

# On the pathogenesis characteristics of chronic atrophic gastritis from the perspective of deficiency, stagnation and blood stasis

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**Abstract:** Chronic atrophic gastritis (CAG) is a digestive system disease with a high prevalence and a high cancer rate developed by a combination of factors. Its pathogenesis is complex. There is currently no exact name of the disease in traditional Chinese medicine and modern medicine also lacks excellent treatments. Therefore, it is very important to explore the etiology and pathogenesis of CAG, understand its prognosis and prognosis, and prevent cancer. Based on ancient books and classics and researches on CAG in recent years, this paper summarizes the pathogenesis of this disease as "deficiency", "stagnation" and "blood stasis", in order to provide a theoretical basis for the comprehensive clinical treatment of CAG.

**Keywords:** chronic atrophic gastritis; etiology and pathogenesis; deficiency; stagnation; blood stasis

## 1. Introduction

Chronic atrophic gastritis (CAG) is a common digestive disease, and histology is mainly characterized by the reduction or even disappearance of the glands propria of the gastric mucosa caused by inflammatory cell infiltration. Globally, the incidence of CAG is high, with a prevalence of 23.9% in the general population using serological testing; With pathological biopsy, the prevalence is 33.4% [1]. With the change of social environment and dietary structure, the prevalence and malignant transformation rate of CAG have increased year by year, but there is still a lack of standardized and effective clinical treatment options. Based on this, it is of great significance to fully grasp the etiology and pathogenesis of CAG and timely and effective intervention and treatment to prevent cancer.

The pathogenesis of CAG is complex and there are many causes, which has attracted the attention of countless clinical researchers. Western medical studies have confirmed that the occurrence of CAG is often related to HP infection, dietary stimulation, alcoholism, history of NSAID taking and autoimmunity, etc, and its essence is similar to exogenous evil, improper diet, and long-term body deficiency in Chinese medicine theory, Therefore, this paper intends to elaborate the pathogenesis characteristics of CAG from the perspective of integrated traditional Chinese and Western medicine.

## 2. An overview of the understanding of CAG in Chinese and Western medicine

There is no name for CAG in traditional medicine, but the common symptoms such as stomach pain and fullness, noisiness and acid reflux, nausea and vomiting, etc, are in line with the ancient doctors' discussion of "epigastric pain", "gastric ruffian", "vomiting" and "noisiness" and other diseases. The relevant records of this disease can be traced back Huangdi Neijing, Ling Shu said "Stomach disease, abdominal distention, epigastric pain", Plain Question mentioned that "Cold qi in the stomach, and cold limbs, so pain causes vomiting." All of the above shows that the basic pathogenesis of stomach diseases are caused by middle warmer qi activity block, dysfunction of ascending and descending of spleen-stomach qi. Ancient physicians attributed the cause of this disease to improper diet, irregular living, irregular mood, emotional maladjustment body deficiency-oriented and evil qi. The detailed discussion laid the foundation for the development of spleen and stomach disease treatment in later generations.

Western medicine divides CAG into multifocal atrophic gastritis (type B atrophic gastritis) and autoimmune atrophic gastritis (type A atrophic gastritis) [2], the former is more common in the antrum

and has a multifocal distribution, and the latter is related to the autoimmune matrix. The onset of the disease is insidious and most patients have no obvious symptoms, symptomatic patients are often manifested as irregular epigastric pain, fullness, acid reflux heartburn, belching hiccups, nausea and vomiting and other dyspeptic symptoms, microscopic manifestations are mainly reflected as gray-white granular or nodular gastric mucosa, often accompanied by vascular exposure and erosion, but the severity of the patient's symptoms and microscopic pathological changes are not clearly correlated. Western medicine research is mainly related to gastric microcirculation function, gastric mucosal damage repair mechanism, precancerous lesion prevention, dietary environment and host factors, which happens to have a very high similarity with the traditional Chinese medicine(TCM) pathogenesis of this disease "deficiency", "stagnation" and "blood stasis".

### 3. Pathogenesis characteristics of CAG

#### 3.1 Deficiency

The spleen and stomach are the source of blood biochemical which are acquired. They are also known as the official of the granary, and have the function of receiving and transporting water valleys. Such as the opinion that "drink into the stomach, overflow the essence, infuse the spleen, disperse the spleen, blong to the lungs, regulate the waterway, infuse the bladder, water nymph scattered, and the five classics are parallel..." originates from Plain Questions. Under physiological conditions, the spleen and stomach have sufficient qi and blood to normally rotten and polished food, and the spleen's transmission and dispersal of fine substances such as essence, qi, blood, and fluid are basically guaranteed. If the congenital endowment is insufficient, the body, spleen and stomach are deficient, the source of qi and blood is lacking in biochemistry, and the middle warmer is unable to promote nutrition throughout the body. Manifested as epigastric discomfort, fatigue, short breath, lazy words, muscle wasting, etc. As Puji Fang mentioned that "those who work weakly, their qi and blood are weak, and their honor and guard are insufficient... Therefore, the splenogastric qi is stuffed and gastric distention"; On the other hand, because of dysfunction of spleen, the qi is not full, and it is difficult to fix the blood, so that the blood travels outside the vein. Shen Mingzong of the Qing Dynasty said in Jin Gui Brief Notes: "The blood of five-internal sixorgans depends on controlling of splenic qi", if the stomach is deprived of blood for a long time, the gastric mucosa gradually thins or even shrinks, which is reflected in the pale face and so on. Modern studies [3] have found that rats with splenasthenic syndrome have symptoms such as loss of appetite and mental malaise during the modeling process, which is similar to the clinical manifestations of CAG spleen-stomach deficiency syndrome, and the pathology is manifested as gastric mucosal atrophy and thinning, mucosal microvascular damage; Cheng Ruodong [4] studied the TCM types pattern of CAG and PLGC based on the logistic regression model, and the results showed that splenasthenic syndrome was mostly present in 1056 patients with CAG precancerous lesions, and this type was closely related to pathological manifestations such as gastric mucosal atrophy and intestinal metaplasia; Zhu Fangshi [5] collected 9995 CAG cases and analyzed the composition ratio of medical evidence types, and found that the pathogenesis of 6 common clinical types of CAG was still spleen and stomach weakness. The Theory of Spleen and Stomach said that "the abundance of vitality is not harmed by the qi of the spleen and stomach, and then it can nourish the vitality. If the qi of the stomach is weak, and the diet is doubled, then the spleen and stomach are injured, and the vitality cannot be filled, and the cause of all diseases is also born", Therefore, Chinese medicine advocates that people with physical weakness should have a regular daily life, regulate cold and temperature, prevent six sexual immoralities, exercise diligently, and strengthen their physique.

CAG is a chronic disease, patients with long-term illness are often accompanied by anemia, shortness of breath, fatigue and other symptoms, microscopic manifestations of gastric mucosal edema, pallor, vascular texture exposure [6], which is essentially consistent with the so-called "deficiency" in Chinese medicine, which may be related to the autoimmune process that destroys the acid-producing mucosa. When the gastric mucosa atrophy and metaplasia, the reduction or disappearance of parietal cells will lead to too little gastric acid and lack of intrinsic factors, while bacteria multiply in the stomach not only produce nitrite and promote carcinogenesis, but also lead to terminal ileal cobalamin malabsorption, which in turn causes megaloblastic pernicious anemia, and pernicious anemia lacking cobalamin is the hematological manifestation of CAG in the terminal stage of autoimmune gastritis [7]. The exact mechanism of this condition is unknown, but studies have found that it may be caused by a range of autoimmune phenomena and is often associated with other primary autoimmune diseases [8]. Iron deficiency anaemia is also a common manifestation of autoimmune atrophic gastritis and is likely to precede pernicious anemia. Based on Faber's observations more than a century ago [9], Hershko et al.

conducted a series of prospective studies in patients with iron deficiency anemia, showing that 40 out of 150 patients (27%) had CAG<sup>[10]</sup>. Another study found that 83 (52%) of 160 patients with autoimmune atrophic gastritis showed iron deficiency anemia<sup>[11]</sup>, suggesting that iron deficiency anemia may be the most common hematologic manifestation of CAG, which perfectly explains the patient-related symptoms. The causes of CAG are often rarely linked to autoimmune aspects, so it is important to re-identify and treat autoimmune gastritis.

### 3.2 Stagnation

Shuo Wen Jie Zi said: "Stagnation, condensation". It is explained that stagnation is condensation, aggregation, poor flow, not fluency, in line with the food accumulation, qi stagnation, evil gathering and other aspects mentioned in Chinese medicine theory. Ye Tianshi's Clinical Evidence Guide Medical Case mentions: "If the spleen should rise, it will be healthy, and the stomach should be lowered." The spleen lord rises clear, the stomach lord descends turbidity, the spleen and stomach cooperate with each other, and the water valley goes down, there is no congestion and blockage. If the spleen and stomach are uncoordinated and the valley is not transported, it will lead to a variety of stasis diseases.

#### 3.2.1 Diet and CAG

The spleen belongs to Taiyin and wet soil, likes dryness and dislikes wetness, and wetness is Taiyin earthy qi, and obscenity is very easy to attack the spleen and stomach; the stomach belongs to Yangming and dry soil, likeing to moisturize and irritable, and dry heat can damage the spleen and stomach fluid. The spleen and stomach help each other, and the evil qi suffer from each other and fights each other, which is more prone to wet heat production, and stomach diseases arise. This disease often comes from the mouth, if the diet is spicy, greasy, excessive wine and meat, and the overnight food is stagnant in the stomach, it is easy to produce phlegmatic hygrois and hot, inhibit the medium warmer machine, and produce abdominal pain, bloating, noisy and other symptoms, such as Lan Chamber Secret said "The person who anoints the sorghum, the humid heat is depressed inside and becomes full"; The True Story of Medicine said "The cause of the disease is mostly from indulgence in the mouth and stomach, like bitterness, drinking hot wine and frying... So stomach pain". As early as Huangdi Neijing's inner scripture, it was mentioned that dietary inadequacy was the most common factor in internal injuries. All this illustrates the importance of dietary stasis in the development of CAG.

Western medicine has also found in the study of this disease that the SLC39A11 polymorphism in the zinc transporter gene ZIP11 is related to chronic gastritis, and is affected by eating spicy food<sup>[12]</sup>, and the higher the intake of spicy food, the more it affects the function of zinc carrier against oxidation and apoptosis of gastrointestinal cells. In addition to genetic differences, factors such as diet or nutrition are important components of the gastric environment, and intake of fruits or vegetables rich in vitamin C, folate, carotenoids, and green tea can prevent gastric cancer<sup>[13-15]</sup>. Conversely, a high intake of lean meat, processed meat, salt, and salt, and metal content of preserved foods increases the risk of cancer<sup>[16-17]</sup>. In addition, based on the study of Shinozaki<sup>[18]</sup>, it was found that a long-term high-protein diet can inhibit the gastric atrophy of Mongolian gerbils infected with *Helicobacter pylori* and prevent CAG by promoting acid secretion. Therefore, it is recommended that CAG patients eat small and frequent meals daily, eat light and soft, eat slowly, and mainly focus on high-calorie, low-fat, and low-fiber foods.

#### 3.2.2 Emotions and CAG

Emotional factors are also the key to stomach discomfort. The main drainage of the liver promotes the mobilization of the spleen and stomach, Danxi Xinfu said: "All depression is in the middle warmer", so liver dysfunction will produce spleen and stomach diseases. If the mood is low and easy to be irritated, the liver wood is too hyperactive, restricting the spleen and stomach, and the qi is not declared; Or all day depressed that injured medium warmer, stomach loss of harmony, movement disorders, qi congestion, those all will cause stagnation of qi, the symptoms will be stagnation of the abdomen, belching, chest and flank fullness, upset and irritability, good and too rest, etc. Qi "depression" is actually qi "stagnation", qi is the root of people which is smooth and accessible, liver depressed long time will cause hot and fire, in addition to seeing red eyes, bitter mouth, tongue infrared, stomach body without fluid moist, easy to produce atrophy, thus developing into CAG.

In Chinese medicine, depression is often called emotional disorder, and in Western medicine, it is manifested as symptoms of mental and psychological factors. If the body is in a state of anxiety and depression for a long time, it will cause gastrointestinal dysfunction, and the mechanism is that increased secretion of motilin may cause reflux of gastric contents, causing damage to the mucosa of the digestive tract, resulting in chronic inflammation<sup>[19]</sup>. Studies have shown<sup>[20]</sup> that the onset of CAG is often closely

related to environmental, social and psychological factors, and patients have a series of psychological symptoms such as low mood, anxiety and even depression due to lack of full understanding of the disease and fear of cancer, in addition to physical symptoms such as stomach fullness and pain. This mental state acts on the body at the same time, resulting in abnormal organ function with qi disorder, many changes, and the disease is difficult to heal.

### 3.2.3 HP infection and CAG

Traditional Chinese medicine often says that "where evil is gathered, its qi will be empty", which shows the damaging effect of "evil" on the body. "Evil" can be extended to "poisonous evil", "poisonous evil" is rich in connotation including foreign poisons such as furuncle poison, harsh poison, warm poison, filthy poison, etc, internal poison such as ambush poison, stasis poison, phlegm poison, dirty poison, etc, and the occurrence of CAG is mainly caused by infecting damp-heat toxin. Damp-heat toxin, mostly through the mouth in the gastrointestinal tract, hidden as harm, and its appearance depends on damp pathogen, wet sticky heavy, long-term choreography heat, humid heat beat, easy to block gastrointestinal blood tract and qi, damage the stomach body, so that it loses nourishment, and gradually atrophies. This is similar to the pathogenic characteristics of HP, first, HP as an external sensation of evil, mostly by ingestion; Second, HP infection often causes erosion and exudation of the gastric mucosa, mainly red, which is in line with the fiery nature of humidity, heat, poison, and evil; Third, HP should not be eradicated, attached to the mucosa, and difficult to heal. Moreover, Hp infection is mostly yin asthenia, humid heat<sup>[21]</sup>, wet essence is heavy turbidity and tangible evil, easy to gather in the meridian blood network, obstruct the qi; The fiery evil fries and burns the liquid, consumes the yin qi, and the two combine into poisonous evil, eroding the stomach body, causing ulceration and atrophy, and even becoming a disease. This basically confirms that there is a certain connection between HP and humid heat poison. HP infection is not only a common pathogen of CAG, but also one of the driving factors of carcinogenesis<sup>[22]</sup>. Studies have proved<sup>[23]</sup> that due to the proliferation of Hp and long-term invasion of the stomach, the resulting inflammatory response will seriously damage the gastric mucosal tissue, causing mucosal atrophy. In addition, Hp infection accelerates the transformation of gastric precancerous lesions into gastric cancer to a certain extent<sup>[24]</sup>. Therefore, eradication of Hp can improve the state of gastric mucosa, effectively alleviate the progression of CAG and prevent the occurrence of gastric cancer, and effectively link the theory of humid heat and poison in traditional Chinese medicine with the mechanism of HP infection in Western medicine, which is more conducive to the treatment of CAG.

### 3.3 Blood stasis

Traditional Chinese medicine has the saying of "long-term illness must stasis", and CAG is a chronic disease, which does not heal for a long time, evil qi enters the stomach, the airway is not open, the blood network is damaged, and it is easy to make turbid poisonous septic blood accumulate, often manifested as stomach pain like knife cutting or needle pricking, or vomiting blood, black stool, purple stasis of the tongue, sublingual veins are tortuous, such as Yi Lin Gai Cuo: "Where abdominal pain, always does not shift, is bruising". Secondly, the spleen and stomach are Yangming more qi and blood that can easier block qi and blood than other organs, if the spleen can not control blood, suffering heat or cold are easy to make blood stagnation, so congestion is a pathological product of CAG development to the later stage, on the contrary, it can also become its causative factor. In addition, if the spleen and stomach qi and blood are insufficient for a long time, the veins are lost in nourishment, the wind of the evil is easy to invade, and the evil poison is easy to attach, so that the internal organs are lost, the pathological products in the body can not be discharged in time, the tendons and muscles are accumulated, at last the gastric mucosal glands can be atrophied, intestinal and even intraepithelial neoplasia. Treatise On Blood Patterns: "All incurable diseases are always caused by bad stasis." Therefore, CAG treatment from the treatment of "blood stasis" not only inherits the wisdom of ancient sages, but also conforms to the effectiveness of clinical medicine.

Modern medical research has also found that the blood flow of the gastric mucosa determines the ability of the stomach to resist injury, and the blood flow of CAG patients is generally in a viscous state, which is consistent with the "blood stasis" of traditional Chinese medicine. Ischemic hypoxia status of the gastric mucosa is associated with local microcirculation disorders, which are important early targets for the pathogenesis of acute gastric mucosal injury caused by NSAID, ethanol, hydrochloric acid, and stress<sup>[25]</sup>. If microvessels are damaged leading to rupture, plasma leakage, extravasation of red blood cells, platelet adhesion, or fibrin deposition, this can lead to stasis of blood vessels. On the other hand, in the study of Chiou, S.K. et al., the prominent role of Survivin protein in the gastric mucosal defense mechanism was demonstrated - inhibition of apoptosis, and the expression level in gastric mucosal epithelial cells directly exposed to destructive substances such as acid and NASID was much higher than

in gastric microvascular endothelial cells, and this expression pattern and the existing anti-apoptosis function of survivin protein itself protected the integrity of the gastric mucosa and avoided gastric mucosal damage [26-28]. Based on this, Western medicine treatment often starts from improving gastric microcirculation, protecting gastric mucosa, and eliminating inflammation.

As mentioned above, CAG disease to the late stage of poisonous evil, easy to become cancerous, the development process can be roughly summarized as "spleen and stomach weakness→ qi, food, humidity, heat, evil accumulation→ septic stasis→ turbid poison diffusion→ evil qi flourishing and asthenia of healthy energy ", which is consistent with the development model of gastric carcinoma (GC) - "superficial gastritis→ atrophic gastritis→ intestinal metaplasia and dysplasia →GC", obviously, the CAG stage can be called the precancerous stage If at this time, the characteristics of its key etiology and pathogenesis can be grasped " deficiency", "stagnation" and "blood stasis", and the individual differences of different patients in different environments are "symptomatic", it can slow down cancer and prolong the disease.

#### 4. Conclusion

CAG as a chronic disease, slow onset, long course, in line with the characteristics of most chronic diseases, this paper through a simple combing of the etiology of CAG, summarize the basic pathogenesis of the disease as " deficiency", "stagnation" and "blood stasis", and at the same time combined with Western medicine on the pathogenesis of CAG and find out the similarities. This leads to a more comprehensive understanding of the disease, hope to be used as an innovative point to provide some guidance for clinical work.

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