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## **Oral ulceration**

### What are oral ulcers?

Oral ulcers are characterised by a loss of the mucosal layer within the mouth. This loss may be acute or chronic, localised or diffuse. This is one of the most common oral problems presenting in primary care and can arise as a result of a number of disorders. Some of these relate to problems around the oropharynx but there is a wide variety of systemic disorders that can also give rise to these lesions. See also the separate Problems in the Mouth and Some Dental and Periodontal Diseases articles.

# How common are oral ulcers? (Epidemiology)[1]

Oral ulceration is a common condition. 25% of the global population are thought to be affected by recurrent aphthous ulcers, one of the most common causes of oral ulcers; and the prevalence of oral ulcers in children has been reported as 9%.

Possible causes of aphthous ulceration include the following:

- Smoking cessation.
- Positive family history.
- Deficiency of iron, zinc, folic acid or vitamins B and D.
- Hormonal factors ulceration can be an issue in the luteal phase of the menstrual cycle.
- Local trauma to the mucosa in the mouth.
- Exposure to foods such as chocolate and peanuts.
- Anxiety.

The incidence of oral cavity cancers is rising in the UK, with Cancer Research UK statistics showing 12,422 new cases on average per year from 2016-2018, an increase of 37% since the early 1990s. [2]

## **Aetiology**

These lesions can arise as a result of a vast number of (sometimes overlapping) disorders detailed in the two sections below. The most common causes are local trauma and recurrent aphthous ulceration.

### Local causes of oral ulcers

#### Mechanical trauma

- The most common cause of oral mucosal ulceration.
- It is most often caused by dentures, braces or sharp/broken teeth.
- It can also be due to tongue or cheek biting, scratching with fingernails, or eating rough foods.
- Any ulcer usually starts to heal within 10 days following removal of the cause. Persistence after the presumed cause has been removed should lead to urgent further investigation.

### Chemical injury

- This can arise from direct contact of oral mucosa with aspirin (leaving white plaques which slough off).
- Bisphosphonates can also cause chemical burns if allowed to dissolve in the mouth rather than taken as instructed (swallowed whole with a glass of water, whilst sitting upright).
- This can also be caused by improperly cleaned/rinsed dentures which are then replaced in the mouth. Ulcers associated with dentures usually occur in a line along the gums. They are usually more painful than mechanical ulcers.

### Thermal injury

Thermal injury arises from mucosal contact with hot food or liquids.

• Although the palate is most commonly affected, these injuries can also occur on the lip, tongue or oropharyngeal region.

### Recurrent aphthous ulceration [1] [3]

- These are also known as 'canker sores'.
- The condition is characterised by clearly defined, painful, shallow round or ovoid ulcers not associated with systemic disease. They are not infective.
- They usually begin in childhood and decrease in frequency/severity with age.
- Around 40% of cases have a family history.
- In predisposed people, the following may precipitate ulceration:
  - Local trauma.
  - Stress.
  - Food sensitivity (eg, chocolate, coffee, peanuts, almonds, strawberries, cheese and tomatoes).
  - Hormonal change (they tend to subside during pregnancy).
  - Cessation of smoking.
- Typically, aphthous ulcers heal within 10-14 days and leave no scar.

#### Infective ulcers

- Primary herpetic ulceration can occur (herpes simplex virus type 1
  (HSV-1) and type 2 (HSV-2)). Secondary nonspecific bacterial
  infection of chronic ulcers can delay the healing process. Primary
  herpetic gingivostomatitis is primary symptomatic infection with HSV
  involving the mouth.
- Human herpesvirus 8 (HHV-8) is associated with Kaposi's sarcoma of the gingiva.

- Candida albicans is a normal commensal but it can overwhelm other microbes in certain situations, such as those who have received long-term antibiotics or steroid inhalers, or in the immunocompromised. It is common in babies. White coating plaques are characteristic of oral candidiasis (thrush).
- Many systemic infections can cause oral ulcers- see the 'Systemic causes' section, below.

## Neoplastic conditions [2] [4]

- Squamous cell carcinoma (SCC) lesions account for 90% of all oral neoplasia, with malignant melanoma, lymphoma and metastases accounting for the remaining 10%.
- Tobacco smoking is the main avoidable risk factor and is linked to 65% of cases in the UK. Alcohol further increases the risk and is thought to be a factor in 30% of cases.
- Incidence varies significantly geographically in the UK oral cancers account for 3% of all cancers and are the 8th most common cancer. The largest number of cases globally is in India, which has one third of the global number of cancers and one quarter of the total global number of deaths. This is likely to be due partly to tobacco consumption, including the chewing of betel. [5]
- SCC may start as white lesions (leukoplakia) or red lesions (erythroplakia): white patches carry a 5% risk of malignancy and red lesions are malignant until proven otherwise (50% risk).
- Spread occurs via the submandibular and cervical lymph nodes;
   these will be involved on presentation in 30% of patients.
- These often present as slow-growing, painless, non-healing ulcers with raised borders, usually on the lateral aspect of the tongue, the floor of the mouth or on the soft palate.

#### Irradiation ulcers

 Ulceration occurs either acutely (as a result of direct damage to epithelial cells) or more long-term, secondary to epithelial atrophy and damage to underlying blood vessels.

- The acute reaction usually begins during the second week of radiation, presenting as erythema followed by spotty mucositis which coalesces to form areas of ulceration covered by a yellowwhite pseudomembrane with a bright erythematous border. The lips are often involved.
- Exquisite pain and burning may be present. Healing generally begins
  as therapy ends and is usually complete within 3-4 weeks, although
  the discolouration and mucosal atrophy may be lifelong.

### Ischaemic ulcers: necrotising sialometaplasia

This is an uncommon disorder that gives rise to large areas of deep ulcers on one side of the hard and sometimes the soft palate. This condition is probably associated with an ischaemic event and is associated with factors such as smoking, alcohol use, denture wearing, recent surgery and systemic disease. It can also be a feature of bulimia nervosa. The clinical and histopathological features may mimic those of SCC.

## Systemic causes of oral ulcers

Although aphthous ulcers are not associated with systemic disease, mouth ulceration can occur with systemic disease. In these conditions, medication for symptom control may be required and there may be need for concurrent antimicrobial treatment for secondary infections. However, ultimately, the underlying cause needs to be addressed.

The following are systemic causes of oral ulcers:

- Autoimmune conditions:
  - Behçet's disease.
  - Kawasaki disease.
  - Systemic lupus erythematosus (SLE).
  - Granulomatosis with polyangiitis.

- Dermatoses:
  - Lichen planus.
  - Erythema multiforme.
  - Pemphigoid.
  - Linear IgA disease.
  - Dermatitis herpetiformis.
- Inflammatory conditions:
  - Crohn's disease.
  - Ulcerative colitis.
  - Reactive arthritis.
- Pharmaceutical agents by various direct and indirect mechanisms:
  - Methotrexate and other cytotoxic agents used for chemotherapy.
  - Non-steroidal anti-inflammatory drugs (NSAIDs).
  - Bisphosphonates.
  - Nicorandil.
  - Propylthiouracil.
  - Recreational drugs such as cocaine.
- Systemic infections:
  - Viral infections Coxsackievirus A (hand, foot and mouth disease and herpangina), Epstein-Barr virus, cytomegalovirus, HSV-1 and HSV-2, varicella-zoster virus and as a complication of HIV infection.
  - Bacterial infections tuberculosis, secondary syphilis.
  - Fungal infections candidiasis.

- Inherited conditions:
  - Epidermolysis bullosa.
- Various miscellaneous conditions:
  - Haematological disease, notably vitamin B12, folate and iron deficiencies.
  - Coeliac disease.
  - Chronic kidney disease.
  - Strachan's syndrome.
  - Sweet's disease.

## Oral ulcer symptoms

#### **History**

Ask about:

- Pain. Most ulcers are painful and therefore present early; the notable exception is oral carcinoma in its early stages.
- Duration. Ask how long the ulcer has been present and if it is a recurrent problem.
- Recent dental problems or changes.
- Symptoms of systemic illness.
- Perception of cause. (The patient may relate it to a specific event or cause.)
- Past medical history.
- Medication.
- Smoking and alcohol use.

#### **Examination**

- Examine the lips and ask the patient to open their mouth (and to remove dentures if present): look at the buccal mucosa, tongue (including under the tongue), the gums and the teeth.
- Note lesion location, size and associated features (eg, pigmentation, bleeding, presence of plaques or sloughed mucosa).
- Examine the hard palate (looking for previous trauma, pigmentation and telangiectasias).
- Using a tongue depressor, ask the person to protrude their tongue and say "aah" in order to assess the oropharynx.
- Palpate a lesion with a gloved finger: tethering or induration is suspicious and warrants further investigation.
- Look for local lymphadenopathy and signs of systemic disease.

### **Investigations**

In many instances investigations are not required and diagnosis is clinical. If history or examination suggests it then blood tests may be required. (FBC, ESR, ferritin, folate, B12, HIV and coeliac screen for example.) Referral for specialist secondary investigation where relevant is discussed below.

## Oral ulcer management<sup>[6] [1]</sup>

### **General principles**

- Establish the cause.
- Avoid any trigger factors such as oral trauma and any food or drink which seems to trigger the ulcer.
- Recommend a dental review if there is local trauma for example, from sharp or broken teeth or ill-fitting dentures or orthodontic appliances.
- It is important to establish the diagnosis in each case, as many of the causes of these lesions require specific management in addition to local treatment.

- Local treatment aims to protect the ulcerated area, to relieve pain, to reduce inflammation, or to control secondary infection. The available options are discussed below, but if the symptoms are mild and infrequent then treatment may not be needed.
- An unexplained ulcer of more than three weeks' duration warrants an urgent specialist review via the two-week wait referral pathway. [7]

#### Simple mouthwashes

- A warm saline mouthwash (half a teaspoon of salt in a glassful of warm water or dilute compound sodium chloride mouthwash with an equal amount of water) has a mechanical cleansing effect and may relieve the pain of traumatic ulceration.
- Use until the discomfort and swelling ease.

#### **Antiseptic mouthwashes**

- Used in the management of secondary bacterial infection.
- May accelerate the healing of recurrent aphthae.
- Chlorhexidine is helpful for aphthous ulcers and also useful in the treatment of denture stomatitis and as prophylaxis in the prevention of oral candidiasis in immunocompromised patients. It is available as a mouthwash, gel and spray. It can stain teeth if used regularly.

#### Corticosteroids

- Topical agents are available as oromucosal dissolvable tablets, mouthwashes, pastes and inhaler sprays.
- It is most effective if applied in the 'prodromal' phase of aphthous ulcers.
- Hydrocortisone oromucosal tablets should be allowed to dissolve next to an ulcer and are useful in recurrent aphthae and erosive lichenoid lesions.
- Beclometasone dipropionate inhaler 50-100 micrograms sprayed twice daily on the oral mucosa can be used to manage oral ulcers although this is an unlicensed indication. Alternatively, betamethasone soluble tablets dissolved in water can be used as a mouthwash to treat oral ulceration although this is also unlicensed.

- Systemic corticosteroid therapy is reserved for severe conditions such as pemphigus vulgaris.
- Oral thrush is a potential side-effect of treatment.

#### Local analgesics

These have a limited role, as short duration of action precludes good maintenance of analgesia throughout the day. They are mainly indicated for intolerable and intractable pain of chronic ulceration (such as with major aphthae). Options include:

- Local anaesthetic: lidocaine 5% ointment, lozenges or spray containing a local anaesthetic are available to apply to the ulcer.
   Care must be taken not to produce pharyngeal anaesthesia prior to eating (risk of choking).
- Anti-inflammatory preparations: benzydamine and flurbiprofen are NSAIDs. Benzydamine mouthwash or spray may be useful, especially in reducing the discomfort of post-irradiation mucositis. However, the full-strength mouthwash can cause some stinging and can be diluted with an equal volume of water. Flurbiprofen lozenges are licensed for the relief of sore throat.
- Choline salicylate gel may provide relief for recurrent aphthae but excessive application or confinement under a denture irritates the mucosa and can itself cause ulceration. Choline salicylate is the active ingredient in the commonly used Bonjela®, available over the counter.

### Other agents

- Carmellose gelatin paste (eg, as Orabase®) is available over the counter.
- Adcortyl in Orabase® is no longer available in the UK.
- Low-dose oral doxycycline (eg, 20 mg bd for three months) can be helpful in the management of periodontitis.
- Systemic analgesics may be needed in some cases.

 Multiple systemic treatments have been proposed for recurrent aphthous ulceration; however, no single treatment has been found to be effective so there is no conclusive opinion regarding the best systemic intervention.<sup>[8]</sup>

## Referral<sup>[1]</sup>

Guidelines from the National Institute for Health and Care Excellence (NICE) advise the following: [7]

- Consider referral under the two-week suspected cancer pathway to an oral or maxillofacial surgeon if there is unexplained ulceration in the oral cavity lasting for more than three weeks.
- Consider urgent referral to a dentist for an appointment within two
  weeks those who have a red or red and white patch in the oral cavity
  consistent with erythroplakia or erythroleukoplakia. A dentist can
  refer directly under the two-week suspected cancer pathway if the
  lesion is suspicious.

Also refer urgently people with unexplained red or white patches which are painful, swollen or bleeding.

The NICE suspected cancer guidance no longer advises who should be referred routinely, but their CKS page on aphthous ulcers suggests that we refer if ulceration is severe and does not respond to topical treatments or systemic corticosteroids. [1]

Refer to a dentist where dental problems are considered the cause of ulceration (tooth damage, denture problems, etc).

## **Further reading**

- Taylor J, Glenny AM, Walsh T, et al; Interventions for the management of oral ulcers in Behcet's disease. Cochrane Database Syst Rev. 2014 Sep 25;
   (9):CD011018. doi: 10.1002/14651858.CD011018.pub2.
- Flint S; Oral ulceration: GP guide to diagnosis and treatment. Prescriber March 5, 2006.
- Herpes simplex oral; NICE CKS, October 2021 (UK access only)
- Candida oral; NICE CKS, May 2021 (UK access only)

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