The concept of the Zangxiang attribution of spleen in traditional Chinese medicine: implications for clinical practice and research

Yi-Qin Huang¹, Qi-Ming Zhang²*

¹College of First Clinical Medicine, Shaanxi University of Chinese Medicine, Xianyang 712046, China. ²Experimental Research Center, China Academy of Chinese Medical Sciences, Beijing 100700, China.

*Corresponding to: Qi-Ming Zhang, Experimental Research Center, China Academy of Chinese Medical Sciences, NO.16, Nene Street, Dongcheng District, Beijing 100700, China. E-mail: Zhang_917@126.com.

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**Abbreviations**
TCM, traditional Chinese medicine; TLR4, Toll-like receptor 4; MyD88, myeloid differentiation factor 88; NF-κBp65, nuclear transcription factor κBp65.

**Citation**

**Abstract**
Both traditional Chinese medicine (TCM) and modern medicine have the concept of spleen. The description of the spleen of the same name in the two disciplines is roughly identical in shape and position, but it is different in functional connotation. The immune, hematopoietic and blood regulation functions of the anatomical spleen in modern medicine cannot match the functions of the spleen in TCM, such as transportation, transformation, commanding bleeding, and dominating muscle and limbs. The spleen is a different organ in TCM and modern medicine. From the function perspective, this paper establishes the relationship between the spleen and the five zang-organs (It refers to the internal organs of the human body.) of TCM. The author believes that the immune and hematopoietic functions of the spleen in modern medicine should belong to the kidney of TCM, and the function of regulating the blood volume of the spleen in modern medicine should belong to the heart of TCM. By establishing the relationship between TCM and modern medicine of the spleen, we hope to provide a new method of TCM treatment for the clinical treatment of spleen-related diseases and provide new ideas for the modernization of the theory of Zangxiang (The physiological function and pathological changes of zang-fu organs are manifested in external signs.) of TCM.

**Keywords:** spleen; five zang-organs; Zangxiang; traditional Chinese medicine
Background

The spleen is located in the left quarter of the rib, between the bottom of the stomach and the diaphragm, the deep side of the 9th to 11th ribs, and the long axis is consistent with the 10th rib. It is supported and fixed by the gastrolienal ligament, the spleen and kidney ligament, the diaphragmatic spleen ligament, and the spleen and colon ligament. It is the largest lymphatic organ of the human body and stores blood, hematopoiesis, clearing aging red blood cells, and immunity [1]. Traditional Chinese medicine (TCM) describes the location of the spleen as: “Spleen and stomach are connected by membrane” in Suwen Taiyin Yangming Theory (Huangdi from the Western Han Dynasty 91 B.C.E.-32 B.C.E.), “spleen is one inch and two in the middle of the stomach, three inches and six in the heart, and three inches and six in the kidney” in Introduction To Medicine (Bing-Wu Jiang 2013 C.E.), “spleen attached to the spine eleven vertebrae” in Zhenjudaocheng (Ji-Zhou Yang from the Ming Dynasty 1601 C.E.), its function is mainly transportation, transformation, commanding bleeding, and dominating muscle and limbs. It can be seen from the above that the spleen of traditional TCM is equivalent to the anatomical spleen of modern medicine in location. However, the two cannot correspond in function, so the two are not the same organ. In order to explore the relationship between the anatomical spleen and the spleen of TCM, this paper is based on the theory of five-zang organs of TCM and the function of the anatomical spleen of modern medicine, and we hope to find the corresponding relationship between anatomical spleen and the five zang-organs of TCM.

Function of spleen

Based on modern anatomy, the spleen mainly comprises three functions: immunity, hematopoiesis and regulation of blood volume.

Immunity

The spleen is the largest lymphoid organ and the most important peripheral immune organ in the human body. There are three main types of immune function: (1) blood filtration. Pathogens in the blood, senescent dead cells, immune complexes and other foreign bodies can be removed here; (2) immune response. The spleen is the body’s main antibody-producing organ; (3) Secretions of immune factors. It secretes complement components and cytokines to regulate the immune response [2].

Hematopoietic function

Spleen hematopoiesis begins in the fifth week of embryonic development, when hematopoietic stem cells from the embryo’s liver enter the spleen through blood and multiply, differentiate and develop in the spleen. After birth, hematopoietic stem cells go dormant and the spleen loses hematopoietic function. The hematopoietic function of the spleen can be reactivated in cases of major blood loss, bone marrow fibrosis, and other blood diseases [3].

Blood regulation

The spleen tissue contains a large number of blood sinuses, which can store about 20% of whole body of blood. The spleen is different in size, and the amount of blood stored is highly variable. The regulation of its blood volume is dominated by the visceral nerve. As the smooth muscle relaxes, the volume of the spleen increases in order to accommodate more blood. As smooth muscle contracts, stored blood can be introduced into the bloodstream to play a role in the regulation of blood volume [3].

The attribution of spleen function in the theory of TCM

According to the theory of TCM, the five zang-organs include the spleen, lungs, kidneys, liver and heart. The main physiological functions of the spleen are to govern transportation and transformation, command blood and dominate muscles and limbs. Its function is similar to the digestive system, coagulation and anticoagulation system and motor system of modern medicine. The main physiological functions of the lung are to dominate Qi (in TCM, it refers to the most fundamental and subtle substance that constitutes the human body and sustains life activities and also has the meaning of physiological functions.) and control respiration and its function correspond to the respiratory system function of modern medicine. The kidney’s main functions are to store essence, control growth, development and reproduction, regulate water metabolism, and its function involves the urinary system, reproductive system, hematopoietic system, immune system and material energy metabolism system of modern medicine. The main physiological functions of the liver are to store blood and maintain a free flow of Qi, which is similar to the function of visceral the nervous and somatic nervous system in modern medicine. The main physiological functions of the heart are to control the blood and vessels and govern the mind. Its function is similar to that of the circulatory system and the mental nervous system [4].

The spleen’s immune function belongs to the kidney of TCM

The immune function of the spleen mainly includes filtering blood, immune response and secretion of immune factors. Bone marrow is the main source of immune cells. The immune function of the body is mainly performed by immune cells such as lymphocytes and granulocytes produced by hematopoietic stem cells in bone marrow [5]. In TCM, it is believed that “the healthy Qi is in the body, and the evil cannot be dry” in Neijing (Huangdi from the Western Han Dynasty 91 B.C.E.-32 B.C.E), that is, the kidney essence is sufficient, the healthy Qi is strong, and the body’s immune function is normal. On the contrary, the body’s immunity is low, which is caused by the lack of kidney essence and the lack of healthy Qi. More scholars also believe that the body’s immune function is closely related to the kidney of TCM [6]. As the material basis of kidney function, the function of kidney essence is very similar to that of stem cells. For example, Jin-Sheng Zhang believes that kidney essence and stem cells have multi-differentiation potential from the origin of life [7]. From the perspective of physiological function, kidney essence and stem cells have the functions of blood circulation, repair, reproduction and development. Finally, it is pointed out that kidney essence and stem cells are identical substances. Studies have shown that patients with kidney deficiency have a significant decrease in immune function, which essentially involves changes in the activity of human-related immune cells and factors [8]. Clinical experiments have shown that the number and activity of T lymphocytes and natural killer cells in patients with kidney deficiency are decreased, and the complement and immunoglobulin involved in humoral immunity are lower than those in the normal population. There is abnormal activation of B lymphocyte function, and obvious atrophy of immune organs such as the thymus and spleen, and ultrastructural damage of immune organs [9, 10]. Most kidney-tonifying Chinese medicines have immune pharmacological effects, which can improve immune function and strengthen cell phagocytoses such as Cordyceps sinensis, Cistanche deserticola, anter, and Corcus officinalis [11]. Therefore, the clinical use of the kidney-tonifying method can improve or restore its immune function [6]. For example, Huang Min established the model of kidney essence deficiency in pregnant rats by compound stress method, and gave the suspension of classic ancient prescription of Chinese medicine Zougui pill to observe the effect of tonifying kidney and filling essence method on the microscopic and ultrastructural changes of spleen and the expression levels of Toll-like receptor 4 (TLR4), myeloid differentiation factor 88 (MyD88) and nuclear transcription factor κBp65 (NF-κBp65) in the related immune pathways of pregnant rats [12]. The results showed that the tonifying kidney and filling essence method could effectively regulate the immune imbalance of pregnant rats by improving the spleen structure and up-regulating the expression level of the TLR4 / MyD88 / NF-κBp65 immune pathway.

In summary, kidney essence and stem cells have the same identity. From the source, the immune function comes from the kidney essence stored in the kidney of TCM, and the patients with kidney deficiency
can have obvious immune dysfunction, manifested as obvious destruction of the structure and function of immune cells and immune organs. Clinical treatment from the perspective of tonifying kidney and replenishing essence can significantly improve their immune function. Therefore, the immune function of the spleen can be attributed to the functional category of the kidney of TCM.

The hematopoietic function of the spleen belongs to the kidney of TCM

Hematopoiesis is the production of new blood cells. Physiologically, the spleen plays a hematopoietic function in the embryonic period, and its function is performed by hematopoietic stem cells. Hematopoietic stem cells are a kind of stem cells with high self-renewal, directional differentiation and self-repair ability after injury. They can produce all kinds of blood cells, including lymphoid cells, myeloid blood cells and platelets. Pathologically, hematopoietic dysfunction mainly manifests as anemia signs such as blood cell reduction, pale complexion, and pale lips and nails. These manifestations are consistent with the blood deficiency manifestations (lusterless complex) of TCM. TCM believes that the metaplasia of blood originates from kidney essence, as Zhu Bing Yuan Hou Lan (Yuan-Fang Chao from the Sui 610 C.E.) says: "kidney stores essence and essence is formed by blood." According to modern medical research on stem cells, Zhang Jin pointed out that hematopoietic stem cells are part of the kidney essence and the complete function of the heart is closely related to kidney essence [5]. When the kidney essence is sufficient, the function of hematopoietic stem cells is normal. Based on the differentiation of hematopoietic stem cells, the microenvironment in which hematopoietic stem cells are located, and the coordination of kidney, liver and spleen on blood metabolism, Lu Yan thinks that sufficient kidney essence can promote the differentiation of hematopoietic stem cells, the proliferation of hematopoietic stem cells, and the potential of hematopoietic stem cell proliferation [13]. It can be seen that blood circulation is closely related to the kidney essence stored in the kidney of TCM. In addition, kidney-tonifying Chinese medicine can promote the proliferation and differentiation of bone marrow hematopoietic stem cells/progenitor cells, improve the hematopoietic microenvironment, and promote the recovery of bone marrow hematopoietic function [14]. The decrease of blood cells in patients with kidney deficiency can be significantly improved by nourishing kidney essence treatment. For instance, Yuan-Tian Wu used a kidney-reinforcing prescription (empirical formula of Chinese medicine Busui Shengxue decoction) to treat 59 patients with aplastic anemia [15]. The results showed that compared with 58 patients in the control group (treated with stanozolol and cyclosporine), the blood red blood cells, hemoglobin and platelets of patients using Busui Shengxue Decoction were significantly higher than those in the control group. From the perspective of nourishing kidney essence, it can accelerate the relief of anemia symptoms. Liu Jian used a multi-center clinical experiment to treat 187 patients with chronic aplastic anemia with an empirical Chinese medicine formula, Bushen Tianjin Fang granules. After six months of treatment, it was found that the total effective rate was 98.8% [14]. The number of hemoglobin and platelets increased significantly. Before treatment, hemoglobin ≥ 40g/L, platelets ≥ 10 × 10^12 /L; the higher the value, the better the curative effect.

In summary, physiologically, hematopoietic stem cells and kidney essence can produce blood cells. Pathologically, the hematopoietic dysfunction caused by abnormal hematopoietic stem cells has a significant effect from the perspective of nourishing kidney essence. Therefore, the hematopoietic function of the kidney essence plays an important role, so the hematopoietic function of the spleen can be attributed to the kidney of TCM [16].

The function of regulating blood volume of the spleen belongs to the heart of TCM

The spleen contains many blood sinuses, which can store about 20% of the body’s blood. The spleen stores blood when the human body is at rest and quiet. When the human body is in a state of stress, such as exercise, blood loss, and hypoxia, the sympathetic nerve is excited, the secretion of catecholamines increases, the capsule and septum of the spleen contract, and the stored blood is discharged into the blood circulation [3]. Under the rhythmic contraction of the heart and vasomotor contraction, the blood is redistributed to ensure the blood supply to important organs, such as the heart and brain, to regulate blood volume. The role of the spleen in participating in the function of the circulatory system to regulate the blood volume is similar to the function of the heart Qi in TCM to promote the blood to run in the pulse and transport the blood to the whole body to nourish the viscera. As Sawen Weilun (Huangdi from the Western Han Dynasty 91 B.C.E.–32 B.C.E) said: "The heart governs the blood vessels," and the heart plays a leading role in the circulation of the whole body of blood. The spleen can also store blood, which is consistent with the "pulse" function in TCM to store blood. The spleen can be understood as the "pulse" in TCM. Therefore, from the perspective of blood flow in TCM, the function of the spleen in regulating blood volume is dominated by the function of the heart in storing and controlling blood vessels. Modern research from the perspective of blood circulation shows that the main blood vessel function of the TCM heart is consistent with the function of the circulatory system. For example, Li Lan observed the effect of left ventricular ejection fraction (EF) and aortic peak blood flow velocity (AV) on cerebral vascular blood flow parameters in 185 hospitalized patients with cardiovascular disease using a Doppler-echocardiogram instrument [17]. The results showed that the peak systolic flow (Vmax) of the left common carotid artery in patients with heart Qi deficiency and other syndrome types was (63.5 ± 18.4) cm/s and (69.76 ± 18.7) cm/s, respectively. The difference between the two groups was statistically significant (P < 0.05). It can be seen that heart Qi deficiency can lead to dysfunction of the heart-governing blood vessels, which can be manifested through the circulatory system. The circulatory system and the heart governing blood vessels have common points. In addition, the circulatory system function is abnormal; from the perspective of TCM, tonifying heart Qi has a good clinical effect. For example, Li Yan and others used ligature of the left anterior descending coronary artery of rats to replicate a rat model of heart failure after myocardial infarction [18]. After successful modeling, Codonopsis and Astragalus were continuously administered for 9 weeks. The results showed that the Qi-supplementing drugs Astragalus and Codonopsis could significantly improve the symptoms of heart Qi deficiency, such as quietness, curling up and fatigue, significantly increase the maximum rate of increase /decrease of left ventricular pressure in model rats (P < 0.05), delay the decrease of myocardial systolic function and reduce the area of myocardial infarction after myocardial infarction in rats. In recent years, some scholars put forward that heart failure can be regarded as heart-governing blood vessel function failure of TCM from the perspective of clinical symptoms [19]. When heart failure occurs due to continuous venous congestion, blood can be retained in the spleen, resulting in congestive splenomegaly, insufficient effective circulating blood volume, dyspnea, fatigue, decreased exercise tolerance, oliguria and renal function damage. In this process, due to heart failure, cardiac systolic function decreases, and the spleen cannot discharge the retained blood into the blood circulation to increase the effective circulating blood volume. It can be seen that the regulation of blood volume by the spleen is affected by the function of the heart governing blood vessels.

In summary, the function of the spleen to regulate blood volume is to discharge the stored blood into the blood circulation. Under the rhythmic contraction of the heart, the blood in the circulatory system is redistributed to the whole body to ensure the blood supply to important organs such as the heart and brain. Its function is similar to TCM’s in that the heart Qi drives it to run in the pulse and transports the blood to the whole body to nourish the viscera. Therefore, the circulatory system is very similar to the function of the diagnostic governing blood and vessels. In addition, heart failure can be regarded as heart-governing blood vessel failure of TCM. When heart failure occurs, the systolic function of the heart is low, systemic venous
congestion occurs, blood is retained in the spleen, heart failure occurs, the rhythmic contraction and vasomotor effect of the heart decrease, and the spleen cannot discharge the retained blood into the blood circulation. It can be seen that the low function of the heart governing blood vessels will also affect the function of the spleen in regulating blood volume. Therefore, the function of regulating the blood volume of the spleen can be attributed to the function of the heart governing blood vessels.

Conclusion

The spleen is the largest peripheral immune organ of the human body. Its functions include immune function, hematopoietic function, and blood volume regulation function. The functions of the spleen in TCM are to govern transportation and transformation, command blood and dominate muscles and limbs. The function of the anatomical spleen in modern medicine is different from that of the spleen in TCM (Figure 1). According to the different functions, the spleen can be divided into five zang-organ of TCM. The immune and hematopoietic functions of the spleen correspond to the functions of the kidney, storing essence, generating marrow and transforming blood, which can belong to the functional category of kidney in TCM. The function of regulating blood volume of the spleen belongs to the function of the circulatory system, which is consistent with the function of the heart governing blood vessels in TCM. It can belong to the functional category of heart in TCM. The corresponding relationship is shown in Table 1. To explore the corresponding relationship between the anatomical function of the spleen and the spleen of TCM, to further sort out the understanding of the same name organ “spleen” in TCM and modern medicine, to provide some theoretical basis for the treatment of clinical diseases such as immunosuppression and hypersplenism from the kidney and heart of TCM. In order to provide a new method of TCM treatment for clinical treatment of spleen-related diseases and to provide new ideas for the modernization of the theory of Zangxiang in TCM.

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Table 1 Spleen function of Traditional Chinese Medicine viscera attribution

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