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Review Article

Pathophysiology of Mouth Ulcers

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ABSTRACT

Mouth ulcers, also known as aphthous stomatitis, are common, painful lesions that affect the mucosal surfaces of the oral cavity. Their pathophysiology is complex, involving genetic, immunological, and environmental factors. Although the exact cause remains unclear, dysregulation of the immune system plays a central role. Inflammatory responses are triggered by the activation of T lymphocytes, which lead to the release of cytokines, resulting in epithelial cell damage and ulcer formation. Genetic predisposition, stress, trauma, nutritional deficiencies (especially of B vitamins, folic acid, and iron), and microbial factors have all been implicated as contributing factors. The local tissue response is characterized by an imbalance between pro-inflammatory and anti-inflammatory mediators, with the upregulation of cytokines such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF- α), and interferon-gamma (IFN- γ). This results in increased vascular permeability, edema, and neutrophil infiltration, which further exacerbate the lesion. Treatment strategies often focus on symptomatic relief, while ongoing research aims to elucidate the precise molecular mechanisms involved to develop more targeted therapies. Understanding the pathophysiology of mouth ulcers is critical for improving treatment outcomes and minimizing recurrence. Treatment options include over-the-counter pain relievers, topical medications, and avoiding irritants. In most cases, mouth ulcers will heal on their own within a week or two. However, if they persist or are accompanied by other symptoms, it is important to seek medical attention. The diagnosis and treatment of oral lesions are often challenging due to the clinician's limited exposure to the conditions that may cause the lesions and their similar appearances. This review aims at a systematic approach towards the diagnosis of oral ulcers based on their clinical and histopathological features while eliminating unrelated factors. Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosal diseases characterized by recurrent and painful ulcerations on the movable or nonkeratinized oral mucosae. Clinically, three types of RAS, namely minor, major, and herpetiform types, can be identified. RAS more commonly affects labial mucosa, buccal

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mucosa, and tongue. Previous studies indicate that RAS is a multifactorial T cell-mediated immune-dysregulated disease.

INTRODUCTION

There are several potential causes of mouth ulcers, including stress, hormonal changes, food sensitivities, and certain medical conditions. They can also be triggered by injury to the mouth, such as biting the inside of the cheek or brushing too aggressively. While most mouth ulcers will heal on their own within a week or two, they can be treated with over-the-counter medications or home remedies to help alleviate pain and speed up the healing process. If mouth ulcers persist or are accompanied by other symptoms, it's important to seek medical attention to rule out any underlying health issues. Mouth ulcers are also common in patients converted to mTOR inhibitors. Again, such ulcers usually resolve spontaneously, but they can be problematic. In one prospective randomized study in which renal transplant recipients were converted at 1 year from a steroid-free regimen of tacrolimus and MMF to sirolimus and MMF, oral ulceration occurred in 9 of 15 converted patients. (*Eur J Oral Sci.* et .al. 2018 Dec12)

Pathophysiology of Mouth Ulcers

Aphthous ulcerations are initially and primarily the result of T cell-mediated immune dysfunction but also may involve neutrophil and mast cell-mediated destruction of the mucosal mucosal epithelium. Mouth ulcers, also known as aphthous ulcers, are small, painful sores that develop inside the mouth. They are a common condition that affects most people at some point in their lives. The exact cause of mouth ulcers is unknown, but they are thought to be triggered by a combination of factors, including:

Trauma: Injury to the mouth, such as biting the inside of your cheek or brushing your teeth too hard, can cause mouth ulcers.

Stress: Stress can also trigger mouth ulcers.

Certain foods: Some foods, such as acidic fruits, spicy foods, and nuts, can irritate the mouth and cause ulcers.

Hormonal changes: Women may experience mouth ulcers during their menstrual cycle or during pregnancy.

Certain medications: Some medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), can cause mouth ulcers as a side effect.

Underlying medical conditions: Certain medical conditions, such as Crohn's disease, celiac disease, and vitamin deficiencies, can also cause mouth ulcers. Mouth ulcers typically heal on their own within 1 to 2 weeks. However, there are a number of things you can do to relieve the pain and promote healing, such as:

Avoid irritants: Avoid foods and drinks that irritate your mouth, such as acidic fruits, spicy foods, and nuts.

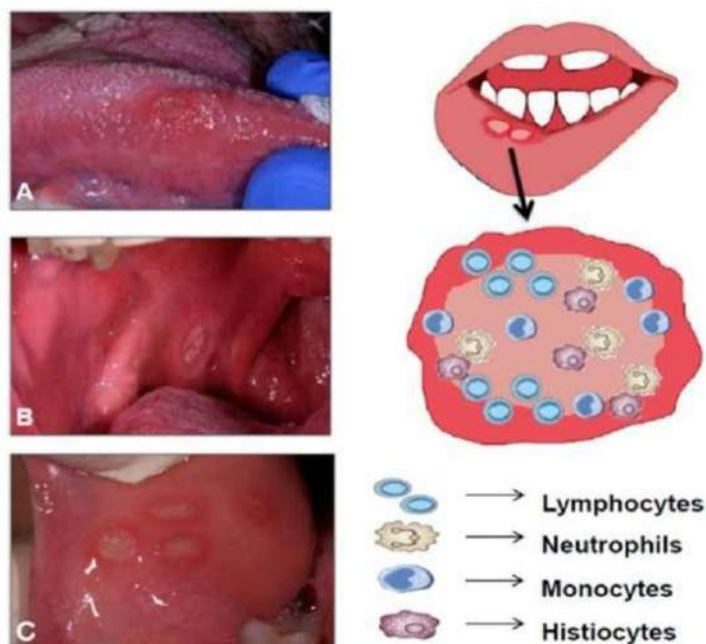
Use a mouthwash: Use a mouthwash that is designed for mouth ulcers.

Apply a topical medication: Apply a topical medication, such as a corticosteroid cream or gel, to the ulcer.

Over-the-counter pain relievers: Take over-the-counter pain relievers, such as ibuprofen or acetaminophen, to relieve the pain.

Causes of mouth ulcers: -





There's no definite cause behind mouth ulcers, but certain risk factors and triggers have been identified. People assigned female at birth, children, adolescents, and those with a family history of mouth ulcers have a higher risk of developing them.

Triggers Include:

- minor mouth injury from dental work, hard brushing, sports injury, or an accidental bite
- dental braces
- toothpaste or mouthwash that contains sodium lauryl sulfate (SLS)
- an allergic response to oral bacteria
- bacterial, viral, or fungal infections in the mouth, such as hand, foot, and mouth disease
- sensitivities to acidic foods and beverages like strawberries, citrus fruits, pineapple, chocolate, and coffee
- certain nutrient deficiencies, especially vitamin B9 (folate), vitamin B12, zinc, and iron
- hormonal changes, such as those that occur during menstruation or pregnancy

- emotional stress
 - lack of sleep
- Mouth ulcers can also be a sign of conditions that are more serious and require medical treatment, such as:
- celiac disease
 - inflammatory bowel disease (IBD), including ulcerative colitis
 - diabetes
 - HIV
 - some autoimmune diseases, including:
 - lupus
 - oral lichen planus
 - Behçet's disease, a rare condition that causes inflammation throughout the blood vessel oral lichen planus
 - Behçet's disease, a rare condition that causes inflammation throughout the blood vessels

Mouth ulcer symptoms

Symptoms of mouth ulcers may vary depending on their cause, but they typically include:

- painful sores that may be yellow, white, or red

- sores on the inside of the mouth, such as on your tongue or the insides of your cheeks or lips
 - areas of redness surrounding the sores
 - pain that worsens when you eat, drink, or talk
- You may have more than one mouth ulcer at the same time.

Mouth ulcers are not usually contagious unless they're caused by an infection such as hand, foot, and mouth disease. Canker sores are the most common type of mouth ulcer, with 20% of people having a canker sore at least once. There are three main types of canker sores:

- Minor
- Major
- Herpetiform

Minor canker sore

Minor canker sores are small oval or round ulcers measuring under 5 millimeters (mm). They heal within 1 to 2 weeks and don't cause scars.

According to Derm Net New Zealand, 80% of people with canker sores have minor canker sores, making them the most common type.

Major canker sore

Major canker sores are larger and deeper than minor ones. They often measure over 10 mm. They have irregular edges and can take weeks or months to heal. Major canker sores can result in long-term scarring.

Herpetiform Canker Sore

Herpetiform canker sores are pinpoint-sized, occur in clusters, and often appear on the tongue. Sometimes the clusters can merge to form one large sore. Herpetiform canker sores have irregular edges and often heal, without scarring, within 1 month. They're called "herpetiform" because they may resemble the sores caused by herpes. Herpetiform canker sores are not otherwise associated with herpes infection.

Sr. no	Common name	Scientific name	family	Chemical constituents	uses
1	Guava leaves	Psidium guajava	myrtaceae	Flavonoid, tannin	Antimalarial, antiulcer, analgesic
2	Indian cherry leave	Cardia dichotoma	boraginaceae	Flavonoid alkaloid	Headache and ulcer
3	Liquorice	Glycyrrhiza glabra	Leguminosae	Saponin, flavonoid	Expectorant, Anti-inflammatory
4	Turmeric	Curcuma longa	zingiberaceae	curcumin	Anti arthritic, antiulcer
5	Pomegranate flower	Punica M L	punicaceae	Gallic acid, ellagic acid	Peptic ulcer, oral and anal ulcer
6	Betel leave	Piper bette L	piperaceae	Alkaloid, amino acid	Antifungal, anti oxidant
7	Aloe vera	Aloe barbadensis miller	liliaceae	Anthraquinones, vitamin, lignins	Anticancer, antidiabetic
8	Capsicum	Capsicum annum	Solanaceae	Capsaicin, paprika, aloe resin	Stomach pain, mouth ulcer
9	Noni fruit	Morinda citrifolia linn	rubiceae	Flavonoid, phenolics	Abnormal menstruation, fever, blood pressure

Diagnosis Of Mouth Ulcers

Your doctor will be able to diagnose mouth ulcers through a visual exam. You might be tested for other medical conditions if you have frequent, severe mouth ulcers.

1. Pain or discomfort in the mouth, particularly when eating, drinking, or talking.
2. Redness or swelling in the affected area.
3. White or yellowish sores or lesions inside the mouth.
4. Difficulty in chewing or swallowing.
5. Tingling or burning sensation before the appearance of the ulcer.
6. Fever or swollen lymph nodes in severe cases.
7. Bad breath or a foul taste in the mouth.
8. Difficulty opening the mouth fully.
9. Feeling generally unwell or fatigued.
10. Recurrent outbreaks of mouth ulcers.
11. Sores that do not heal or continue to grow in size.
12. Ulcers that spread to the lips, gums, or throat.

Cold sores are also more likely to cause additional symptoms beyond the lesions, including:

- fever
- fatigue
- malaise
- swollen lymph nodes in the neck

Both types of lesions can cause a burning or tingling sensation on the skin that may start a few days before the lesions appear. However, this sensation is more closely associated with cold sores.(Chiang CP,et.al.2019)

Aphthous ulcers

Aphthous ulcer is another name for a canker sore. The medical term “aphtha” has a few definitions but is mostly used to refer to a small ulcer.

Mouth Ulcer Treatment

Most mouth ulcers don't need treatment.

However, if you get mouth ulcers often or they're extremely painful, a number of treatments and home remedies can decrease pain and healing time. These include:

- covering the ulcer with a paste made from baking soda
- using other topical pastes
- placing milk of magnesia on the ulcer
- using a mouth rinse made from salt water and baking soda
- using a mouth rinse that contains a steroid to reduce pain and swelling
- applying ice to the ulcer
- placing a damp tea bag on the ulcer
- taking supplements if you have deficiencies in certain nutrients, including vitamin B9 (folate), vitamin B12, zinc, and iron
- using over-the-counter topical products that are made with benzocaine, like Orajel and Anbesol (Hausmann JS, et.al., 2019)

Treatment Of Mouth Ulcers

The treatment for mouth ulcers is broadly divided into two categories:

Symptomatic Relief

Various OTC and prescription formulations are available for topical application to provide relief and promote faster healing of the mouth ulcers:

- Topical gels containing anesthetics like benzocaine and lidocaine are used to give relief from pain.
- Antiseptics can be used to prevent and treat infections associated with mouth ulcers.



- Use of chlorhexidine gluconate mouthwash can decrease the duration of the ulcer.
 - Antibiotic Mouthwash containing Tetracycline helps in reducing the size of the ulcer and the pain associated with it.
 - Oral painkillers like diclofenac are used to relieve pain.
 - Oral Steroids and Mouthwashes containing dexamethasone are prescribed in cases of severe ulceration.
 - Drugs used in the treatment of gastrointestinal ulcers such as sucralfate may also provide some relief in mouth ulcers.
 - Dental lasers can be used to perform cautery, a kind of mini-surgery on mouth ulcers to promote healing Supportive care. (Kirkham, et.al., 2018)
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