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Redescription of Zang Spleen Model in Modern Anatomico-functional Terms

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Traditional Chinese Medicine (TCM) conventionally described Zang organs according to the Zangfu manifestation theory. Current TCM studies showed that the network of stomach-pancreas-intestine and the hypothalamic-endocrine-immunological axis or the mitochondria may represent the Zang Spleen. Zang is described as a set of interrelated parts rather than an anatomical organ. This paper reviewed how the Zang Spleen could mean the same anatomical organ but with added dimension. Re-inclusion of intestinal lymphoid and lymphatic structures with their related vigilant immunological functions would help restoring the anatomical functional tie. The one Spleen-Pancreas-Intestine Complex with the gastro-intestinal digestive system and lymphatics linking the immunologically vigilant spleen and intestines may be taken as the Zang Spleen "situated internally". Zang Xiang "external manifestations" may be expressed as functional features of that one structure as it serves to encounter food with digestion, related stomach functions, guarding interface, a lympho-circulatory transport system, and utilization of the assimilated essence for energy and vegetative balance, nourishment of brain and muscles to cater for life, and also functional features of the intricate interrelationship between that structure and the whole body neuro-endocrine balance, the influence on tone and dynamics of the whole internal viscera, stabilizing blood in circulation, body fluid perfusion-drainage balance, the immunological homeostasis and body defense, idea formation and intention mechanisms to face life. These correspond well with Zang Spleen described, and meet its essential meaning more closely than previous models. This anatomico-functional model can better interpret TCM literature and be easily understood by current science.

Key words: Zang Spleen, Zang Xiang, anatomical functional structure, organ complex, modern medical science

Introduction

This paper is a step to describe Traditional Chinese Medicine (TCM) mechanisms in scientific terms. With a different language, Zang Spleen seems quite different from the anatomical organ, the spleen. In fact, for most modern TCM workers, the Zang Spleen describes digestive functions, with nothing concerning the spleen organ itself. For framing future research, this paper aims to identify meaningful and

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useful modern anatomico-physiological homologues and states that match TCM Zangfu networks and functions. To start with, it is presumed that TCM and western medicine essentially started with the same body bio-physiological features, being different only after long cultural separation[1]. By reviewing the TCM Zang Spleen, understanding the limitations of modern models, and reinterpreting it in that presumptive perspective, a useful model can be deciphered. A similar model has been developed and described for the Zang Kidney[2].

A note to clarify the wording used. TCM texts capitalize the first letter to denote a word significantly different from modern medical usage. Here, for clearer and easier reading, Zang Kidney, Zang Spleen, Zang organs are abbreviated with prefix as zKidney, zSpleen, zOrgans respectively[3].

Ancient and Orthodox Zang Spleen Model : From Anatomy to Function

TCM ancient literature anatomically described many body parts. Internal Zang-fu were classified as five Zang organs, six Fu organs and six extraordinary Fu organs. That was an anatomico-functional classification, since the zOrgans, Zang, are solid organs, to depict organs which collect and store, being different from the Fu or zViscera which are hollow, through organs that receive and let through. In contrast, the word organ in western medicine means a list of fully differentiated structural and functional units specialized for some particular function.

To start with, the spleen was described anatomically in one of the most ancient TCM texts, Eighty Eight Classic Medical Questions (Nan Jing)[4]. In Nan Jing "The Spleen weights two jin and three liang, is three cun wide and five cun long, and has a half jin of clustered fatty tissue". The description corresponds to the spleen with the attached fatty tissue which must have meant pancreas. Illustrated Supplement for Classified Classics, Leijing Tuyi[5] stated that "the Spleen ….form like a blade, omentum shared with stomach, on its left". Much later in 1796, it was depicted in Zhoushi Jingluo Compendium, and the Spleen diagram clearly represented the anatomical spleen and pancreas[6]. The actual anatomy was not described in Huang Di Nei Jing, the earliest classic, which somehow mentioned "the spleen(-pancreas) as connected to the stomach by a membrane" [7]. In TCM, same as in modern physiology, the Zang Spleen has a dominating influence on food handling and energy metabolism.

The book Classified Classics[8], similar to an earlier commentary by Wang Bing[9], stated that "The Zangfu organs situated internally are manifested externally (physiological and pathological features reflected externally), thus called Zang Xiang". Zang solid organs and Fu hollow organs form the core while the other body parts are functionally related to them. Ancient Chinese scholars observed that the body as a whole varies with environment in adaptation. Expressed in holistic terms according to their refined understanding of the universe, the body core would function and vary with nature according to Yin Yang and harmony principles. Diseases would be due to disturbances of nature on poor body constitution and adaptation. Then, the interrelationship between various body parts were used to account for inner harmony and its disturbance. This is the Zangfu manifestation (Zang Xiang) theory which expressed the Zang organs as functional organ networks in the body systems, generalizing from the

physiological functions and pathological features of the Zangfu organs. Xiang, or manifestations, in Chinese refers to the picture as well as the equivalent symbolization of things.

The understanding of Xang Xiang is highly important to clinical TCM. Current workers tried to understand it through diseases and from clinical methods being used. Nevertheless, Zang organs are essentially different from terms of western scientific medicine. This could be due to the fact that the concepts of Zang organs and Zang Xiang were developed since ancient time. Over the centuries after Nei Jing, as TCM described the body in terms of functional entities away from anatomy matters during the course of time, there is now insignificant correlation between anatomy and functional physiopathology. The difference has led to divergent views on handling TCM words when confronted with modern science:- as necessary technical terms, as similar things but different only in breadth and dimension, or validity questioned.

Currently on Zang organs, TCM is more in a way of describing a set of interrelated parts rather than one anatomical organ. In current TCM literature, the main physiological functions and features of the zSpleen are: "governing transportation, transformation and upflow of the clear and governing blood and fluids; internal-externally interconnected with the zStomach, with Meridian connecting as zSpleen-Stomach which forms one important organ complex that basically handles food by digestion, absorption, and distributing its essence. After birth, the continuation of basic body functions and life, and the transformation of Qi, blood and body fluids are all dependent on transportation and transformation of the food essence by the zSpleen-Stomach organ complex. This complex is therefore the source of all metabolisms: the postnatal life foundation. It dominates the four limbs by influencing the muscles, opening through the mouth, and manifesting its luster externally in lip, as saliva in secretions, and as thoughts in mind." [10]

Modern Network Zang Spleen Model

In modern medicine, anatomy, function and physiology have to be closely related. For present TCM scholars, the pancreas-intestinal model coupled with the stomach is used. This model has been derived from the traditional Spleen-Stomach theory 脾胃論, put into modern perspective[11]. To explain the Zang Xiang for the Zang Spleen, investigations were done over the whole body[12]. It was noted that zSpleen deficiency is associated with vegetative neural changes in having reduced sympathetic and increased parasympathetic activity[13], reduced blood cAMP and dopamine levels, reduced gastric electric waves and movement waves associated with reduced gastric tension and increased intestinal motility[14]. Most of these are summarized at the turn of the century by Wei [15], and further expanded by his Beijing team[16]. Motilin is increased in zSpleen deficiency[17]. A deficiency of zSpleen Qi was found to correspond to an insufficiency of digestive enzymes and a reduction of enzyme activity, interfering with digestion. There is associated delay and reduction in oral salivary amylase secretion after acid induction in zSpleen deficiency patients[18]. Decreased intestinal absorption function and reduced intestinal epithelial homeostasis with cell damage are noted in zSpleen deficiency[19]. Gastric epithelial cAMP is reduced[20]. A number of immunological alterations[21-23] were noted, though not specifically related to the spleen as such[24,25]. Differences were found in the different types

of zSpleen disorders. All these were investigated to illustrate the associated body changes in the various types of zSpleen disorders apart from gastrointestinal function.

Researchers in China from the integral, organ, cellular and microscopic levels to investigate for the essential meaning of Zang Xiang, have move away from a solid organ representation of Zang to a network representation. The word Zang currently, takes a rich meaning, including its many interrelated body parts and their functions, and its relationship with other body parts, demonstrating the mutual positive and negative influences among the body systems. The scientific study on zKidney was one of the earliest works in this reform for this modern reinterpretation. Researches have demonstrated that the hypothalamic, adrenal and ovarian function are closely related to zKidney[26,27]. Hypothalamus-pituitary-ovary-adrenal dysfunction was notable in zKidney dysfunction[28-30]. It was thought that the hypothalamus-pituitary-ovary-adrenal axis represents the zKidney. Further study on other hypothalamic functions such as thyroid and sex hormone axis and immunological functions[31] revealed that the Immune-endocrine axis[32] and zKidney function are closely related. A network model has been used to explain the Zang Xiang. With its success, TCM workers followed the same way to expose other Zangs, including the zSpleen, in a similar network of many organs. It was popularized that each Zang organ is not separate, but can be explained only in its relationship with the other Zang organs as a whole.

That model is justified by Zang Xiang conceptual frameworks, which is vital in TCM theory, applications and therapy. Choosing the more important relational Zang Xiang as the core concept in keeping up with its meaning, modern workers justified it by the network medicine offered by the perspective of systems biology. It needs be noted that systems biology integrates data in models mainly to assess observations not otherwise assessable with the reductive approach. For the Zang to go modernized, it becomes a conceptual framework and nothing like a real complex. Theoretical models can influence or direct diagnosis and therapy, or even act to pool clinical experiences. However, models certainly cannot be viewed as real complexes as they may change from time to time with new experience and observation. In contrast, there has been little change in all those centuries in the TCM Zang core concept that a real Zang exists. Not based on the usual solid acceptable standards in mainstream medicine, the network model to represent Zangs suffers from not being easily accepted since there can be many other ways to combine for similar networks. In fact, the model led by Wei (Model A) has not by itself enough distinguishing features from similar models for the zHeart, zLung, zKidney or zLiver deficiency[33].

Leaving the representation by solid organs, going still further away from the network model, a new representation emerged. Since the 1980's, Liu and his Guangdong team led researches to study the relationship between zSpleen and mitochondria[34,35]. It was believed that mitochondria, "the powerhouses of the cells" that produce most of the chemical energy used by the cells, represent zSpleen (Model B). The mitochondria are important in the Krebs cycle in the body, a series of energy-yielding steps in the catabolism of carbohydrates as they catalyze oxidation reactions that form ATP, an energy carrying molecule. As zSpleen deficiency is concerned with energy metabolism, the mitochondria for most of the chemical energy used by the cells, would explain zSpleen being "the origin of all metabolism vital to

life" [36]. It is hypothesized that in mitochondria, the ATP formed in the Krebs cycle during carbohydrate metabolism may represent the Qi, and the succinate monoacyl CoA supports hemoglobin or the Blood, both central to zSpleen physiology[36]. Researches in gastric epithelial cells supported as they showed mitochondrial pathological changes related to the degree of zSpleen dysfunction. In zSpleen Qi or Yang deficiency, gastric mucosa may be normal, while pathological gastric mucosa and mitochondria would be worse and more often found in patients with zSpleen Yin deficiency and zSpleen deficiency with stagnate Qi[20]. Besides, the degree of zSpleen dysfunction is related to degree of gastritis, and the disturbance in the gastric epithelial zinc and copper metabolism and enzyme systems[37]. Decreased intestinal absorption function as a characteristic essential to zSpleen deficiency is related to decreased mitochondrial function[38,39]. Quantitative and qualitative changes of mitochondria with decreased number of the enzyme secreting cells and zymogen granules necessary for normal digestion would explain the interference with digestion of proteins as in zSpleen Qi deficiency with abdominal flatulence, abnormal stools and undigested food in the stool after the intake of a high protein diet. Use of zSpleen Qi reinforcing concoctions would protect these gastric mitochondrial changes[40], even 3D-dimensionally[41]. Decreased number and quality of mitochondria leading to less ATP formation would explain for less fuel or zSpleen Yang for absorption and transportation of nutrients to the cells. Insufficient mitochondrial energy induces symptoms like lanquor, lethargy, lassitude to talk, abdominal distention after exhaustion, and these symptoms occur in patients with worse degree of zSpleen deficiency, particularly those associated with stagnate Qi from zLiver antagonism[42]. The possibility is raised that deranged cellular K^+/Na^+ pump with mitochondrial dysfunction may cause dampness seen in zSpleen deficiency. Notably, mitochondrial density and energy dependency are highest in brain and skeletal muscles, the body parts closely related to zSpleen function. Mitochondrial abnormalities in number and structure were found in myocardium, liver, gastric mucosa, and skeletal muscles in zSpleen Qi deficiency in mice[43-45]. The zSpleen is related to health of muscles and brain, and mitochondira produce energy to muscles and brain. Deficient zSpleen Qi patients had thin musculature and their mitochondria are fewer with more structural changes. Use of zSpleen-Yin recuperation herbs was found to restore muscle mitochondrial number and structure[46], brain mDNA metabolism[47] and mitochondrial changes[48] in aged mice. Thus mitochondrial changes are used to explain the effect of zSpleen on muscles and brain. It may be said that this representation by mitochondria is useful to attribute the pathophysiology of zSpleen dysfunction to defective energy processes, but describes the mechanism at tissue level rather than the zOrgan level.

In short, the current Zang Spleen description is not matched for function with anatomy. Anatomy was understood sufficiently in ancient times, and the zSpleen as an entity was not challenged. When modern TCM workers confronted the western view in anatomy and physiology; they took the western medical framework to describe the zSpleen. To overcome the long cultural gaps, most TCM scholars justified their observations and experience by taking the main function of the zSpleen for its digestive concepts and functions. Unable to include the spleen, some alleged that this word has been a misnomer[49,50] or poor equivalent[51]. In the end, after all the efforts, the modern representation of zSpleen with digestive structures and

neuro-endocrinal-immunological network or with the mitochondria still do not have anything related to the actual organ, spleen, for which the Zang is so named.

Blind Spot in Modernizing Zang Concepts

Western Medicine once followed a reductionist path to understand the body part by part. The body was understood by component systems, including digestive, respiratory, excretory, endocrine etc. In describing the digestive system, the immunological system would be separate. The importance of immunological events has all along been unintentionally downplayed in all discussions in food handling pathophysiology. This placed a gap and obstacle to restore meaning and understanding of TCM Zangs in a modern context when TCM workers used this western framework in the construct of zSpleen.

Here it is believed that the ancient started with essentially the same anatomical organ but with a wider dimension. To review effectively, the limitations of modern TCM framework obscured by blind spots must be recognized. The zKidney can be used as example. In zKidney, the blind spot as TCM used western medical framework in Zang explanation, was the lost importance of musculature, which re-emphasis helps in understanding zKidney[2]. Then, it should allow identification of the added dimension to the named anatomical organ to match each zOrgan in structural terms.

By the same token, zSpleen can be better described only when it is re-emphasized that food taken in may both be used as well as guarded. TCM has passed on since ancients times with food understood primarily in a comprehensive view as both positively and negatively acting. Ancient Shen Nong tried thousands of plants whether nutritive or poisonous, and graded them in a system of homology of food and medicine. Cumulated experiences were used to improve health and treat diseases. After all, while the body takes in external substances for the benefit of nutrition, the body also faces things foreign not being tolerated. The western perspective isolating the digestive system in body discussions would highlight only the nutritive processes. In general, food is both nutritive to be useful as well as pathogenic or antigenic to be guarded, and processed through the respective digestive mechanisms and vigilant immunological mechanisms. Comprehensive food handling concepts essentially put these back all together. To rediscover the anatomico-functional zSpleen, there is need to re-include the actual anatomical vigilant spleen in reframing its theoretical framework.

New Anatomico-functional Zang Spleen Model

Let us presume that in ancient TCM, the zSpleen was essentially started or defined as a structure with a name and configuration consistent with anatomy, while the frame model of Zang Xiang, generalizing manifestations of physiology and pathology were added on top of it later[2]. Then finding out the initial ancient anatomico-functional structure of zSpleen, the derived Zang Xiang functions can be reviewed in a better perspective.

I. Anatomical Spleen Essentially Inside Zang Spleen

The intestinal mucusa, apart from absorption, is a primary host defense and recognition organ. Currently,

most of the orthodox TCM texts have not addressed defense and immunity when referring to zSpleen. In fact, the description in Nan Jing and the diagram of Zang Spleen in Zhoushi Jingluo Compendium depicted the pancreas and the spleen together. The anatomical spleen is a lymphopoeitic organ. Before the immune system was elaborately defined in western medicine, the spleen was linked with the liver and intestines by the portal circulation. It is now known to be an important organ in blood and immune disorders.

The immune system, composed of cells and molecules, has an innate and an adaptive response. The innate immune response, comprising natural killer cells, mast cells, dendritic cells, phagocytes, cytokines, complements, and acute phase proteins, represents the first line of defense to an intruding pathogen. It is non-specific, without memory, and response to substance which the body regards as foreign or potentially harmful. The adaptive immune response, comprising T and B cells, cytokines and antibodies, display a high degree of memory and specificity, and can evoke a more potent response on second exposure to the pathogen. The adaptive immune response frequently incorporates cells and molecules of the innate response in its fight against harmful pathogens[52,53]. The immunity cells form a system of defense. Only a few cells of each specificity are stored as template for mass production at times of antigen stimulation. Each episode of stimulation contributes to the concept of "self" [54].

The lymphatic system and the circulatory system helps to circulate these immune cells, allows regulation and clearance of foreign materials, and promotes confrontation against foreign pathogens. The intestinal mucosa is one of the three major sites of external confrontation, the other being skin surface, and the lung epithelium. In reviewing the histology of the small intestine, there are a lot of Peyer's patches which are lymphopoietic follicles beneath epithelial M-cells (Membranous or 'Microfold' cells) scattered between the transportation enterocytes. In fact, there are much more immunity events going on here than other body parts because of the much larger quantity of pathogens to handle.

In any stream of medicine, defense is a necessary concept. In TCM, the concept of defense has been described. In fact, Ying and Wei have been described early since Huangdi Neijing: "Ying is the essence of nutrient granary….Wei is the defense with nutrient granary"[55]. Here, Ying 營 (buildup, battalion) is translated as "coalition". Food absorbed produced the nutritious coalition, Ying 營 , and nutrients, Yang 養 . In the current refined TCM concept, Ying is the coalition battalion formed from absorbed food, forming a defense circulating in the blood, while the Wei Defense move along with it externally to traverse among tissues throughout the body[56]. Wei may be analogous to the immune cells, and Ying Qi becomes a Qi energy of defense and resources in the circulation. In a sense, TCM had tied nutrition and defense together. It is only much later in the Ying and Qing dynasties that defense is better expounded in concept in infectious diseases. The zSpleen is recently believed to be much immunologically related[57,58]. Diseases of chronic inflammation, probably those closely related to immunological damage, including glomerulonephritis[59] and hepatitis[60,61], are found to have damp-heat causally significant to the disease. Damp-heat syndrome is related to zSpleen[62], and inflammation is related to immunological problems. With so many immunological and defense associations, the anatomical spleen cannot be disregarded, especially

when food processing should include guarding vigilant mechanisms.

II. Defining the Functional Anatomical Zang Spleen

The Zang Spleen, in the ancient Chinese, could mean the same anatomical organ but with added dimension. The organ mass around the spleen, taken as Spleen-Pancreas-Intestine Complex associated with the digestive system as well as lymphatics linking the vigilant spleen and intestines form ONE piece of functional structure and that could be the zSpleen[63,64]. It is intimately related to the stomach together in function.

This is one functional structure, because they can be seen as one integral, closely interactive, closely inter-coordinated complex. Digestion of food materials, guarding of pathogenic and antigenic materials from food are served by the Intrinsic Functions of that one functional structural complex. Intrinsic functions include mediating the comprehensive nutrient intake and food processing functions.

This view with a structural base allows a re-understanding and a coherent construct of the zSpleen and Zang Xiang manifestations into three inter-reacting levels. From the one zSpleen Anatomical Structure, there are Intrinsic Structural Functions, and all of these are supported with Internal Interactive Complex Mechanisms.

Essentially it serves five areas: digestion, related stomach functions, guarding interface, a lympho-circulatory transport system, and utilization of the assimilated essence for vegetative and energy balance for life. The internal support would be a host of neural, immunological endocrine, receptor mechanisms among others to achieve homeostasis and to cater for energy and life needs. These would produce external observable Zang Xiang manifestations.

III. Better Understanding Supports the New zSpleen Model

This present view of zSpleen, as a functional structural complex closely interacting with supporting mechanisms, would be able to embrace known features and current findings which in the new light also become evidences for this model. This one functional structural complex includes the spleen-pancreas-intestinal complex working with the stomach together. It may be taken as three parts interacting, with external and internal components for digestive and immunological processing functions.

One part of the complex, the pancreas-intestine provides the needed external mechanisms for digestion. The integral body needs nutrition, and digestion is well described in western medicine. Through digestion, nutrients from food are assimilated to support all metabolism. Internally, food nutrients need to be transported to all parts of the body. Most of the food nutrients like sugars and amino acids are absorbed directly into intestinal capillary blood and ascend up through the portal circulation for hepatic metabolism. On the other hand, chylomicrons are carried by and transported first into the lymphatic vessels in the intestinal villi. Chylomicron-rich lymph then drains into the systemic lymphatic system and finally via the blood to the tissues throughout the body for utilization. That corresponds to what TCM described as Essence dissemination that the zSpleen transports water and essential nutrients around the body. TCM described that “the zSpleen with the stomach moves its fluids”[65]. The other way called nutrient redistribution is with the predominant part flowing through the portal circulation.

These nutrients that pass through the liver first go through metabolism, ascend upwards to the lung and is thereafter redistributed to the whole body. With all these, the zSpleen is said to govern transportation and transformation[8].

Another part of the complex, the spleen-intestine provides antigen-pathogen recognition and primary host defense mechanisms. Food provides antigens that body mechanisms may discriminate. The mucosal associated lymphatic tissues and intestinal lymphatics form one important functional group as sampling site, recognition vehicle and guarding modifier for food handling. Researches showed that the mucosal related guarding mechanism starts maturing as food (and microbes) are first introduced into the gut after birth. Food taken in should call for discrimination originating from the "self" in recognizing and eliminating non-self foreign matters. However, before birth, while its absorptive function is ready, the immunity apparatus of the intestine is still immature. At birth, while intestinal absorption gradually assumes full function, many more maturational changes occur in the immunity apparatus: increase in primary at-site lymphopoisis with germinal centers, and maturation of immunoglobulin specificity. In fact, polyclonal TCR ß-chain production becomes more oligoclonal and specific only after enteral feeds and microbial colonization[66]. Dietary compounds can affect the formation of postnatal lymphoid follicles[67]. Even in the matured gut, the "self" is constantly remodeled. At steady states it recognizes diverse dietary and bacterial antigens in promoting intestinal tissue homeostasis. The intestinal epithelium plays a role in the generation of immune responses through sampling of foreign antigens via Toll-like receptors TLRs, expressed by epithelial cells, and NOD-like receptors NLRs[68]. Epithelial M cells transfer particulate antigens from the lumen to the underlying immune cells in the lymphoid follicles. Dendritic cells (DCs), as the preeminent antigen-processing cells, present antigen to the immune system to activate both naive and memory T cells. They directly sense intestinal contents by extending their dendritic processes into the intestinal lumen. Also, these cells and macrophages in the subepithelial Peyer patches sense degraded luminal contents transcytosed by M cells. The dendritic cells take these immune messages to the intestinal mesenteric lymph nodes, then the immune system and the spleen. Immunologic memory is a feature of both T and B lymphoid cells. The host's immunologic history, its food antigens, viral, and microbial exposures may all affect the behavior of its sensors. Returned immune messages to the intestinal mucosa recognizing food and bacterial pathogens and antigens interact for further processing. Immunological reactors with cytokines, and chemokines, together with host and microbial metabolites are key molecular mediators of intestinal homeostasis.

The health of the intestinal mucosa affects general health. The cells of the gut epithelium (goblet cell, Paneth cell, M cell, enteroendocrine cell, and absorptive enterocyte), forming an essential mucosal barrier, are closely related to each other to preserve the mucosal digestive and guarding functions. TLR signaling in the intestinal epithelial compartment is crucially involved in the maintenance of intestinal homeostasis and tissue repair[69]. These signals also positively regulate the sampling of luminal contents by DCs of the underlying intestinal lamina propria[70]. Commensal floral interactions with TLRs have been shown to mediate tolerance to food antigens. For example, TLR4-dependent signals provided by the intestinal commensal flora inhibit the development of allergic responses to

food antigens[71]. Beyond the gut, apart from the general immune system, the spleen is involved[72,73]. Blood-borne cell precursors seed the spleen and develop into immature conventional DCs[74] which drive the adaptive immune response. Conventional DCs include both the lymphoid tissue-resident DCs and migratory DCs. In the intestine, TLR5 signaling activates these DCs in the lamina propria[75]. DCs are essential for expression and for stimulation of innate cells[76], and they activate immune cells like Th17 lymphocytes[77], a Th17 differentiation. These Th17 cells produce cytokines that stimulate mucosal antimicrobial defenses and tissue repair during an adaptive response. In short, TLR5 signaling stimulates the innate production of Th17-related cytokines by T cells in spleen and mucosa[76]. Also the DCs acquired properties in the lamina propria of the intestine and enhance conversion of regulatory T cells in the gut important for intestinal homeostasis. To note, this is dependent on TGF-β and retinoic acid, a vitamin A metabolite from food[78]. The protective mucosal response of sIgA production to stimuli is also dependent on the spleen. Thus intestinal mucosal homeostasis supported by the spleen is critical to preserve a healthy intestinal epithelial function. In zSpleen deficiency syndrome patients, the turnover rate of epithelial cells was hastened, showing a short life span, and inflammatory changes appear[79]. In those with disharmonic zLiver-Stomach type, even metaplasia may occur.

Externally the immune system interacts with the intestinal homeostasis with food and microbes. Internally, the nutrient and guarding functions contribute to protective or aggressive dynamics of the immune cells. In adaptive immunity, the Th17 lymphocytes are the main producers of Th17-related cytokines[77] which contribute to adaptive immunity in response to various inflammatory and infectious diseases[80]. Patients with zSpleen deficiency have T cell subset changes, with reduced total T cells and helper T cells but not regulatory T cells[81]. Symptoms of weak defense and immunological problems are prominent in zSpleen disorders. TCM describes the coupling of Ying (nutritious coalition as battalion) and Wei (defense traversing tissues)[56].

Another part of the complex, the stomach-intestine works in gut motility. In support of this functional zSpleen structure, internal neuro-endocrine mechanisms are closely linked. The enteric nervous system ENS is able to regulate such complex and diffuse motility functions by its vast network throughout the gastrointestinal tract. The ENS for gut movement consists of a continuous ganglionated plexus between the circular and longitudinal muscle layers of the muscularis propria, and a plexus in the submucosa, in the wall of the gastrointestinal tract. The gastrointestinal peristalsis consists of an ascending contraction and a descending relaxation that facilitate food bolus towards the anal end. In essence, the intestine directs food transportation, while the stomach affects the accepting capacity. These are inter-dependent, relying on the internal closely interactive mechanism as a series of physical, neural and hormonal messages between stomach and intestine.

On top of these structures, the ENS is connected to the central nervous system through axons in both directions, largely in the vagus nerve. More than 90% vagal fibers are afferent fibers, and the vagus functions mainly to initiate activity of the integrated circuits in the ENS rather than to coordinate gut function by direct signaling. The gastrointestinal hormonal secretions are coordinated with the vegetative neural system for gut movement. Motilin is released from M cells

of the duodenum and jejunum into the blood during fasting or interdigestive period to improve peristalsis in the small intestine, helping to clear out the gut in preparation for the next meal[82]. This 22 amino acids hormone is structurally related to ghrelin, which is secreted by the stomach and regulates gastric function limiting food intake by increasing satiety and affecting energy homeostasis[83,84]. Other mediators of satiety include glucagons like peptide-1(GLP-1) are mainly produced by intestinal L cells. PeptideYY_{3-36} which is released in response to a meal[85], reduces appetite and inhibits gastric motility, thereby increasing efficiency of digestion and nutrient absorption after a meal. PeptideYY neurons may also play a coordinating role through visceral, motor, and sympathetic output targets[86]. Cannabinoid receptors present in neurons and endocannabinoids synthesized in the gastrointestinal tract are modulated by feeding. The gastrointestinal hormonal secretions interacting with these neural receptors are modulated by feeding and nutritional status, and influence several important aspects of nutrient processing, including gastric secretion, gastric emptying, and intestinal motility[87]. These intricate inter-relatedness to facilitate smooth operational mechanisms influences the vegetative balance over the smooth muscles to assure smooth performance for function. Problems may manifest in zSpleen Qi deficiency with dyspepsia and in zSpleen Yang insufficiency with constipation.

The balance of upflow and downflow cycling movements affect the motility, secretory, assimilative, absorptive and transporting functions of the digestive tract, as well as the functional activities of the vegetative nervous system of the gut and the gut hormones. The distention or mucosal stimuli in the peristaltic reflex are relayed to sensory neurons to cholinergic interneurons. These are coupled to vasoactive intestinal peptide VIP and nitric oxide synthase NOS neurons caudad, as well as acetylcholine and tachykinin SP, SK neurons orad. Somatostatin, opioid, and γ-aminobutyric acid GABA neurons exert a modulatory influence on VIP and NOS neurons[88]. As they directly involve internal smooth muscle coordination, they contribute to the basal tone of internal structures. Thus the vegetative neural and hormonal environment would indirectly affect the general ascending and descending tone of the whole internal viscera. Intestinal VIP is reduced and SP increased in zSpleen deficiency rats[89]. TCM described that the body upflow and downflow related to the zSpleen-Stomach coupling would influence the whole body function. Poor synchrony[90] means poor internal health.

The internal closely interactive mechanism as a series of physical, neural and hormonal messages between stomach and intestine facilitate food transport towards the anal end. In the oral end, salivary alpha-analysis for salivary flow and amylase activity, a measure of endogenous adrenergic activity, can be a good marker of zSpleen deficiency[91] particulary after acid stimulation. Food handling needs be coordinated with the oral muscles. The ganghionated plexus extends from the top upper esophagus to the bottom anal sphincter. Secretomotor neurons in the small and large intestine also regulate water and electrolyte secretion, and in the stomach, stimulate acid secretion. It is notable that both digestive and guarding mechanisms for food start at the mouth. Dyspepsia behaviour is a form of gastrointestinal dyssynchrony. Self-guarded mechanisms against certain food can also cause dyspeptic behaviour. When compared to other supportive mechanisms not so dependably facilitated,

the close link of these mechanisms to the zSpleen structure as one functional complex can be appreciated.

In another perspective, the influence and interplay of food and microbes in the zSpleen complex affect the general body. Ghrelin secreted by stomach modulates body energy homeostasis, influencing the muscles, physique and development[82,87]. Food nutrients also support the whole body and limbs. While diet, e.g. a "Westernized" diet, may induce obesity and increase body fat deposition, the generation of obesity is also related to a change of intestinal microbiota, which if remaining unchanged as shown in mice, the obese phenotype would be protected from developing[92]. As over 90% of the phylogenetic types present in the gut microbiota belong to the Firmicutes and the Bacteroidetes divisions, the dramatic shift in microbiota composition with the reversal of the Bacteroidetes-Firmicutes ratio as seen in obese individuals indicates the substantial changes to the functional gut ecosystem. The obesity-associated microbiome harbors a substantial increase in genes encoding enzymes involved in the breakdown of dietary polysaccharides, related with increased capacity of the obese microbiome for energy extraction from the diet. Gordon[93] demonstrated that the gastrointestinal microbiota is directly involved in the regulation of energy homeostasis in both mice and man. This change in gut microbiota can be called a type of zSpleen dysfunction.

The skeletal muscles are particularly rich in mitochondria. Neuromuscular disorders like myasthenias, amyotrophic lateral sclerosis, and muscle atrophies are particularly responsive to treatment by tonifying zSpleen-stomach herbs[94-96]. In TCM words, the zSpleen influences the muscle and dominates the four limbs. Inadequacies are seen in zSpleen Deficiency Syndromes. Concoctions fortifying zSpleen improve muscles and their mitochondria in these patients[97].

The whole body function is also affected in fluid redistribution as food nutrients enter intestinal lymphatic and portal circulation. As portal blood enters lung circulation while lymphatic nutrients enters general circulation, they affect the general blood perfusion and lymphatic drainage circulatory pattern. Perfusion-drainage imbalance with bloatedness is quite common in zSpleen disorders. It is sometimes severe and can appear similar to gross edema. Diuretics usage may not be needed, since it is quite ameliorable with therapy that improves body quality and rid body of bloatedness by its better circulatory and lymphatic forces. The traditional view that lymphatic capillaries are passive channels needs to be challenged[98]. Thus while zSpleen governs transportation and transformation, it affects dampness recycling.

The fluid may be associated with waste metabolites as inflammatory materials. Locked in interstitium, channels and vessels, it is analogous to Damp-heat described in TCM. Dermatitis and eczema, is related to perfusion-drainage imbalance interlocked with inflammation. In dermatitis patients, swelling and bloatedness of varying degrees are common even in non-affected areas, suggesting lymphedema which are often underdiagnosed. Inflammatory disorders are particularly responsive to treatment, depending on acuteness, by mild or heavy purgation and which is commonly used in TCM therapies.

Inflammatory signals may arise with a dysfunctional mucosal immune system, as related to malfunction of the intestinal epithelial barrier, the specifically designated entry ports that allow controlled induction of food and microbial immune signals, cellular memory, and the vigilant spleen[99]. Really, it is estimated that

T cells associated with the small intestinal epithelium alone may account for more than 60% of the total body lymphocytes[100]. Faults in immune reactivity against intestinal flora or dietary antigen can lead to disease, inducing local and often also systemic inflammation[101]. At the signal of inflammation or injury in the body, the undifferentiated monocytes in the reservoir of the spleen would increase their motility, exit the spleen en masse, accumulate in injured tissue, and participate in wound healing. The spleen is a site for storage and rapid deployment of monocytes and splenic monocytes are a resource that the body exploits to regulate inflammation[102]. In animal models with zSpleen deficiency, there is evidence of microscopic damage in the spleen[103].

The spleen is highly related to platelet and immune cells. Vascular permeability is affected by chemokiness released by spleen. Changes in platelet sufficiency and immune cells also affect blood vessel wall integrity. These are also related to nutritional state and composition. When the degree of zSpleen deficiency progresses, the degree of anemia and low albuminemia would be related to immunological changes[104]. TCM physiology describes coupling between nutritive Coalition and the protective Defense, which serves also for internal protective mechanisms in the vessels. It may be said that through good nutrients and immunological competency, the zSpleen regulates and keeps blood circulating inside the blood vessels, or in TCM words, zSpleen rules and stabilizes Blood. In zSpleen deficiency associated with dysfunctional Blood-ruling, impaired platelet aggregation is seen in half of the cases[105]. This may be attributable to defective mitochondria which are rich in platelets[36]. Defective intestinal mucosal homeostasis seen in zSpleen dysfunction may also increase intestine epithelial breaks and inflammatory changes with associated microcirculatory reactions[106] which affect blood vessels in the whole body. TCM describes that zSpleen Qi deficiency may lead to loss of control and blood flows outside from vessels, with various hemorrhagic symptoms and diseases, such as chronic uterine bleeding.

Higher up, the internal neural and hormonal interactive mechanisms together with nutrients influence brain. The nutritious conglomerate of nutrients with a variety of composition that arrive at the brain promote ideas. Dietary tryptophan affects brains serotonin, essential oils are essential for the brain, and chocolates stimulate joy are examples. Proficiency in nutrients reduces thought apathy. TCM described that the zSpleen carries nutritive coalition, and Ying carries intentions, facilitating thoughts in mind. Neural adaptations with hormones determine programmed behaviour through specific hormone receptors in the brain. Health and strength in all these structures and internal mechanisms enhance brain nourishment.

In conclusion, the Zang Spleen can be perfectly expressed by a functional anatomical zSpleen, which anatomical mass is made up of the Spleen-Pancreas-Intestine Complex with the gastro-intestinal digestive system and lymphatics linking the vigilant spleen and intestines. Its functional expressions or external Zang Xiang is observed in the associated interactive components, with the pancreas-intestine, the spleen-intestine, and the stomach-intestine complexes interacting. The whole complex serves all functions described under traditional Zang Spleen:- to encounter food with digestion, related stomach functions, guarding interface, a lympho-circulatory transport system, and utilization of the assimilated essence for energy and vegetative balance, nourishment of brain

and muscles to cater for life. The internal support would be a host of neural, immunologic, endocrine, receptor mechanisms among others to achieve homeostasis and to cater for energy and life needs. Their action domain during food digestion and guarding may subserve the immunological homeostasis and body defense, energy metabolism including mitochondrial function, the influence on dynamics of the whole internal viscera, stabilizing blood in circulation, body fluid perfusion-drainage balance, muscle health, and idea formation and intention mechanisms to face life.

Functional Anatomical Zang Spleen, Evidence and Validation

Three main approaches stand out in past studies on Zangfu physiopathology: to review the original TCM classics on theory and applications, to expose TCM classical knowledge with modern interpretation and experimental proof and to research by clinical studies. The key is to keep them relevant to, and consistent with, the ancient texts and current usage in disease and therapy relating to zSpleen. This present model will be reviewed for its supporting evidences in contrast with the past model, a Pancreatic-gastro-intestinal Hypothalamic-Endocrine-Immunological network model[12], or a representation by mitochondria[107]. To note, the past models discuss immunological events as being associated rather than the consequence of the main structural complex.

I. Validating with ancient texts

To validate it, its meaning may be checked for consistency (True T/ False F) with ancient texts. To reduce comparing through the tremendous volume of many ancient texts, Nei Jing and Nan Jing may be used as the 'gold standard'. Two points are essential for any modern model (Table 1).

Table 1. Comparison of models with meaning in Nei Jing and Nan Jing (T: consistent, F: inconsistent)

	Nei Jing, and Nan Jing	Models A, B	Present Model
1. Zangs, solid zOrgans in contrast to Fu, hollow zViscera	T	(F)	T
2. Zang Spleen refers to matters around spleen-pancreas-intestine	T	(F)	T

Thus, the present model is sound and more acceptable as it is more consistent with its usage in Nei Jing and Nan Jing.

The next validation step is to check for any word "spleen" appearing throughout Nei Jing and Nan Jing. Taking aside its use in Spleen Meridians, any such word with context and meaning inconsistent with the current interpretation would be incongruent and treated as an outlier. The less the number of outliers, the more representative this model would be. Going through Nei Jing for incongruence, in time for example, one may come across "The zSpleen Qi traverse the mouth. A healthy zSpleen allows the mouth to discriminate all grains and crops"[108]. Here again can be justified by the

neuro-endocrinal receptor mechanisms depicted in the present zSpleen model. One may also come across "The zSpleen mainly directs defense"[109]. This is justified by the spleen-intestine immunological setup for body defense in the present model and not in past models. To go completely just through Nei Jing would need to be covered in another article. Similarly, after Nei Jing, one can validate the same with other ancient texts.

II. Supporting the model with pathophysiology understanding

One may go through the list of understanding in zSpleen pathophysiology in ancient texts, and see how the past model or the present model covers and comprehends better in attributing function or dysfunction to their components (+ present, – absent).

Table 2. Features (+ present, - absent) in models as related to pathophysiology in texts

	Models A, B	Present Model
1. The zSpleen governs transportation, transformation[8]	+	+
2. The zSpleen governs upflow of the clear[110]	+	+
3. Essence dissemination up to Lung[111]	+	+
4. The zSpleen opens through the mouth[112]	+	+
5. The zSpleen carries nutritive coalition, Ying[113]	+	+
6. Ying, the essence of nutrient granary[55]	+	+
7. Wei, the defense with nutrient granary[55]	(–)	+
8. Overeating damages the zSpleen[38]	(–)	+
9. The zSpleen mainly directs defense[109]	(–)	+
10. The Spleen rules Blood[114]	(–)	+
11. The Spleen packs Blood[4]	Indirect	+
12. Blood develops zSpleen[115]	Indirect	+
13. zSpleen and zStomach inside-out related[10]	+	+
14. Gastrointestinal epithelial health related to zSpleen[20]	+	+
15. Various dampness diseases with swelling and fullness zSpleen related[116]	Indirect	+
16. Damp-heat common in zSpleen dysfunction[62]	(–)	+
17. The zSpleen influences the muscles[117]	+	+
18. Muscle mitochondrial changes related to zSpleen deficiency[46]	+	+
19. The zSpleen dominates the four limbs[7]	+	+
20. Manifest as saliva in secretions[118]	+	+
21. Manifest as thoughts in mind[119]	+	+
22. As the origin of all metabolism vital to life[120]	+	+

Going through the list (Table 2), the present model is more plausible as it better explains more of the points listed. It portrays the Zang Xiang manifestations more comprehensively. The standard text described the zSpleen, governing transportation, transformation[8], governing upflow of the clear[110], with essence dissemination up to lung[111], carrying nutritive coalition, Ying[113], the essence of nutrient granary[55], with Wei as the defense with nutrient granary[55], ruling Blood[114], blood developing zSpleen[115], zSpleen and zStomach inside-out related[10], various dampness diseases with swelling and fullness zSpleen related[116], influencing the muscles[117], dominating the four limbs[7], manifesting as saliva in secretions[118], thoughts in mind[119] and as the origin of all metabolism vital to life[120]. Now there really is a Zang organ "situated internally.

Any future observations found as being enlightened by this model frame would further support its usefulness. For example, when peristaltic gut movements were found to contribute to upward lymph flow despite the low pressure in lymphatic[121], it further substantiates the importance of zSpleen Qi in perfusion-lymphatic balance, which imbalance causes bloatedness. It is noted that clinically the use of senna in a tiny dose 3mg. daily would reduce significantly within weeks bloatedness associated with zSpleen dysfunction[122]. Massage of the abdomen is also believed to improve bloatedness, all probably by the same peristaltic mechanism. Further demonstration of whole body perfusion-lymphatic balance to peristaltic up-down synchrony in man would lend support to this relationship. Also for this model, when it is noted that parenteral nutrition (not through mouth) rather than enteral feeding does not produce a protective defense immunological state[123,124], it further substantiates that immunologic state is related to food going through the gut processes depicted in this model. Besides, appetite disorders can be alleviated by the use of therapy on motility mechanisms. Other similar studies to illustrate the importance of zSpleen for health with better immunity, and studies to demonstrate the interactive function between the associated mechanisms of zSpleen would strengthen its validity. The degree of the closeness of the interactive links can be explored by the degree of smoothness in internal facilitation over that of other less linked mechanisms.

III. Validating with usage in disease therapy

Success with zSpleen therapies has been used as supporting evidence pointing to zSpleen dysfunction being treated (Table 3). Distinction should be made between diseases which are internationally categorized and zSpleen dysfunction, a body state which can be coexistent with various diseases.

Table 3. Effectiveness (+, –) on zSpleen dysfunction with therapy on model components

	Models A, B	Present Model
1. Regardless of disease types, their associated mitochondrial change related to zSpleen deficiency, can be remedied with zSpleen herbs.	+	+
2. Inflammatory problems associated with zSpleen disorders can be remedied with zSpleen herbs.	–	+

In diseases not related to gastrointestinal disorders, like uterine prolapse, macular retinitis, myasthenia, regardless of disease types, treatment of associated zSpleen dysfunction would help the diseases[12]. Here the present model would need much more experimental support. But it is here that the model should predict that, further study on therapy with quality food would strengthen the zSpleen and alleviate inflammation associated with zSpleen problems. Such therapies may consist of modulation in amount and food quality, and abstinence from spicy and highly flavoured food. For example, food modification is useful for relieving allergic dermatitis. Confirming these in future or lack of disconfirming evidence would support the present model. The finding of dietary manipulation (with cereal grains, diary products, yeast, citrus, and foods belonging to the nightshade family) in patients in certain forms of rheumatoid arthritis and ankylosing spondylitis, even without clear evidence of classic allergy, resulting in gradual mitigation of disease now may need not be ignored[125]. The model also can explain that Qi tonics like astragalus, ginseng and atractylodes are notably immune promoters and strengtheners. There are such supporting reports, scattered maybe due to the lack of the current zSpleen framework to guide.

Concluding Remarks

This approach by no means refutes scientific findings of previous workers. Previous compromise retains only the digestive mechanisms to achieve any necessary anatomico-functional coherence. This approach expands that concept with the anatomical base and internal interacting mechanisms into one coherent structural-functional complex. This is made possible by recognizing the importance that food processing requires transport, digestive as well as guarding mechanisms. This understanding helps in the formation of an entity with the densely placed components of a food transport unit closely tied with the network of internal neuroendocrine structures for motility support, and a food digestion unit closely tied with internal mechanisms of energy balance and intestinal mucosal homeostasis, immunological mechanisms supporting. The interplay of the components in the complex affects each other and the whole body in life.

I. Advantages of the present anatomico-functional model over previous models

1. It would be easier to understand that the ancient people referred to one piece of structure rather than grouping many disparate functional entities in a network.
2. This single structure supports functions including digestion, related stomach functions, food and microbe guarding interface, a lympho-circulatory transport system, and utilization of the assimilated essence for vegetative and energy balance for life. The internal support would be a host of neural, immunologic, endocrine, receptor mechanisms among others to achieve homeostasis and to cater for energy and life needs. Most if not all of the corresponding described functions of the zSpleen can be explained.
3. The motility, secretory, absorptive, assimilative and transporting functions of the digestive tract can be understood.
4. This structure now includes the anatomical spleen, which name is present in zSpleen itself. It has not been embraced in previous models.
5. Inclusion of intestinal immunological guarding mechanisms embraces defense mechanisms,

important to understand inflammatory disorders associated with zSpleen.

6. Understanding intestinal epithelial integrity as related to immunological homeostasis helps to understand inflammatory disorders associated with zSpleen.
7. The statement that "Ying is the essence of nutient granary….Wei is the defense with nutient granary", untouched by previous models, can now be better explained by taking the nutritive and vigilant properties for food in this model in account.
8. The physiology and pathology of the internal supportive complex of neural, immunologic, endocrine and receptor function can be used to explain the external manifestations of Zang organ networks and Zang Xiang features.
9. The statement that "the zSpleen mainly directs defense"[109], can be explained better with this model. This verse has seldom been quoted but in fact is contained in an important line in Neijing, where the essential main function of each Zang is stated. Another verse that reads "the zSpleen mainly directs defense, enabling it to encounter food"[126] becomes explicitly clear in the light of this model. Besides, this model explain better how imprudent "overeating damages the zSpleen"[55], for apart from the associated neuro-endocrinal disturbance, the change in intestinal homeostasis associated with change in gut bioflora related to imprudent food can how be related.
10. This model provides a match between anatomy and function of the Zang organ. This is more acceptable to modern science. This platform can pull ancient Zang concepts to modern medicine and will allow elaborations on zSpleen and diseases in plain words.

This anatomico-functional structural formation is an integrated system. It is richer in breadth and depth than former models. The anatomico-functional model would expand our framework to probe for more useful research and observations to understand and utilize the TCM concepts, and build TCM models based on scientific acceptable structures to elaborate ancient literature on health and diseases of zSpleen. The important past observations are retained while the present model offers a more stable comprehensible entity. This paper together with the similar paper on zKidney help to redefine Zang and Zang Xiang in terms of a functional structural complex as the internal Zang, with its Zang Xing manifestations expressed externally, and illustrate an approach applicable to understand all the five Zangs. This functional structural complex as the internal Zang may be viewed more succinctly as an "organ complex". Western medicine describes organs and systems, with the word organ meaning a fully differentiated structural and functional mass in one unit specialized for some particular function, and system meaning a related organ group interactive for some particular specialized function. In contrast, this "organ complex" means a cluster of organs packed together in one, being closely interactive for some related specialized function. Organ clustering could have phylogenetic origin in facilitating close interaction.

II. Help further understanding

Previous findings can now be re-interpreted with this model. Further studies should relate how treatment to strengthen the intestinal homeostasis and peristaltic synchrony would strengthen the zSpleen and alleviate zSpleen symptoms.

TCM classifies zSpleen dysfunction by its clinical symptom complex according to zSpleen

Yin (its material and structures), zSpleen Yang (its intrinsic energy and reserve), and zSpleen Qi (its propulsive and energy functions). Most of the zSpleen disorders can be understood by the upflow, circulating, and disseminating actions of the zSpleen Qi, as supported by the zSpleen Yang. In zSpleen deficiency, the diagnostic criteria in common are poor appetite, abdominal fullness after meal, loose bowel movements, and pale or sallow complexion, with symptoms of fatigue, asthenia, and wasted muscles. Deficiency disorders include zSpleen-Yang deficiency with added cold limbs, and fear of cold, zSpleen-Stomach-Yin deficiency with general wasting, a dry mouth and lips with a shrunken smooth and bare, red tongue, collapse of central or zSpleen Qi with down-bearing of organs, flaccidity, vertigo and blurred vision. Easy bleeding and bruises is referred as zSpleen not ruling circulation. Loss of appetite or epigastric upset with rapid hunger is attributable to zStomach diseases, while indigestion, abdominal distension after meals and loose stools are attributable to zSpleen diseases. In this comprehensive model, these classical syndromes of zSpleen dysfunction and symptom complexes could now be further delineated with modern anatomical structures and physiological mechanisms at those many interrelated levels. The intestinal epithelial integrity besides mitochondrial states can be useful markers. Inflammatory markers of the mucosal and body immune system may be correlated with the subtypes of zSpleen disorders. There may be correlated with digestive and gut motility indicators. Besides searching for biochemical or physiological markers, additional anatomical and physiological assessment should improve defining the different zSpleen dysfunction syndromes.

A diagnosis of zSpleen dysfunction would then, apart from the diagnostic label of zSpleen Yang, Yin, or Qi deficiency, comprise of the fuller diagnosis with the various levels of derangement specified. These may be at multiple levels including higher neuro-endocrinal axis, the target organs and peristaltic synchrony, the action sites like epithelial homeostasis, the food and microbes with its varying ecosystem, and the person's self-adjustable prudency behaviour.

All these may allow better clinical differentiation and application in treatment, with the Zang organ and Zangfu manifestation theory in concert with modern medicine. TCM therapy of zSpleen dysfunctions has been useful to treat gastrointestinal disorders, to support patients with muscular debilitation and in diseases with zSpleen deficiency like organ prolapse and energy disorders. Therapy in TCM is based on the clinical syndrome diagnosed. Other modules of treatment could then be explored and coordinated with herbal treatment for the type of zSpleen deficiency. These may be active or passive manipulative treatment with various forms of diets, particularly relating it to intestinal homeostasis. Developing tests for stability or facilitative cohesiveness of internal interactive mechanisms of zSpleen, including digestive, immunologic aspects on one hand and neuro-endocrinal aspects on the other hand, may develop good indices to measure zSpleen strength and how use of food, or neutraceuticals, including probiotics and vitamin A, may strengthen it. Therapy under the present model allows manipulation and treatment at the various levels. Understanding perfusion-drainage imbalance in relation to intestinal wave for up-down synchrony, how the up-down synchrony of intestinal wave affect neurohormonal states produce body upflow downflow balance, and relating intestinal immunity with vascular permeability would help to enhance understanding.

As zSpleen deficiency is a systemic disorder, dysfunction of vegetative nervous system of gastrointestinal tract coexists. The majority of zSplenic deficient patients with chronic diarrhea and peptic ulcer have an overactive parasympathetic nervous system. Through balancing the upflow and downflow cycling movements, the functional activities of vegetative nervous system can be restored to help other multi-organ disturbances. Moreover, as energy-expenditure discrepancy and imprudent diets should affect the coalition battalion towards defense, good diet mix may be worked out for prescription to improve immunity against diseases and inflammation.

The intestinal system has all along been seen as a digestive system. Only recently it has been understood to be well linked with immunological surveillance. Now it is established to be the important site for the development of a immunological ecological system for host interreacting with microbes. Chinese medicine somehow saw in ancient times that link between the gut and spleen. Recent advances have established the reciprocal interactions of the intestinal microbiota and immune system[127]. It consolidates the need for the concept that the whole system is meant for digesting and guarding. It should help future medicine to understand how taking food pattern could affect even the immunological development of the "self" for the person to protect himself and to match and tolerate his environment better. Chronic inflammatory disorders are often related to immunological mismatch. Starting with dietary deviations, the intestinal food and microbe ecological system may in time and in development become so mismatched that neuro-endocrinal and immunological adjustment along his own initially matched self integrity profile become problematic to face the environment. Imprudent food, or poor intestinal homeostasis from odd meal time and lifestyles, would affect the gut, or in other words, the organ cluster of the zSpleen, and in due course the body is inflicted with mismatch problems such as gastrointestinal motility disorders and chronic inflammatory disorders including dermatitis. Understanding the parts of zSpleen in this model helps understanding treatment of the related areas. It reemphasizes the TCM integral concept that zSpleen health affects all areas of the body.

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以解剖與功能關連結構重劃中醫脾臟模組

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本文以現代醫學理解的層面描繪傳統中醫學說中的 [脾] 臟。傳統中醫學說以「臟象學說」演繹臟腑，而過去數十年，現代研究中醫 [脾] 臟理論時，基於臟象與現代醫學的神經、內分泌及免疫系統功能的密切關係，提出把胰、腸、胃、自主中樞神經、內分泌及免疫組成網路功能來演繹 [脾] 臟。臟腑臟象被看為一組相互關聯的結構而不是獨立的器官，其後亦另外提出 [脾] 臟可被看作細胞線粒體般演繹。總之 [脾] 臟功能不能與其解剖結構作出聯繫，亦不涉及以其起名的器官「脾」。古代中醫的「脾」字使用亦當作不恰當，說其本身是胰臟。本文會重新審視 [脾] 臟，由其消化及能量代謝的層面切入，並研究「迎糧」的腸道淋巴及免疫反應機能，具體把中醫 [脾] 臟的結構與功能互相連結，終將人體迎接食糧的整體功能結構、脾臟胰臟腸胃一體、包括消化系統及腸道相關淋巴組織至脾器官的免疫機組，視為「居於內」的 [脾] 臟。至於接受及防備食物的結構功能，包括 (1) 消化代謝、胃功能、衛護界面、淋巴液循環運轉系統及營養應用運化、能量代謝平衡調節、滋養肌肉、腦部及意識來應付生命，配上 (2) 腸胃及全身神經及內分泌的互動緊密機制，影響內臟動力、穩定血管流注、身體內水液灌流排液平衡、免疫持平、身體防禦等機能，則視為「觀於外」的 [脾] 臟臟象。這 [脾] 臟範式與中醫學的脾臟本質意義相距不遠，但比過去的模式更為貼切，能成全主流基本要求標準，因其中解剖與生理的密切關連。因此，這模型比起過去的理論模型，較易為現代科學的同儕所認受，其中提出臟器群的特色可供主流醫學參考。本文亦介紹古籍及現代研究複證的方法，有助於中西醫學發展，並帶來獨特及具啟發性的看法。

關鍵字：中醫脾臟、臟象、功能解剖結構、臟器群、現代醫學

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