

# Common Triggers of Oral Ulceration and Updated Clinical Treatment Options

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## Abstract:

This study synthesizes existing literature to provide a comprehensive overview of oral ulceration, including its types, adverse impacts, contributing factors and practical management strategies. Oral ulceration encompasses diverse forms, with some being self-healing via the body's immune system, while severe cases may lead to oral nerve damage and intense pain if left unaddressed. Its etiology is multifactorial, involving the interaction of multiple elements rather than single independent triggers. Key contributing factors include genetic predisposition, impaired immune function, psychological stress, infections by viruses, bacteria or fungi, poor oral hygiene, physical trauma, nutrient deficiencies and unhealthy lifestyles such as staying up late and low physical activity levels. For patients, core management measures include documenting individual triggers, maintaining oral hygiene, adhering to a balanced diet, managing stress and using medications rationally under medical guidance. This study aims to enhance public awareness of oral ulceration, equip individuals with knowledge to self-prevent and manage the condition and contribute to the popularization of oral health-related medical knowledge among the general public.

**Keywords:** Oral ulcers; etiology; measurement.

## 1. Introduction

Oral ulcers are common and painful diseases that can destroy the oral mucosa. Global prevalence is estimated between 20% and 25%. Although this disease has almost no threat to life, severe pain when eating and speaking leads to malnutrition, and anxiety reduces quality of life. For patients with frequent recurrence, oral ulceration is a kind of chronic and distressing disease. Since ancient times, oral ulceration has been described. Historically, Chinese

doctors thought that "excessive heat", vitamin deficiency, and trauma can cause oral ulcers. However, systematic scientific research began in recent years. Oral ulcers are a complex inflammatory disorder involving multiple factors. The core pathological basis is that T cell-mediated autoimmune response, which can lead to local destruction of oral mucosal epithelial cells and ulcer formation. Lifestyle and local modification can be used to manage the symptoms. In China, scientists pay more attention to genes and

heredity. Also, government funds support the research on the modernization of traditional Chinese medicine. The scientists try to explain the mechanism with a molecular biology approach. The Chinese doctors are more willing to offer Chinese patent medicine such as watermelon frost and Bing Peng San[1,2]. The doctors combine Chinese and Western medicine. They totally study the Western methods. Chinese scientists are studying how to extract ingredients from natural plants such as licorice and astragalus to make medicine. In a foreign country, the immune system is a more important research point. Also, the scientists study the genetic diversity. Their method for treating the oral ulcers is standardized. They adhere to evidence-based medicine grading systems. Western doctors use physical therapies such as laser treatment earlier compared to Chinese doctors. Western country has a more mature framework and more mature management of immunosuppressive agents. Scientists in a foreign country tend to focus on the study of the development and application of molecular targeted drugs and biologics. The global research shift from symptomatic treatment to etiological and personalized therapy. Many researchers study the target treatment for a specific inflammation cytokine, such as TNF- $\alpha$ , especially for Behcet disease. Researchers focus on creating more effective local or systemic immunomodulators and biological agents. Up to now, due to unclear pathology, doctors can only treat symptomatic in order to inhibit pain, promote healing, and reduce recurrence frequency. However, all of these treatments cannot cure once and for all. The final goal is to find the pathogenic principle and find effective methods to prevent all kinds of oral ulcers. This includes identifying high-risk populations by genetic testing. Maintaining oral ecological balance via microbiome modulation, and implementing artificial. An oral ulcer is a kind of chronic recurrent disease. It is regarded as a clinical model for studying chronic, recurrent, painful mucosal disease. An oral ulcer is a disease that combines basic and clinical medicine.

## 2. Definition of Oral Ulcer

Oral ulcers are small sores that form on the mucous membranes of the gums, lips, tongue, inner cheeks or roof of the mouth[3]. The ulcer surface is round or oval, with a white or yellow center. It is a membrane composed of fibrin, necrotic cells, and inflammatory cells. The periphery is slightly congested, red and swollen. Most of them are often painful, making eating, drinking and speaking uncomfortable. Oral ulcers can be classified in two ways. First is clinical classification. Minor Aphthous Ulcer(MiAU) is the most common kind(80%). It is painful but heals in 7 to 14 days, which is a short time. After treat-

ment, scarring does not remain. Major Aphthous Ulcer(MjAU) is more serious. The ulcer's diameter is larger than 1 centimeter. It is deeper than MiAU. MjAU can reach the submucosa and even the muscular layer. Herpetiform Ulcer(HU) looks like clusters of 1 to 3 millimeter ulcers, which are like herpes. If someone catches this, headache and fever also happen. Herpetiform Ulcers need to heal in 10 to 30 days. The pain is severe. Fever, lymphadenopathy occur meanwhile[4]. The healing process is slow, taking weeks to months. When it is treated, scarring is left. The second one is etiological classification. Recurrent Aphthous Stomatitis(RAS) has an unknown etiology, probably linked to immunity, genetics or nutrient deficiency. Traumatic ulcers are caused by mechanical or chemical irritation, such as biting. The oral ulcer has many kinds of shapes, which is like the cause. After removing the trigger, the traumatic ulcer can be treated. Infection-related Ulcers are mainly caused by the HSV virus, tuberculosis and candida. Gingival redness, hand-foot-mouth disease with rashes are the main symptoms. Infection-related Ulcers are mainly in children. Systemic Disease-related Ulcers are mainly caused by Behcet's disease and autoimmune disease. The skin and mucosa are destroyed. Neoplastic Ulcers are malignant ulcers. They are indurated, irregular edges and progressive. Most of them are on the tongue or the floor of the mouth.

## 3. Influence of Oral Ulcers

### 3.1 Local Factors

Most local factors are mechanical trauma, caused by teeth biting or toothbrush abrasion. They will result in a wound. This process mostly occurs when chewing. If the wound is not treated, it will develop into an ulcer because the oral mucous membrane is destroyed. There are a large number of bacteria in the oral cavity. The damaged site exhibits a high propensity for bacterial colonization, thereby triggering inflammation and ultimately leading to an oral ulcer. Similarly, eating some sharp food, such as biscuits, can also cause oral abrasions. Excessive oral hygiene can also cause oral ulcers. As noted earlier, excessive brushing of teeth may destroy the oral mucosa and form ulcers. Analogously, chemical stimulation can also result in oral ulcers forming. Frequent use of powerful antibacterial ingredients, such as toothpaste or mouthwash with a high concentration of ethanol, will result in oral mucosa destruction. On the other hand, excessive oral hygiene may disrupt the beneficial bacterial environment. These beneficial bacteria can inhibit the excessive proliferation of the pathogen, such as Streptococcus, triggering local inflammatory responses and inducing oral ulcers.

### 3.2 Systematic Factors

Immune system diseases and nutrient deficiency are the major systemic factors. A classical immune disease is Behcet disease, which is a kind of chronic systemic vasculitis. First, this disease can cause inflammatory damage to the micro blood vessels of the oral mucosa, resulting in ulceration. Second, the gene of Behcet disease shows a high correlation with the HLA-B51 gene. The gene may increase the susceptibility of the oral mucosa to inflammation. The HLA-B51 gene may promote pro-inflammatory T-cell subsets such as Th1 and Th17. This process increases cytokines such as IFN- $\gamma$  and IL-17 secretion.

Nutritional deficiency is a normal factor of recurrent aphthous ulceration (RAA). B vitamins, C vitamins, iron, and zinc are the four factors strongly associated with ulcers. B vitamins are involved in metabolism, oral mucosal repair, and immune system regulation. When B vitamins are not taken enough, inflammatory cheilitis may occur. Also, if Vitamin B9 is not taken enough, DNA can not be formed quickly, causing the ulcer to remain cured in a short time. Inflammation produces a lot of free radicals, which can attack the cell membrane, protein, and DNA. Pro-inflammatory cytokines are also released a lot. The main functions of vitamin C include antioxidation, immune enhancement and reducing pro-inflammatory cytokines such as IL-6[5]. Vitamin C can enhance wound healing capacity. Iron is a necessary mineral for haemoglobin synthesis. It is a factor of wound repair. Zinc is a mineral that can promote wound repair and DNA synthesis. The time needed to repair the oral mucosa is strongly associated with Zinc. Low concentration of zinc in blood prolongs oral healing time and increases recurrent oral ulcers.

### 3.3 Genetic Factors

Genetic factors show a strong connection with RAA. 30%-40% of patients report a family history. An individual who has a parental history of recurrent aphthous ulceration exhibits significantly elevated disease risk. The concordance rate is much higher in identical twins than in fraternal twins. IL-1 $\beta$ , IL-6, and TNF- $\alpha$  are pro-inflammatory cytokines. They cause excessive inflammatory responses and induce mucosal damage. HLA-B\*51 and HLA-DRB1 genes are two important genes in the human leukocyte antigen. The HLA-B\*51 gene is connected with Behcet's disease. HLA-B\*51 mistakes recognize self-mucosal proteins as antigens, triggering an immune attack. HLA-DRB1 gene variation may lead to hyperactivation of CD4+T cells by antigen-presenting cells, triggering Th1 and Th17 immune responses. Subsequently, pro-inflammatory mediators are released and the oral mucosal barrier is disrupted. Concurrently, impaired regulatory T cell function can-

not effectively suppress the inflammatory attacks targeting the mucosa. NLRP3 is a kind of gene that can control innate immunity. It may release more IL-1 $\beta$ , triggering the oral ulcers. MUC19 belongs to the mucin gene family, which can encode important protective glycoproteins in the saliva and on the mucosa. Mucin can prevent pathogen adhesion and neutralize acidic substances. Moreover, it can promote epithelial repair. If MUC19 is abnormally expression may cause insufficient secretion of salivary mucin, weaken the mucosal barrier, making the oral tissue more vulnerable to mechanical damage and micro invasion or chemical irritation. The mucin repairing ability decreases and the oral ulcers are difficult to cure.

### 3.4 Psychological

Stress and anxiety are important factors in psychological factors. Stress disrupts immune function, increasing inflammatory factors, triggering ulcer formation. Depression is an indirect factor. It may worsen oral hygiene, reduce immunity, or even lead to poor nutrition. For example, iron and vitamin B12 may be deficient. Sleep disorders such as insomnia and staying up late reduce sleep quality, impairing mucosal repair and immune regulation, increasing ulcer susceptibility.

### 3.5 Lifestyle Factors

Dietary habits are important. Mineral and vitamin deficiency weaken mucosal integrity[6]. Oral hygiene is important. Brushing teeth is a good habit. Otherwise, bacterial imbalances may contribute to chronic ulcers. However, over-brushing or using SLS toothpaste to brush the teeth may destroy the mucosa. If someone is obsessed with drinking, a nutritional deficiency will occur. The oral mucosa will be dehydrated. The tissue is stimulated. For women, during the menstrual cycle, ulcers form frequently because progesterone delays healing and IgA drops. During the pregnancy, hormonal shifts trigger ulcers and iron or folate may be deficient.

### 3.6 Medical Factors

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used to relieve pain, reduce inflammation and lower fever. The most representative examples are aspirin and ibuprofen. They work by inhibiting cyclooxygenase enzymes such as COX-1, which can produce prostaglandins, chemicals that promote inflammation, pain, and fever. However, NSAIDs promote bleeding[7]. When NSAIDs inhibit COX-1, less prostaglandin E<sub>2</sub> is produced. Prostaglandin E<sub>2</sub> has an effect on protecting the mucosa. Prostaglandin E<sub>2</sub> promotes mucus secretion, maintains mucosal blood flow and helps tissue repair. Most oral ulcers caused

by NSAIDs are superficial ulcers, such as aphthous ulcers. Chemotherapy is another factor that affects oral ulcers[8]. Chemotherapy drugs such as 5-FU, methotrexate and docetaxel. On the first two days, chemotherapy drugs disrupt DNA and RNA synthesis. Oral epithelial cells are killed and the mucosa becomes thinner. Also, the drug's metabolism generates reactive oxygen species(ROS), damaging cellular membranes and mitochondrial function, causing apoptosis. In 5-7 days, matrix metalloproteinases(MMPs) are activated. MMP-1 and MMP-3 concentration increase, which has an effect on decomposing collagen and destroying the mucosa. Meanwhile, the Bax and Bcl proportions are imbalanced. Oral epithelial cells are killed more frequently. In 7-14 days, the completeness of the oral epithelium is lost. Bacteria or fungi colonize the lamina propria. At this time, large ulcers form. The diameter is larger than one centimeter. Its surface is covered by a pseudomembrane. Normally, oral ulcers can be restored. On 3-5 days is inflammation resolution time. Neutrophils clear necrotic tissue. In 5-10 days, granulation tissue forms. New blood vessels form and fibroblast proliferation. On 10-21 days, epithelial reform. Basal stem cells differentiate into epithelial cells to cover the wound. However, chemotherapy causes several problems. First, insufficient angiogenesis in the granulation tissue. The restoration delay and bleeding. Second, epithelial margins become thinner. Proliferation of stem cells is restricted, leading to only monolayer epithelial coverage. Only minor friction can cause ulcer recurrence. Third, the pseudomembrane is persistent. It is hard to clean the infection and necrotic tissue.

#### 4. Treating Method for Oral Ulcers

Anti-inflammatory drugs such as lidocaine gel and glucocorticoid patches. Lidocaine gel is a kind of local anesthetic drug. It provides fast-acting pain relief and serves as an adjunct to other therapies. Glucocorticoid patches can direct delivery of anti-inflammatory drugs to ulcer surfaces, offering significant advantages such as strong target capability, few side effects. It is one of the preferred approaches for treating recurrent aphthous ulcers. In order to clean the bacteria in the mouth, brushing teeth is important[9]. For people whose oral mucosa is weak, a soft-bristle toothbrush is a good choice. Dental floss can clean the spaces between teeth to reduce food debris. Mouthwash, especially mild salt water or chlorhexidine or other mouthwash containing antibacterial ingredients, but some mouthwash that contains ethanol should be avoided. Also, whitening toothpaste should be avoided because it contains peroxides and may aggravate ulcers. If someone wears braces or dentures, they cover the metal edges with

orthodontic wax in order to prevent friction. The denture must be cleaned and soaked each night. If someone is a patient with dry mouth, keeping moist with gum or artificial saliva spray without sugar.

If someone has oral ulcers because of Vitamin B, C, zinc and iron, eating vegetables, eggs, beans, and oranges can significantly solve this problem without pain. Eating whole wheat bread, eggs, milk, spinach and salmon can offer Vitamin B[10]. Beef, oysters, black fungus. Tea and coffee, especially concentrated tea, should be avoided because they reduce the ability to absorb iron. Spicy food or overly sour food, such as lemon, overly hot or fried food, should be taken in less. In order to prevent inflammation, blueberries, turmeric, olive oil, and deep-sea fish are good foods. Honey, yogurt, which contains probiotics, can help the oral mucosa repair. Overly sour fruits such as pineapple and lemon should be avoided. Immune system improvement can treat oral ulcers. High-quality sleeping quality is necessary. Staying up must be avoided. Avoiding electrical equipment for at least one hour before bedtime can significantly achieve this. Reducing stress can also help the immune system. Doing yoga three times a week can reduce inflammation in the body.

#### 5. Environment and Lifestyle Improvements

At home and office, an air humidifier can keep humidity between 40%-60%, which can prevent oral drying. If someone who catches asthma or other kinds of diseases that require to use of inhaled corticosteroids(ICS) should rinse their mouth immediately in order to avoid local immunity. If someone needs antibiotics, they should combine them with probiotics to promote intestinal digestion. When staying up late, rinsing with aloe vera juice instead of regular mouthwash can significantly help reduce inflammation and maintain moisture. Traditional Chinese doctors recognize oral ulcers are caused by Dysfunction of the organs, upward flaming of fire-heat, or accumulation of dampness-heat. Doctors distinguish the patients' constitutions. For heart fire ascending type patients, who have red and painful ulcers, drink light bamboo leaf tea and lotus seed heart 2 grams. For spleen and stomach damp-heat type patients who have halitosis with ulcers, boil 30 grams of coix seeds and red beans in water. Also, if the patients are not willing to drink medicine, an external treatment method is a good choice. Evodia rutaecarpa(wuzhuyu) plaster is suitable for recurrent ulcers. The powder herb mixed with vinegar should be applied to the Yongquan acupoint on the soles to guide fire downward. For the oral ulcers caused by Behcet disease, coicosterone

is an effective medicine to reduce the inflammation[11].

## 6. Conclusion

There are many kinds of oral ulcers, including Minor Aphthous Ulcer(MiAU), Major Aphthous Ulcer, Recurrent Aphthous Stomatitis(RAS) and so on. The cause of oral ulcers is complex. There are no obvious factors that can cause oral ulcers. It is a very complex mechanism: infected wound, bad immune system, genetic factors, terrible living style and other diseases interact with each other. Most oral ulcers can be treated by themselves. For example, MiAU and RAS usually only last for about seven to fourteen days. For those serious oral ulcers, such as herpetiform ulcers, many methods can be used to treat. Both Western countries' and Chinese doctors have many kinds of medicine for treating most oral ulcers. There are many people who can benefit from this paper. Common people can understand all kinds of oral ulcer symptoms. Many measures can be used to prevent and treat oral ulcers. The paper can help more people reduce the risk of catching or getting crazy about oral ulcers. There are some limitations in this paper. Firstly, this paper only refers to Chinese and English language databases on the CNKI website. This paper probably omits other meaningful studies published in another language, such as Spanish or French. Secondly, in order to introduce many kinds of oral ulcers and their treatment method, this paper precludes an extremely detailed exploration of any single type. Finally, the conclusions of this review are derived from the analysis of existing secondary literature. The strength of the evidence and conclusions is therefore constrained by the quality of the primary studies. Meanwhile, there are not enough samples in this field, which probably impacts the accuracy rate of the summarized findings. Based on the current research in this paper, in basic research areas, future studies should combine many technologies, including genomics and microbiome, in order to study the mechanism of oral ulcers. Society should pay more attention to the stress on the common people.

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