anti-inflammatory signals, altered vascular permeability, and fibroblast activation may convert post-infectious inflammation into chronic tissue injury and further compromise endometrial receptivity [3,10-13]. Accordingly, the therapeutic goals for CE should extend beyond infection control to include resolution of inflammation, tissue repair, and restoration of endometrial function [5-7,13].

In TCM, CE is commonly understood within the categories of leukorrheal disease, abdominal pain in women, and infertility, with emphasis placed on the interactions among dampness, heat, blood stasis, and deficiency and on their dynamic changes over the disease course [18-20]. Juxtaposing the immune microenvironment with TCM pathogenesis is not intended to establish a simplistic equivalence between the two theoretical systems, but rather to generate testable research questions. Focusing exclusively on CE, this review examines alterations in the immune microenvironment, TCM pathogenesis, and therapeutic strategies, with the aim of providing a clearer conceptual framework for research on

integrated Chinese and Western medicine.

2. The Immune Microenvironment of the Normal Endometrium

2.1 Mucosal Barrier and Innate Immunity

The normal endometrium must maintain a dynamic balance among antimicrobial defense, immune tolerance, cyclical tissue remodeling, and embryo implantation [14-16]. The epithelial barrier, mucus, antimicrobial peptides, complement, and the local microbiota together constitute the first line of defense. Neutrophils, macrophages, dendritic cells, and natural killer (NK) cells participate in pathogen recognition, phagocytic clearance, initiation of inflammation, and tissue repair [14,16]. The numbers of these cells are not constant; their proportions and functions vary across the menstrual cycle. For example, uterine NK cells increase markedly during the late secretory phase and mainly contribute to vascular remodeling and maintenance of local homeostasis [14-15].

Under physiological conditions, innate immunity must promptly limit pathogen spread while avoiding an excessive inflammatory response [16]. Insufficient recognition and clearance may allow pathogens to persist, whereas excessive inflammation or failure of timely resolution may damage epithelial and stromal structures. Endometrial health therefore depends on an immune response that is proportionate, regulatable, and capable of timely termination [14-16].

2.2 Adaptive Immunity and Reproductive Tolerance

T and B lymphocytes and their secreted cytokines participate in antigen-specific immune responses. The balance among helper T-cell subsets influences the intensity and duration of inflammation, whereas regulatory T cells help restrain excessive immune activation and maintain reproductive tolerance [14,16]. B cells are relatively sparse in the normal endometrium, while persistent or abnormal plasma-cell infiltration usually indicates local chronic inflammation [6-9]. Thus, stronger immunity is not necessarily better in the reproductive tract; coordinated regulation among antimicrobial defense, immune tolerance, and tissue repair is essential [14-16].

3. Dysregulation of the Immune Microenvironment in Chronic Endometritis

3.1 Pathogen Recognition and Initiation of Inflammation

The onset of CE is often associated with invasion by pathogenic microorganisms or disruption of the normal microbial composition within the uterine cavity [11,13]. Once these exogenous stimuli are recognized by the endometrial epithelium and local immune cells, a series of defensive responses is triggered, including the release of chemokines and proinflammatory cytokines that recruit neutrophils and monocyte-macrophage populations to the site of infection [10-11,13]. A moderate inflammatory response facilitates clearance of harmful stimuli. However, when the stimulus persists or the host cannot effectively terminate the response, local defense mechanisms may gradually shift toward a pattern of chronic tissue injury [3,13]. The persistence of CE therefore cannot be attributed solely to incomplete pathogen clearance and may be more closely related to altered patterns of host immune response [11-13]. Clinically, focusing only on conversion of pathogen tests to negative status often fails to explain why some patients show poor recovery of symptoms, endometrial morphology, and reproductive capacity [3,5-7].

3.2 B-Cell and Plasma-Cell Infiltration

Among the microenvironmental changes in CE, the presence of plasma cells is a relatively characteristic finding and is currently a commonly used histopathologic marker [6-8]. Under repeated or persistent antigenic stimulation, B cells are recruited to the endometrium and differentiate into plasma cells, which tend to accumulate in the stroma or around endometrial glands [9,12]. Persistent plasma cells indicate that the local humoral immune response has not fully subsided and are often accompanied by abnormal expression of multiple immune-related molecules [9,12]. Nevertheless, plasma-cell counts may indicate the presence of inflammation but cannot, on their own, reliably reflect its severity, disease stage, or the actual functional status of the endometrium [6-8]. Because studies differ in specimen processing, observation methods, and diagnostic thresholds, the clinical significance of small numbers of plasma cells remains controversial [6-8]. Assessment of the endometrial immune state should therefore integrate other immune components, including T cells, NK cells, and macrophages, as well as tissue-morphologic changes.

3.3 Macrophage, T-Cell, and NK-Cell Subsets

Macrophages have dual roles in CE: they may aggravate local inflammation through the release of inflammatory mediators, while also clearing necrotic tissue and supporting angiogenesis and tissue repair [10-11,13]. Persistent polarization toward a proinflammatory state may excessively stimulate fibroblasts, leading to tissue stiffening and structural alterations [13]. Studies have also commonly reported increased numbers of T cells, B cells, and plasma cells in the endometrium of patients with CE, together with possible alterations in the proportions and activities of T-cell subsets [11-13]. Findings regarding NK cells are inconsistent across studies and may be influenced by menstrual-cycle phase, timing of sampling, and interindividual variation [11,13-15]. Therefore, analyses of immune-cell changes should extend beyond numerical increases or decreases to include activation status, tissue distribution, and interactions among cell populations.

3.4 Cytokine Networks and Fibrosis

Proinflammatory cytokines such as IL-1β, IL-6, and TNF-α are often persistently elevated in CE, increasing vascular reactivity and inflammatory-cell accumulation and thereby damaging epithelial and glandular structures [10,13]. Other cytokines, including IL-2, IL-10, and TGF-β, tend to regulate immune responses, limit excessive inflammation, and promote tissue repair; however, their specific alterations are influenced by multiple factors, and published findings are not fully consistent [11-13]. When proinflammatory signaling

remains dominant, fibroblasts may be chronically activated, causing excessive deposition of collagen and other extracellular materials and leading to tissue remodeling. If reparative signals are relatively inadequate, the structure and function of the endometrium may fail to return to normal [13]. Nevertheless, clinical evidence that CE directly causes endometrial fibrosis remains insufficient, and this concept is derived largely from basic research and animal studies. Further confirmation in human tissue is required. Thus, "immune regulation" should not be understood as simply enhancing immune function, but rather as facilitating timely resolution of inflammation and rebuilding the local balance between defense and repair.

3.5 The TLR4/NF-κB/NLRP3 Inflammatory Signaling Pathway

The TLR4/NF-κB/NLRP3 signaling pathway is one potential mechanism currently proposed to explain the failure of inflammation to resolve in CE [13,17]. Recognition of pathogen-associated or damage-associated signals by the corresponding receptors initiates intracellular signaling cascades that ultimately promote the production and release of multiple proinflammatory mediators [13,17]. These mediators recruit and activate additional immune cells, creating an amplification loop of inflammation. Failure to regulate this pathway in a timely manner may aggravate endometrial injury and structural abnormalities and thereby impair endometrial receptivity [13,17]. It should be noted, however, that evidence for this pathway in CE currently comes mainly from cell and animal experiments, whereas direct evidence from human clinical tissue remains limited. This signaling axis is therefore better viewed as an entry point for mechanistic investigation, and its specific clinical role requires validation in rigorously designed human studies.

3.6 Effects of Immune Dysregulation on Endometrial Function

The clinical importance of CE lies not only in inflammation itself but also in its long-term disruption of endometrial function. Abnormal immune-cell infiltration, dysregulated mediator networks, and tissue remodeling may interfere with normal decidualization, regulation of blood supply, and embryo-endometrium synchrony [1-4,11-13]. Transcriptomic studies have also indicated altered expression profiles of immune-response-related genes in the endometrium of patients with CE, which may contribute to reduced receptivity [12]. Even after infection has been controlled, the endometrium may remain unstable if the local immune and reparative environment has not recovered [3,5-7]. Evaluation of treatment efficacy in CE should therefore integrate etiologic findings, inflammatory status, histologic features, clinical symptoms, and pregnancy outcomes rather than relying on a single indicator [5-8].

4. TCM Understanding of Chronic Endometritis

4.1 Disease Classification and Location

There is no exact equivalent of CE in traditional Chinese medicine. Based on clinical manifestations such as profuse yellow and viscous vaginal discharge, prolonged menstruation, abnormal uterine bleeding, dull lower abdominal pain, infertility, recurrent implantation failure, and miscarriage, CE may be classified under the TCM categories of leukorrheal disease (dai xia bing), abdominal pain in women (fu ren fu tong), metrorrhagia and metrostaxis (beng lou), abdominal masses (zheng jia), and infertility [18-20]. The immediate disease location is the uterus (baogong) and uterine vessels or collaterals (baomai), and the disorder is closely associated with dysfunction of the liver, spleen, and kidney and of the Chong, Ren, and Dai vessels [18-19].

In TCM theory, the kidney stores essence and governs reproduction and is the root of the Chong and Ren vessels; the spleen is the source of qi and blood production and governs the transformation and transportation of fluids; and the liver governs free coursing and stores blood, regulates qi movement, and participates in menstruation and reproduction [18-19]. Dysfunction of these three organs may impair fluid transformation, obstruct qi movement, and impede blood circulation, ultimately disrupting the storage and discharge functions of the uterus and the abundance and patency of the Chong and Ren vessels.

The etiology may be understood in terms of external, internal, and miscellaneous causes. During menstruation, the postpartum period, or after birth trauma, the uterine vessels are relatively depleted and the "blood chamber" is open, allowing damp-heat and pathogenic toxins to invade, injure the Chong and Ren vessels, and lodge in the uterus. Emotional injury and constrained liver qi may cause qi stagnation and blood stasis; liver overacting on the spleen further impairs transportation and transformation, generating internal damp-turbidity. Improper diet and excessive consumption of rich, greasy, and sweet foods may likewise weaken the spleen, generate dampness, and allow constrained dampness to transform into heat [18-20]. Repeated intrauterine procedures are regarded as injury by metal instruments; they not only directly damage the uterus and uterine vessels but may also permit pathogenic factors to remain and obstruct the movement of qi and blood [20].

Thus, although CE primarily manifests as a localized uterine disorder, it is essentially the combined result of dysfunction involving the zang-fu organs, qi and blood, and the extraordinary vessels. Its core pathogenesis may be summarized as dampness, heat, blood stasis, stagnation, and deficiency. Damp-heat intermingled with blood stasis constitutes a common pathological basis, while prolonged disease gradually gives rise to deficiency of healthy qi, producing a pattern of root deficiency with branch excess and a mixture of deficiency and excess [18-20].

4.2 Dynamic Evolution of Dampness, Heat, Blood Stasis, and Deficiency

CE is insidious, protracted, and recurrent, and its pathogenesis is not static but evolves continuously as pathogenic factors and healthy qi wax and wane [20]. At onset, damp-heat pathogenic toxins commonly invade the uterus, or spleen deficiency generates dampness that becomes constrained and transforms into heat. Dampness is heavy, turbid, and sticky and readily obstructs qi movement; heat scorches body fluids

and blood and may injure the uterine collaterals. Accordingly, damp-heat predominance is often manifested by profuse, yellow, viscous, and malodorous vaginal discharge, lower abdominal distension or bearing-down discomfort, impeded menstruation, or abnormal bleeding [18-20].

When damp-heat remains unresolved, qi movement becomes obstructed and blood circulation impaired, gradually producing qi stagnation and blood stasis. As expressed in the traditional statement, "initially qi becomes bound in the channels; over time, blood is injured and the collaterals are affected." Blood stasis is both a pathological product of damp-heat obstruction and a factor that further prevents the dissipation of dampness and heat, resulting in recurrent and refractory disease [18,20]. When stasis obstructs the uterine collaterals, abdominal pain may be fixed or stabbing and may worsen during menstruation. Visible lesions such as endometrial congestion, edema, small polypoid changes, adhesions, and fibrosis may also develop and can be interpreted through the TCM concepts that "prolonged disease enters the collaterals" and "prolonged disease forms masses" [19].

As the disease persists, damp-heat and blood stasis continually consume qi and blood and damage the spleen and kidney. Spleen deficiency impairs transportation and transformation, making dampness more difficult to eliminate; kidney deficiency deprives the Chong and Ren vessels of nourishment and the uterus of warming and enrichment, further affecting menstruation, embryo implantation, and maintenance of pregnancy [20]. Patients with constitutional yang deficiency or yang damage caused by chronic illness may also develop congealed cold-dampness and internal blood stasis, manifested by lower abdominal pain relieved by warmth and pressure, clear and thin vaginal discharge, aversion to cold, and cold limbs. Overall, the disease tends to progress from excess damp-heat to qi stagnation and blood stasis, and then from excess to deficiency, with deficiency in turn retaining pathogenic factors. In clinical practice, however, these stages often overlap and are not necessarily sharply demarcated.

Treatment should not be constrained by a single syndrome pattern or a fixed therapeutic method. Instead, the relative predominance of pathogenic factors and healthy qi and the urgency of primary and secondary manifestations should be determined. When damp-heat predominates, treatment should mainly clear heat, drain dampness, remove toxins, and dissipate accumulations. When blood stasis is prominent, treatment should additionally regulate qi, invigorate blood, dispel stasis, and unblock the collaterals. When cold-dampness congeals, the channels may be warmed, cold dispersed, dampness transformed, and vessels unblocked. In chronic cases with spleen-kidney deficiency, qi should be supplemented, the spleen strengthened, the kidney tonified, and the Chong vessel regulated. Healthy qi should be protected even during pathogen-eliminating treatment, while residual dampness, heat, and blood stasis should not be neglected when supporting healthy qi. This reflects the principles of eliminating pathogenic factors while supporting healthy qi, combining attack and supplementation, and treating according to disease stage [18-20].

4.3 Theoretical Links Between TCM Pathogenesis and the Immune Microenvironment

From the perspective of theoretical integration, the TCM pathogenic framework of exuberant pathogenic factors, deficiency of healthy qi, obstruction by blood stasis, and retention of dampness may be used to summarize the dynamic relationship among local infection, immune dysregulation, and impaired tissue repair in CE. "Exuberant pathogenic factors" may correspond conceptually to pathogen stimulation and an enhanced proinflammatory response. In a study comparing histopathology, microbial culture, hysteroscopy, and molecular microbiologic testing, Moreno et al. [21] found that CE was closely associated with intrauterine pathogens and abnormalities of the endometrial microbiota, and that persistent pathogen stimulation could trigger local immune-inflammatory responses. In an LPS-induced rat model of CE, Liu [20] observed increased nuclear translocation of NF-κB p65, elevated NLRP3 and IL-18 expression, and infiltration of chronic inflammatory cells, including plasma cells and macrophages, in uterine tissue, reflecting sustained activation of the inflammatory cascade under a state of "exuberant pathogenic factors."

"Deficiency of healthy qi" may conceptually correspond to insufficiency of the mucosal barrier, immune clearance, and reparative capacity. In 308 infertile women undergoing assisted reproductive treatment, Cuadrado-Torroglosa et al. [22] found that specific KIR genes involved in immunoregulation of uterine NK cells were associated with lower rates of endometrial dysbiosis and CE and with a better response to anti-infective treatment. These findings suggest that inadequate local immune defense may hinder pathogen clearance, creating a state described in TCM as "deficiency of healthy qi with lingering pathogens."

"Blood stasis obstructing the uterine collaterals" may be linked conceptually to impaired microcirculation, tissue edema, adhesions, and fibrosis. Liu et al. [23] demonstrated abnormal expression of HIF-1α, VEGFA, and VEGFR2 and excessive vascularization in peri-implantation endometrium from infertile women with CE, suggesting that local hypoxia and abnormal vascular remodeling may affect endometrial microcirculation and receptivity. In animal experiments, Liu [20] also observed uterine vascular congestion, stromal edema, glandular atrophy, fibrous-tissue proliferation, and tissue adhesions, indicating that persistent inflammation may gradually progress from an intangible state of "stasis" to visible lesions such as adhesions and fibrosis.

The "sticky and lingering nature of dampness" reflects the persistence, exudation, and recurrence of inflammation. In dynamic modeling experiments, Liu [20] found that with prolonged LPS stimulation, the endometrium progressed from early congestion, edema, and inflammatory exudation to epithelial shedding, chronic inflammatory-cell infiltration, and fibrosis, illustrating the difficulty of eliminating sticky pathogenic factors and the protracted course of disease. CE may therefore be summarized as a pathological cycle in which exuberant pathogenic factors damage healthy qi, deficiency of healthy qi allows pathogens to linger, prolonged dampness gives rise to blood stasis, and blood stasis obstructs recovery.

These links, however, represent a cross-system theoretical interpretation; TCM syndromes should not be mechanically equated with a single immune-cell population or molecular marker.

5. TCM Therapeutic Strategies and Potential Immunoregulatory Mechanisms

5.1 Principles of Treatment

TCM intervention for CE should be based on a clear diagnosis and standardized etiologic assessment [24]. When a pathogen has been identified or inflammatory activity is pronounced, standardized anti-infective therapy should receive priority. TCM may be used according to syndrome characteristics to improve symptoms, regulate inflammatory responses, and promote endometrial recovery [24,26-28]. In patients with persistent inflammation, delayed tissue repair, or unsatisfactory recovery of endometrial function, the therapeutic emphasis may gradually shift from pathogen elimination alone to a combination of pathogen elimination and support of healthy qi [27,28].

Syndrome-differentiated treatment should also avoid using the broad phrase “enhancing immunity” to describe all effects. Immune abnormalities in CE may include both excessive inflammatory activation and inadequate clearance and repair; the goal of treatment should therefore be to restore balance rather than unidirectionally enhance any single immune component [25].

5.2 Damp-Heat Accumulation Pattern: Clearing Heat and Draining Dampness While Addressing Toxins

In the damp-heat accumulation pattern, retention of damp-heat in the uterus is the primary pathogenesis. Treatment should clear heat and drain dampness, with toxin-resolving medicinals added as clinically indicated. The herbs listed in the original manuscript—including Patrinia herb (Baijiangcao), dandelion (Pugongying), honeysuckle flower (Jinyinhua), forsythia fruit (Lianqiao), and spreading hedyotis herb (Baihuasheshecao)—may be considered as syndrome-based combination options, but the specific prescription should be adjusted according to the characteristics of vaginal discharge, pain, tongue and pulse findings, and disease duration. Studies have used compound prescriptions containing heat-clearing and toxin-resolving herbs such as Patrinia herb and spreading hedyotis herb, together with blood-invigorating herbs such as red peony root (Chishao) and Salvia root (Danshen), to treat CE and have reported improvements in clinical symptoms, endometrial inflammatory-cell infiltration, and selected indicators of endometrial function [26]. Modified Yiyi Fuzi Baijiang Powder combined with doxycycline has also been reported to improve TCM syndrome scores, endometrial blood flow, and inflammatory indices in CE characterized by qi deficiency and blood stasis complicated by damp-heat [27].

From an immunologic perspective, this treatment method may reduce the release of inflammatory mediators following pathogen stimulation and restrain persistent elevation of proinflammatory signals such as IL-1β and TNF-α, thereby limiting excessive recruitment of inflammatory cells [25,27]. However, existing clinical studies of TCM have mainly used symptom scores, serum inflammatory factors, hysteroscopic findings, and pathological indices as endpoints. These outcomes are insufficient to demonstrate that a particular medicinal directly regulates a specific immune-cell population or signaling pathway. Such hypotheses still require validation using clinical CE tissue samples and targeted studies.

5.3 Qi Stagnation and Blood Stasis Pattern: Invigorating Blood and Unblocking the Collaterals While Clearing Residual Pathogens

Persistent damp-heat and obstruction of qi and blood movement may result in qi stagnation and blood stasis. Treatment should combine clearance of heat and dampness with invigoration of blood, dispersion of stasis, regulation of qi, and unblocking of the collaterals. Potential combination strategies may include Salvia root (Danshen), red peony root (Chishao), peach kernel (Taoren), safflower (Honghua), Corydalis rhizome (Yanhusuo), and Cyperus rhizome (Xiangfu). Greater attention should be given to blood stasis in patients with fixed pain, menstrual exacerbation, or a prolonged disease course. Penning Granules containing blood-invigorating medicinals such as red peony root, Salvia root, Sparganium rhizome (Sanleng), and Curcuma rhizome (Ezhu), as well as kidney-tonifying and blood-invigorating formulas, have shown potential to improve symptoms, endometrial blood flow, endometrial thickness, or histologic indices in clinical studies of CE [26,28].

Therapies that invigorate blood and unblock the collaterals may create favorable conditions for endometrial repair by improving local perfusion and reducing tissue edema and inflammatory exudation [26-28]. They may also influence macrophage activation, fibroblast responses, and extracellular -matrix deposition [25]. The latter mechanisms, however, remain hypotheses derived primarily from current understanding of inflammation and tissue remodeling in CE. They cannot be confirmed solely on the basis of TCM theory or changes in peripheral blood inflammatory factors and should be evaluated through combined assessment of local histology, immune-cell phenotypes, fibrosis-related indicators, and clinical outcomes.

5.4 Cold-Dampness Congealment and Spleen-Kidney Deficiency Patterns: Combining Warming and Unblocking with Support of Healthy Qi

Patients with cold-dampness congealment may present with cold lower abdominal pain relieved by warmth and pressure; treatment should warm the channels, disperse cold, eliminate dampness, and unblock the collaterals. In patients with a protracted and recurrent course accompanied by fatigue, soreness and weakness of the lower back and knees, or recurrent vaginal discharge, treatment may address spleen-kidney deficiency by supplementing qi, strengthening the spleen, tonifying the kidney, and consolidating the root, with blood-invigorating and collateral-unblocking medicinals added as appropriate. Clinical studies in CE with a kidney-deficiency and blood-stasis pattern have shown that adding a kidney-tonifying and blood-invigorating formula to anti-infective therapy may further improve TCM syndrome scores,

endometrial blood-flow parameters, endometrial thickness, and indices such as IL-6 and TNF-α [28]. Research in patients with qi deficiency and blood stasis complicated by damp-heat also suggests that combining healthy-qi-supporting medicinals with dampness-clearing and stasis-resolving medicinals may better reflect the mixed deficiency-excess pathogenesis than pathogen elimination alone [27].

The aim of supporting healthy qi is not simply to increase the intensity of the immune response, but to improve mucosal defense, resolution of inflammation, and tissue-repair capacity, thereby restoring a local immune response that is proportionate, coordinated, and capable of timely termination [25]. In mixed deficiency-excess patterns, excessive warming and supplementation or exclusive pathogen attack should be avoided, as either approach may deviate from the underlying pathogenesis.

5.5 External Therapies

Chinese herbal enemas, acupuncture, heat application, and other physical therapies have been used to some extent for gynecologic conditions such as chronic pelvic inflammatory disease and chronic pelvic pain. Their effects should not be described broadly as "enhancing immunity"; it is more appropriate to characterize them as modulation of local immune-inflammatory responses. A retention enema allows the herbal decoction to remain in the rectum and be absorbed through adjacent pelvic tissues, potentially exerting heat-clearing, toxin-resolving, blood-invigorating, and stasis-dispersing effects. It may alleviate symptoms by improving local circulation, reducing inflammatory exudation, and facilitating resolution of inflammation. In a multicenter randomized controlled study, Hou et al. [29] found that retention enema with the Chinese herbal Yanting Decoction produced greater improvement in local signs and TCM syndrome manifestations of chronic pelvic inflammatory disease than oral administration. However, immune cells and cytokines were not directly measured, and the proposed immunoregulatory mechanism therefore remains to be validated.

Acupuncture, moxibustion, and heat application may improve pelvic microcirculation through thermal effects and acupoint stimulation and may influence neuroendocrine-immune regulatory networks. After acupuncture treatment in patients with chronic pelvic inflammatory disease, Woźniak et al. [30] observed reductions in pain and erythrocyte sedimentation rate, decreased IgM, and increased γ-globulin, suggesting potential anti-inflammatory and immunoregulatory effects. Other forms of thermotherapy, electrotherapy, and pelvic-floor physical therapy may also be used as adjunctive measures. However, direct evidence for their effects on the immune microenvironment remains limited and should be clarified in high-quality randomized controlled trials.

6. An Integrated Chinese and Western Medicine Approach

6.1 Clear Diagnosis and Standardized Treatment as the Foundation

Integrated treatment of CE should begin with a clear diagnosis. The inflammatory state should be assessed comprehensively on the basis of medical history, clinical manifestations, etiologic evaluation, hysteroscopy, and endometrial histopathology [31-32]. Because examination methods and diagnostic thresholds for plasma cells have not been fully standardized, diagnosis should not rely solely on a single symptom, a hysteroscopic finding, or one etiologic test [31-32].

When a pathogen has been identified or infectious activity is pronounced, standardized anti-infective treatment should be the foundation, and antimicrobial agents should be selected rationally according to etiologic and antimicrobial-susceptibility findings [31-32]. When the pathogen has not been identified, empiric anti-infective regimens may be used in accordance with guidelines or expert consensus, with careful attention to indications, treatment duration, adverse effects, and the risk of antimicrobial resistance [31-32,35]. TCM should be used to improve symptoms, modulate inflammation, and restore endometrial function; it should not replace necessary diagnostic procedures, etiologic assessment, or standardized anti-infective management [31].

6.2 Stratified Intervention According to Disease Course and Syndrome Pattern

At the initial stage, when damp-heat manifestations are prominent, treatment may focus on clearing heat, draining dampness, eliminating pathogenic factors, and reducing abnormal vaginal discharge. As the disease becomes protracted and is accompanied by pain, bleeding, or poor tissue repair, blood-invigorating and collateral-unblocking treatment may be strengthened. In chronic, recurrent cases with constitutional deficiency, qi supplementation and spleen strengthening or kidney tonification and consolidation of the root should also be considered. When the syndrome pattern changes, the treatment strategy should be adjusted accordingly. Long-term use of a fixed prescription without renewed syndrome differentiation and reassessment of inflammatory activity should be avoided [36].

This stratified approach may tentatively be linked to stage-specific changes in the immune microenvironment. During active inflammation, attention may focus on pathogen stimulation, release of proinflammatory mediators, and inflammatory-cell infiltration. As inflammation subsides, greater emphasis should be placed on restoration of immune homeostasis, tissue repair, decidualization, endometrial receptivity, and reproductive outcomes. Persistent inflammation in CE may involve pathogen-associated immune activation, TLR and NLR signaling, release of proinflammatory cytokines, and disruption of the endometrial microbiota. Functional recovery after treatment is not necessarily equivalent to pathogen clearance or a reduction in plasma-cell numbers [37].

It must be emphasized that stable, validated correspondences have not yet been established between TCM patterns such as damp-heat, blood stasis, and spleen-kidney deficiency and specific immune cells, cytokines, or stages of inflammation. The stratified model described above is intended primarily to generate research hypotheses. TCM patterns should not be assigned simple and fixed correspondences with individual

immune pathways, and their clinical value must be validated through standardized syndrome assessment, local tissue testing, and prospective studies [38].

6.3 Efficacy Evaluation and Safety Management

Evaluation of CE treatment should not be limited to symptoms such as pain or abnormal vaginal discharge, nor should conclusions be based on a single inflammatory marker. A more appropriate assessment system should integrate clinical symptoms, endometrial inflammatory or histologic changes, recurrence, endometrial function, and pregnancy outcomes. In patients seeking fertility, post-treatment endometrial status and subsequent pregnancy should also be monitored.

Attention should be paid to prescription composition, dosage, treatment duration, and concomitant medications. Medicinals and external therapies should be selected cautiously in patients attempting conception, during pregnancy, in those with hepatic or renal dysfunction, and in those with other comorbidities. Long-term management should also include standardized follow-up, prevention of infection, lifestyle modification, and psychological support when needed.

7. Research Limitations and Future Directions

Evaluation of CE treatment should not be limited to symptoms such as pain or abnormal vaginal discharge, nor should conclusions be based on a single inflammatory marker. A more appropriate assessment system should integrate clinical symptoms, endometrial inflammatory or histologic changes, recurrence, endometrial function, and pregnancy outcomes. In patients seeking fertility, post-treatment endometrial status and subsequent pregnancy should also be monitored.

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8. Conclusion

The development and progression of CE are closely related to dysregulation of the local immune microenvironment. Pathogen recognition, plasma-cell infiltration, alterations in immune-cell subsets, disruption of cytokine networks, and abnormal tissue repair collectively impair endometrial function. The TCM evolution of dampness, heat, blood stasis, and deficiency provides a theoretical basis for stage-specific and individualized intervention. TCM may act by modulating inflammatory responses, improving local circulation, and promoting tissue repair.

At present, the boundaries of the available evidence should be viewed objectively. Standardized diagnosis and anti-infective treatment remain the foundation of management. TCM may serve as an important component of syndrome-differentiated intervention and recovery management, but its specific effects on the immune microenvironment in CE require confirmation in high-quality studies. Future evaluation combining TCM syndrome patterns, immune phenotypes, and clinical outcomes may facilitate development of more targeted integrated Chinese and Western medicine strategies for CE.

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