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Theoretical Research

Understanding the viscera-related theory that the lung and large intestine are exterior-interiorly related

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Abstract

Pairing of the viscera and bowels is an important theory, which provides guidance to traditional Chinese medicine (TCM) clinical practice. Investigating this theory has been the focus of research on the basic theory of TCM. Recently, researchers have performed many studies on the theory that the lung and large intestine are exterior-interiorly related, which is a different point of view to that of previous literature, recent clinical studies and experimental studies, and these recent studies have enforced the theoretical connotation of the statement. However, there are problems in some of these studies including recent clinical studies and experimental studies. In the current article, literature on the viscera-related theory of the lung and large intestine are exterior-interiorly related is reviewed from physiological, pathological, and clinical views, and some opinions on the current research status are discussed.

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Key words: Lung; Large intestine; Viscera-related; Exterior-interiorly related

INTRODUCTION

Previous literature such as Lingshu Benshu^[1], Suwen Qixuexingzhi^[2], and Yi Xue Qi Yuan^[3], discuss that there is a Yin-Yang and exterior-interior relationship between the lung and large intestine. "Exterior-interior" is a relative concept. It is relative to zang-organs; fu-organs are exterior and zang-organs are interior. This corresponding relationship is mutual, which is mainly reflected by mutual connections of physiological functions, mutually affecting pathological changes as well as mutually using the therapeutic principle (e.g., pulmonary disease can be treated by dealing with intestinal disorders and large intestinal diseases can be treated by solving problems in the lung).

THE PHYSIOLOGICAL FUNCTION OF THE LUNG AND LARGE INTESTINE AND MEANS OF CONTACT BETWEEN THE EXTERIOR AND INTERIOR

Regulatory function of the lung refers to the fact that the lung is responsible for ensuring all organs in the human body function in an orderly, temperate, regular and rhythmic manner^[4]. It also means that the lung dominates both the Qi of respiration and the Qi of the whole body^[5-7]. In addition, the lung maintains and regulates the flow of fluids.

The large intestine is an organ of transmission, which is the passage for residues^[8]. In addition, some water in the feces is re-absorbed by the large intestine before transmission. Regulating body water metabolism is another physiological function of the large intestine. It is considered that the large intestine governs body fluids. The large intestine is one of the six hollow viscera. The function of the six hollow viscera is transmission. This physiological characteristic is the most prominent in the large intestine. The physiological function of the large intestine regulating body fluids is closely related to that of the lung concerning the flow of fluids.

The lung and large intestine are interrelated physiologically. However, the question can be asked "What is the exterior-interior method of contact between the lung and large intestine?" First, the meridian network relationship is the basis of the theory that the lung and large intestine have an exterior-interior relationship^[9]. Besides the direct connection through the meridians between the lung and large intestine, the lung meridian of hand-Taiyin is indirectly connected with the large intestine meridian of hand-Yangming through collateral vessels separated from the Lieque point (LU 7). The large intestine meridian of hand-Yangming is indirectly connected with the lung meridian of hand-Taiyin through collateral vessels separated from the Pianli point (LI 6). The collateral vessel branches derived from the meridian strengthen the communication and contact of the exterior-interior meridian. Moreover, meridian divergence of the lung and large intestine abide by the rules of Li-Ru-Chu-He, a circulation routine of twelve divergent channels. All communication of the meridian and collateral vessels indirectly strengthen the link between the lung and large intestine.

Second, the relation of the lung and large intestine being exterior-interiorly related is mainly implemented through the regulation of Qi transformation and fluid. They influence each other physiologically. On the one hand, the lung controls the Qi of the body. Harmonious Qi transformation depends on the regular function of diffusion and purifying, and down-sending function (which means the downward movement and purifying action of lung Qi in contrast to its diffusing action) of lung Qi. Lung Qi can promote the circulation of Qi to the bowel. The reason why the large intestine can conduct is because the bowel is connected to the lung. The conduction of the large intestine cannot be separated from the function of diffusion and purification and down-sending of the lung^[10]. The lung is the source of fluids. It maintains and regulates the flow of fluids. This function of the lung enables the large intestine to be moist and not dry, and it is conducive to the "transfer of objects" function of the large intestine. On the other hand, the conduction function of the large intestine affects the physiological function of the lung. They are interdependent and reinforce each other^[11,12].

Researchers have conducted a series of studies from different angles on the interaction of the lung and large intestine on physiological functions. A study on embryology using histology showed that the lung and trachea evolved from gastrulation foregut, and respiratory epithelium and glands evolved from the original intestinal mesoderm^[13]. The same sources of the structure of the lung, trachea and intestine provide histological evidence for the theory that the lung and large intestine are exterior-interiorly related. Gas in the gastrointestinal tract that is absorbed mainly relies on intestinal blood circulation, and it is originally discharged from the lungs. Under normal circumstances, the gas discharged by this route is 20 times higher than that discharged from the anus^[14]. The lung is a respiratory organ as well as an endocrine organ. Vasoactive intestinal peptide synthesized in the lung can affect vasodilation in the intestine^[15]. Surfactant protein-A (SP-A) gene expression in both the lung and intestine is regulated by the same factors in both organs^[16]. It is currently considered that mucosal immunity is a material basis of the theory that the lung and intestine are related. Normal function of the lung and intestinal tissue relies on the function of sIgA in the gastrointestinal and respiratory mucosa. Mucosal lymphocyte "homing" has become an important method of pulmonary-intestinal immunity^[17]. In addition, a study on pulmonary intestinal micro-ecological changes found that the pulmonary disease state can lead to flora changes in the intestine, and bowel disease may also affect flora changes in the lung. The lungs and intestinal flora are significantly affected when there is disease in the lung and intestine. A previous study on the micro-ecology point of view suggested that the lung and large intestine have an exterior-interior relationship^[18].

THE LUNG AND LARGE INTESTINE PATHOLOGICALLY INTERACT AS WELL AS TRANSMUTE FROM ONE SYNDROME TO ANOTHER

The viscera and bowels are physiologically interconnected and this can lead to pathological interaction. Large intestinal Qi transformation and fluid distribution are regulated by diffusion and purification and the down-sending function of the lung. When a disease develops to a certain extent, syndromes can change between the viscera and bowels; for example, lung dysfunction can cause a variety of syndromes in the large intestine. Conversely, abnormal bowel function can also affect lung function and cause a variety of syndromes in the lung. The exterior-interior transmutation of lung and large intestinal diseases is expressed as three forms: pulmonary disease causes large intestinal disease, large intestinal disease causes pulmonary disease, and comorbidity of the lung and large intestine. It should be noted that large intestinal disease is not relatively superficial and pulmonary disease is not relatively deep. This does not mean that exterior disease involves interior disease when large intestinal disease causes lung disease, and also does not mean that interior disease involves exterior disease when pulmonary disease causes large intestinal disease. It depends on the circumstances and dialectical thinking is required.

Pulmonary disease causes large intestinal disease When pulmonary disease causes large intestinal dis-

ease, this refers to the body suffering from pulmonary disease first and then the function of the large intestine is affected. Dysfunction of the lung Qi in purification and down-sending can affect the large intestine and lead to disorders of conduction function. In ancient times, it was recognized that the etiology and pathogenesis of large intestinal diseases are closely related to that of pulmonary diseases^[19-21]. Clinically, disorders of lung function can lead to constipation. For example, lung Qi deficiency cannot promote Qi movement and this makes defecation difficult. This is called constipation because of a deficiency in vital energy. Lung heat syndrome can also cause constipation because the heat is transferred to the large intestine. In addition, pulmonary diseases can lead to disorders of bowel function diarrhea. For example, a chronic cough could injure Qi and result in the loss of fluid because of Qi deficiency, thereby causing encopresis^[22]. Lung hyperactivity transferred to the intestine can also lead to diarrhea. Dr. Ganren^[23] used Gegen qinlian decoction to treat cough, chest pain, fever and diarrhea. In his medical records, the pathogenesis of diarrhea was considered to be due to a wind-warmth (a warm disease attributable to contraction of wind-heat pathogens) latent pathogen that was obstructed and could not reach the outside of the body but was transferred into the large intestine.

Clinical research on pulmonary diseases that cause large intestinal diseases with cor pulmonale are often complicated by acute respiratory failure, as well as abdominal distention, poor appetite, constipation and other serious intestinal function abnormalities, including intestinal obstruction^[24]. As the disease worsens, the incidence of bloating and constipation significantly increases. The worse the respiratory function (lung Qi deficiency), the more serious the gastro-intestinal disorders. Feng and Lin found^[25] that plasma motilin levels were significantly decreased in acute asthma patients, while those in patients with heart failure and the nongastro-intestinal disease control group did not change. This indicated that there was an intrinsic link between respiratory and digestive diseases. Zeng^[26] found in a study on 102 autopsies, that in the enteritis group, there were mainly intestinal pathological changes, but there were some lung pathological changes, such as pulmonary congestion and edema, alveolar wall fracture and formation of emphysema, as well as a decrease in the number of bronchial stick olfactory goblet cells, bronchial mucous glands and the content of goblet cell mucin and mucopolysaccharide in the majority of cases. In the pneumonia group, lung pathological changes were mainly observed, but there was also some congestion and edema of the intestine. In most cases, it not only caused a reduction of goblet cells of the colon, but also led to a decrease in mucin and mucopolysaccharide in the colon.

Large intestinal disease causes pulmonary disease

Large intestinal disease causing pulmonary disease refers to the body suffering from large intestinal disease first and then the function of the lung is affected. Conduction disorders of the large intestine can cause dysfunction of lung Qi in purification and dysfunction of down-sending and cause coughing and chest distress. The ancient Chinese were aware of the phenomena that large intestinal disease can cause pulmonary disease for a long time^[27]. In addition, bowel Qi obstruction is one of the main reasons for causing lung Qi ascending counterflow. Under physiological conditions, the large intestine must remain unobstructed, and the lung must keep down-sending. If heat is blocked in the large intestine, it will be transmitted upward along the meridians and injure the lung and aggravate coughing, asthma or other symptoms^[28].

From the point of view of modern clinical observations and animal studies, intestinal lesions can cause chest tightness, wheezing and other respiratory symptoms. For example, ulcerative colitis patients have small airway obstructive diseases, and as the course increases, small airway obstructive syndromes are more obvious^[29]. Serious intestinal hormone disorder leads to lung damage and acute respiratory failure symptoms appear. A previous study^[30] Showed that when the superior mesenteric artery of the rabbit was clamped, there was pathological damage in the lung, while there were no abnormalities in any other organs, including the heart, liver, pancreas, adrenal gland and kidney as observed by the naked eye or microscopy. This indicated that there is an intrinsic relationship between ischemic bowel function abnormalities and lung damage, and lung damage has obvious specificity^[30]. When observing pathological changes in main organs, such as the lung, large intestine, small intestine and heart, Feng et al^[31] found that semi-ligation of the rat rectum or small intestine led to colon or small intestine flatulence, chyme stagnation and dry feces, accompanied by lung pathological changes, but no abnormalities in other organs. Specific lung injury was also observed in similar experiments^[32]. A constipation rat model showed that the lungs of rats had pathological changes of pulmonary congestion, hemorrhage, alveolar epithelial swelling, deformation, structural variation, necrosis and increased cell death of alveolar macrophages^[33]. Allograft rejection after small bowel transplantation only occurs in the intestines and lung, and the lung is the first distant organ to show rejection^[34]. It appears that the lung and intestine have a similar immune response system and are similar in development^[34]. Results from the above studies provided some experimental evidence for the theory that the lung and large intestine are exterior-interiorly related.

Comorbidity of the lung and large intestine

Comorbidity of the lung and large intestine indicates that there is no obvious time difference between the on-

set of pulmonary disease and large intestinal disease. There is a cause-and-effect relationship in the etiology of these diseases; therefore, simultaneous treatment of the lung and large intestine can be performed. Xuanbai Chengqi decoction syndrome (Yangming warm disease, unable to defecate despite purgation, panting, phlegm, and constipation; the syndrome is related to failure of lung Qi to descend) is an example of comorbidity of Yangming-intestine and Taiyin-lung^[35]. Another example of comorbidity of the lung and large intestine is Ejiao Huangqin Decoction syndrome. In this syndrome, there is lung dryness with a large amount of intestinal heat. Lung syndrome is characterized by an itchy throat and dry cough, sticky sputum with red blood, with phlegm accumulated in the chest and hypochondrium. Large intestine syndrome is characterized by a burning sensation in the hypogastrium, watery stool, anal burning pain, abdominal pain, diarrhea but difficulty in defecating, symptoms similar to dysentery, and sharp pain in the intestine^[36].

CLINICAL APPLICATION OF THE THEORY THAT THE LUNG AND LARGE INTESTINE ARE EXTERIOR-INTERIORLY RELATED

Based on the theory that the lung and large intestine are exterior-interiorly related, pulmonary disease can be treated by dealing with intestinal disorders, large intestinal diseases can be treated by solving problems in the lung, and simultaneous treatment can be used for comorbidity of the lung and large intestine, to improve clinical efficacy.

Methods to facilitate bowel movement and regulate lung function have been applied to treat lung diseases. This embodies the Chinese medicine theory that the lung and large intestine are exterior-interiorly related, and also provides new ideas for Chinese medicine treatment in modern respiratory critical care^[37]. Methods of simultaneous treatment in the viscera and bowels and treatment of the viscera were used by Yu to treat 72 cases of chronic obstructive pulmonary disease. The results showed that simultaneous treatment of the viscera and bowels in terms of total efficiency or lung function improvement was significantly better than that of treatment of only the viscera^[38]. Better therapeutic effectiveness has been obtained in treating stable chronic obstructive pulmonary disease with Bufei-Tongfu decoction^[39]. Some researchers have described that the method to facilitate bowel movement used in lung excess syndrome was important in defeating illness and shortening the course. A method to facilitate bowel movement used in deficiency syndrome is known as "purgation is a tonifying method"^[40]. The method of simultaneous treatment of the viscera and bowels was used by Song and Wang to treat bronchial asthma cases in

acute attacks. They added rhubarb to herbal medicine prescriptions and obtained satisfactory therapeutic effectiveness^[41]. On the basis of conventional treatment, Xie *et al* added rhubarb, gardenia and other Chinese herbs for a recipe to facilitate bowel movement and clear out the heat to treat 50 patients with acute lung injury. The results showed significant clinical efficacy in the treatment group^[42].

Wang and Sun^[43] considered that there has previously been more focus on the spleen and kidney in the treatment of ulcerative colitis, and the exterior-interior relationship of the lung and large intestine was ignored. The method of treating ulcerative colitis by regulating the lung could improve the cure rate and reduce the relapse rate, and provide new ideas and methods of treatment. Zhang^[44] used various treatments to regulate the lung in treating irritable bowel syndrome and found good therapeutic effectiveness. Liu et al^[45] used Baisu Yuyang decoction to treat intractable peptic ulcers by regulating the lung, and they found that after treatment, the average integral values of chest distress and pain, acid reflux, belching, hiccups and other symptoms were significantly reduced (P<0.01). Wang^[46] used treatment to regulate the lung to treat 52 cases of diarrhea in children. They found that the cure rate was 69.2% and the total effectiveness rate was 94.2% after 2 days of treatment. These observations provided clinical research data for reference on the treatment of pulmonary and large intestinal diseases guided by the theory that the lung and large intestine are exterior-interiorlv related.

However, further studies are required on the theory that the lung and large intestine are exterior-interiorly related. Most reports on this theory are regarding clinical case studies or the personal experiences of practitioners^[47,48], while there only a few clinical studies with a large sample^[49]. Even with randomized controlled trials, there are various issues, such as sample size estimation, blinding method, allocation concealment, randomized implementation, follow-up and eliminated cases, intentional analysis, diagnostic criteria, and inclusion and exclusion criteria^[50]. In clinical studies of drug interventions, although researchers have used the principle that pulmonary disease can be treated by regulating the large intestine, and large intestinal disease can be treated by regulating the lung, or simultaneous treatment in the viscera and bowels, the prescriptions are not the same, even when using the same principle. Therefore, the lack of a uniform standard has limited the clinical application of a valid prescription. The current study mainly focused on the mechanism of injury of the causative agent that interacts between the lung and large intestine in the pathological state. Previous studies on the analysis of the exterior-interior relationship and the functional position of the relevant viscera and bowels have still not clarified this relationship. The conclusions on this theory are based on analysis of experimental results and phenomena, or are interpreted only from the perspective of modern medicine. The connotations and essence of the basic theory of TCM are not fully understood. There is insufficient evidence to prove this theory. The same problems appear in basic research to some degree.

In summary, the lung and large intestine communicate through the meridian network relationship. There is mutual restraint physiologically and they interact pathologically. There are 3 forms of transmission: pulmonary disease causes large intestinal disease, large intestinal disease causes pulmonary disease, and comorbidity of the lung and large intestine. For treatment, the following principles can be used: pulmonary disease can be treated by regulating the intestine; large intestinal disease can be treated by regulating the lung; and simultaneous treatment can be used for treating pulmonary disease and/or large intestinal disease.

In view of the current research status and some problems in the study of the lung and large intestine, it is necessary to adopt principles and methods of evaluation of evidence-based medicine in future clinical studies. It is also important to perform a series of studies based on clinical epidemiological methods, such as investigating symptoms, syndrome type, therapy, prescriptions, exterior-interior syndrome type of transmutation characteristics, conversion factors and timing of common diseases of the lung and large intestine. In this process, the basic principles and methods of the clinical application of the theory should be explored in-depth. In basic research, an animal model is required for standardized experimental study and this should be carried out using multiple different approaches. For example, studies on the biological basis of the theory that the lung and large intestine are exterior-interiorly related, the exterior-interior connection of the lung and large intestine, and channel tropism and pharmacokinetics should be conducted to comprehensively and scientifically interpret the concept and connotations of the theory that the "lung and large intestine are exterior-interiorly related".

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