

# *Study on the pathogenesis and treatment of carotid atherosclerosis from “phlegm, blood stasis and toxicity”*

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**Abstract:** Carotid atherosclerosis is an independent risk factor for the occurrence of ischemic stroke, posing a serious threat to human health. Although modern medicine has achieved some success in the treatment of plaque, there are problems such as large side effects and high recurrence rate. According to the characteristics of carotid atherosclerosis, this paper discusses the etiology and pathogenesis of carotid atherosclerosis in traditional Chinese medicine, and concludes that "phlegm", "blood stasis", and "toxicity" run through the development of atherosclerotic diseases, and that "phlegm", "blood stasis", and "toxicity" are always present. It is believed that "phlegm", "blood stasis" and "toxicity" run through the development of atherosclerosis, and "phlegm, blood stasis and toxicity" is the core mechanism of the disease. In clinical treatment, "resolving phlegm and expelling stasis, detoxifying and clearing the veins" should be the main focus. The prevention and treatment of carotid atherosclerosis based on the theory of "phlegm, blood stasis and toxicity inter-conjugation" provides new ideas and methods for Chinese medicine to prevent and treat carotid atherosclerosis and its complications.

## 1. Introduction

Atherosclerosis (AS) is a progressive vascular disease characterized by the accumulation of lipids and inflammatory cells in the walls of medium and large arteries, and is the main pathological basis of common vascular diseases such as coronary heart disease, cerebral infarction, and disabling peripheral vascular diseases<sup>[1]</sup>. The carotid artery is the most frequently involved part of atherosclerosis because of its physiological and structural characteristics. The carotid artery is one of the main blood vessels supplying the brain, as it is mainly responsible for transporting blood from the heart to the head, face and neck. Because of its superficial location and easy to detect, the carotid artery can be used as a "window" to reflect the status of atherosclerosis throughout the body<sup>[2]</sup>. The findings of various studies have consistently demonstrated that carotid atherosclerosis serves as an autonomous risk factor for cerebrovascular disease<sup>[3]</sup>. Contemporary medical research posits that once atherosclerosis induces damage to the target organs, its reversal becomes arduous. Consequently, the prevention and treatment of carotid atherosclerosis have emerged as focal points in both traditional Chinese medicine (TCM) and Western medicine investigations.

CAS is a modern medical name, and there is no direct record of it in the ancient TCM texts. In view of its lesion site in the blood vessels, it can be categorized as "vessel bi" <sup>[4]</sup>. According to "Suwen", the core mechanism of "vessel bi" is the stagnation of blood. Modern medical research reveals that the main pathological features of CAS are carotid artery intima-media thickening, plaque formation, resulting in obstruction of blood flow, which is consistent with the pathogenesis of "vessel bi" in TCM <sup>[5]</sup>. Combined with clinical practice, modern Chinese medicine scholars believe that CAS is closely related to phlegm, blood stasis and toxin, and that "phlegm, blood stasis and toxin are intertwined" is the core mechanism for the formation and development of the disease. Therefore, this paper discusses the pathogenesis of carotid CAS from the perspective of "phlegm, blood stasis and toxin" to provide reference for its clinical treatment.

## 2. Theoretical discussion

### 2.1 The relationship between "Phlegm" and CAS

Phlegm is a pathological product formed by the malfunction of the body fluid due to gasification, and it can also be used as a pathogenic factor to cause various diseases. Phlegm can be divided into "tangible phlegm" and "intangible phlegm". The "tangible phlegm" refers to the pathological products that are produced in the lungs and stomach and can be expelled from the body, mostly referring to the phlegm that is clinically called "sputum". The "invisible phlegm" refers to the disorder of internal organs, disharmony of qi and blood, fluid stagnation of pathological products, stagnation in the chest and diaphragm, meridians, internal organs, and other parts of the body <sup>[6]</sup>. The disease of phlegm is mainly attributed to the lung, spleen and kidney. Lung, spleen and kidney organ dysfunction, fluid metabolism is the key to phlegm. As the "source of all diseases," said: "phlegm drink, by the qi blockage, fluid can not be, water and drink gas stop in the chest and intestines, knot in phlegm," pointing out that the formation of phlegm is mainly caused by the water and drink stop and collection <sup>[7]</sup>. External evil attack, emotional disorders, dietary disorders, old age and frailty can lead to visceral dysfunction, water metabolism obstacles and the formation of phlegm, phlegm and drink can be used as a pathological factor, further blocking the qi and blood operation, affecting the metabolism of water, resulting in stagnation of the vein tract, the operation of poor and the development of vein paralysis. Chinese medicine believes that phlegm is the key link in the pathogenesis of CAS, and the occurrence and development of CAS are closely related to "phlegm", which contains the development law from "invisible phlegm" to "visible phlegm".

Modern medical researches show that the formation mechanism of CAS is closely related to the lipid infiltration theory, which suggests that the development of CAS is related to lipid deposits in the vessel wall. These lipid deposits are mainly low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C), which are deposited and oxidized in the vessel wall to form oxidized low-density lipoprotein cholesterol (ox-LDL-C), which further stimulates the proliferation and migration of smooth muscle cells in the vessel wall. These smooth muscle cells form foam cells within the vessel wall, which in turn secrete a variety of growth factors and cytokines that promote the proliferation and migration of vascular smooth muscle cells, ultimately leading to the formation of CAS<sup>[8]</sup>. This is consistent with the "phlegm opacity causes disease" theory in Chinese medicine. Numerous studies have shown that the use of phlegmolytic drugs can be anti-atherosclerotic. In clinical practice, treatment with formulas that dissolve phlegm and dispel opacity can significantly improve the extent of carotid atherosclerotic plaques. The mechanism of this treatment may be related to the enhancement of the lipid-lowering effect, the reduction of the degree of inflammatory response and the level of oxidative stress<sup>[9]</sup>. The results of several animal experiments have shown that the Anti-Phlegm Soup has a significant hypolipidemic effect, improves the antioxidative stress ability and inhibits inflammatory factors, thus exerting anti-atherosclerotic effects<sup>[10]</sup>.

## 2.2 The relationship between "Stasis" and CAS

Blood stasis is a pathological product caused by poor blood circulation or stagnation of the blood channels. This blood congestion not only exists as a pathological product, but can also be one of the causes of blood congestion because it can block the channels. According to the description of "Suwen - Paralysis Essay", paralysis lies in the veins when blood is condensed and does not flow, which suggests that stasis and obstruction of vein channels and blood coagulation are the key pathogenic mechanisms for the onset of vein paralysis <sup>[11]</sup>.

From the perspective of modern medicine, the biochemical basis of blood stasis syndrome includes abnormal blood rheology, impaired blood circulation, and changes in the physical and chemical properties of blood. These changes manifest as increased blood viscosity, increased platelet aggregation, and decreased red blood cell deformability, etc. Furthermore, modern medical research has also found that plaque and thrombosis are the major pathological changes of carotid atherosclerosis, and this pathological process has similarities with the Chinese medicine theory of "blood stasis causes disease". Wang Chunye <sup>[12]</sup> and his team conducted an in-depth and comprehensive study and analysis of modern literature on AS, and found that blood stasis was the most common TCM evidence, accounting for 74.13% of the total number of cases. In addition, a large number of studies have shown that blood stasis activating Chinese medicines have a variety of pharmacological effects, such as lipid regulation, anti-inflammation, antioxidant, endothelial protection, etc <sup>[13-14]</sup>. These effects can effectively inhibit the occurrence and development of CAS. For example, blood-activating and congestion-eliminating traditional Chinese medicines can regulate blood lipid levels, lower blood cholesterol and triglycerides, and thus reduce lipid deposition in the blood vessel wall; in addition, these medicines have anti-inflammatory effects, which can reduce the vascular inflammatory response and inhibit the development of atherosclerosis. At the same time, blood-activating and congestion-dissolving TCM can also act as antioxidants, scavenging free radicals and protecting endothelial cells of blood vessels, thereby preventing vascular damage and the occurrence of CAS.

In summary, blood stasis is a significant pathological factor in the development of CAS. One of the essential methods to treat this disease is by activating blood circulation and removing blood stasis.

## 2.3 The relationship between "Toxicity" and CAS

The term 'poison' encompasses all pathogenic factors that significantly harm the structure and function of the body. According to JinGuiYaoLueXi Dian, poison is formed due to the stagnation of evil qi, which is not resolved <sup>[15]</sup>. It can be seen that poison covers a wide range, the ancients believe that all harmful substances can be attributed to the category of poison. According to its different sources, divided into "endogenous poison" and "foreign poison". Internal toxicity mainly refers to the body's metabolic wastes and undesirable substances, such as phlegm, blood stasis, etc. In addition, modern medical doctors innovatively put forward the concept of CAS-related internal toxicity, such as "lipotoxicity, glucotoxicity," etc. <sup>[16]</sup>. External toxins are mostly caused by improper Qi of the time of the day, or contact with daily life, or invasion of the human body due to trauma and infection; modern medical practitioners have also combined with the modern etiological understanding to put forward the concept of external toxins related to carotid artery atherosclerosis, such as cigarette smoke, turbid toxins, and exogenous evil toxins. Whether "wind, cold, heat, fire" outside the evil, or "phlegm, stasis, deficiency" and other internal evil, long accumulated in the body can become poison. External and internal poisons are causative of each other, influencing and promoting each other. These poisonous factors will cause damage to the human body, resulting in poor blood circulation, stasis and damage to the veins, which in turn triggers CAS.

Western medicine believes that the pathogenesis of carotid atherosclerosis is mainly due to

dyslipidemia, hypertension, diabetes and other factors lead to damage to the endothelial cells of the blood vessels, cholesterol and other substances in the blood vessels to form plaques, which in turn triggers the narrowing of blood vessels, blood flow obstruction and other symptoms. At the same time, smoking also causes damage to the endothelial cells of blood vessels and promotes the formation of plaques. This series of factors that promote the formation of carotid atherosclerosis can all belong to the category of "poisonous evil".

### 3. "Phlegm, Blood Stasis and Toxicity" are the main pathologies of CAS

Phlegm, stasis, and toxicity are not only the pathological products of internal organ dysfunction but also the pathogenic factors of carotid atherosclerosis. Carotid atherosclerosis caused by phlegm and stasis is the result of phlegm poison and stasis poison. This means that phlegm and stasis are generated within the carotid atherosclerosis, intertwined with each other, and adhere for a long time, resulting in the disease mechanism of evil poison. Toxicity is believed to be the primary cause of CAS progression and deterioration. The main pathogenetic mechanism for the occurrence of CAS is the blockage and damage of veins by phlegm, stasis, and toxicity, leading to stasis of the veins over a long period of time<sup>[17]</sup>.

Diseases of the human body involve the proper functioning of qi, blood, and bodily fluids. Pathological products such as phlegm and blood stasis can result from the malfunctioning of blood and fluid. Phlegm and blood stasis have the same origin and can affect each other. The term 'same origin of fluid and blood' refers to their common origin in the spleen and stomach. According to Tang Rongchuan, a renowned doctor from the end of the Qing Dynasty, 'blood stasis' and 'phlegm' are two distinct manifestations of the disease of blood and fluids. However, since physiological blood and fluids have the same origin, they will inevitably lead to pathological phlegm and stagnation of each other. In his Treatise on Blood Evidence, Tang Rongchuan pointed out that 'the accumulation of phlegm and water stasis, phlegm and blood stasis intertwine with each other to form a nest.' The concept of 'all phlegm' is described as the origin of all diseases. According to the author, phlegm is congested by the blood, agglomerates due to drinking water, and does not dissipate, leading to stasis. Conversely, stasis can also be embedded in phlegm and dampness. It is important to note that this explanation is based on subjective evaluations and should be clearly marked as such. Carotid atherosclerosis is caused by a variety of internal and external factors that lead to visceral dysfunction. This dysfunction can cause phlegm, blood stasis, and other internal issues that can block the flow of qi and result in stasis of blood within the body. Blood stasis and phlegm are intertwined, and they can attach to the veins and become plaques. Additionally, the accumulation of phlegm and stagnant toxins in the veins can cause damage to the vessel walls, leading to thickening and narrowing of the walls. This can ultimately result in the development of carotid atherosclerotic plaques, and even carotid stenosis or occlusion<sup>[18]</sup>. It is important to note that phlegm and stagnant toxins are intertwined and can cause long-term damage to the veins.

Toxicity can lead to the production of phlegm and stasis. These three conditions are interconnected and can transform into each other, resulting in the formation of toxic phlegm and blood stasis in the same disease. When fluids accumulate, they can become phlegm, and when blood flow is inhibited, it can lead to blood stasis. Phlegm and blood stasis can influence each other, layer by layer, coagulating into a block and accumulating into a larger mass, which can develop into carotid plaque. Toxicity is produced and circulated in the veins, exacerbating the condition of phlegm and stasis that corrupts the body<sup>[19]</sup>. This complex disease is caused by a combination of factors, including phlegm, stasis, and heat. In summary, phlegm initiates CAS, blood stasis is always present in CAS, and toxicity results from prolonged illness and the accumulation of harmful substances in the body. The combination of three factors leads to congestion of qi and blood, damage to the blood vessels, and

deficiency of the blood vessels, resulting in cervical vein paralysis.

#### 4. Treatment of CAS based on "Phlegm, Stasis and Toxin"

The pathological process of carotid atherosclerosis is accompanied by the dominant changes among the three evils of phlegm, stasis, and toxicity, with phlegm and turbidity predominating in the early stage of the disease and blood stasis taking the second place; blood stasis is more prominent later with the progression of the disease; and phlegm and stasis accumulate toxicity in prolonged disease, forming the pathological state of phlegm, stasis, and toxicity intertwined with the three qi<sup>[20]</sup>. Therefore, the relationship between phlegm, blood stasis and toxicity should be emphasized in the treatment, and attention should be paid to the identification according to the different clinical symptoms and physical signs. For patients with phlegm, stasis and toxicity, it is necessary to treat all three elements together, but also to distinguish the lesser and the greater, to treat the root cause of the disease, and to catch the main causative agent.

During the course of treatment, in addition to medication, it is equally important to adjust lifestyle and psychological state. Patients should focus on dietary control, including low-salt, low-fat, and low-sugar options, and increase their intake of dietary fiber. Additionally, maintaining appropriate exercise, such as walking, swimming, or yoga, can help improve the body's immunity. Patients should refrain from smoking and drinking, and prioritize good sleep quality to maintain normal bodily functions. Maintaining an optimistic mindset and avoiding emotional fluctuations can enhance treatment effectiveness and promote disease recovery. The combination of these comprehensive measures can improve treatment outcomes and promote patient recovery.

#### 5. Conclusions

The pathogenesis of carotid atherosclerosis involves three interrelated pathogenic elements: phlegm, blood stasis, and toxicity. These factors are not independent, but rather influence each other. Phlegm and blood stasis can be produced during the process of fluid metabolism, and can further develop into phlegm poison and stasis poison. Toxicity causes heat, while stasis is caused by toxicity. Various pathological factors persist and adhere to each other over time, leading to the formation of phlegm, stasis, and toxicity. These factors are key contributors to the symptoms of carotid atherosclerosis. Therefore, it is often necessary to treat these factors in combination or individually to achieve effectiveness. Treating carotid artery atherosclerosis using the theory of 'phlegm, blood stasis, and toxicity' allows for the utilization of Chinese medicine's advantages in treating chronic diseases. This approach broadens our understanding of disease intervention and provides a new clinical treatment strategy.

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