1. Ulceration

Ulceration is a breach in the oral epithelium, which typically exposes nerve endings in the underlying lamina propria, resulting in pain or soreness, especially on eating spicy foods or citrus fruits. Patients vary enormously in the degree to which they suffer and complain of soreness in relation to oral ulceration. It is always important to exclude serious disorders such as oral cancer (Article 3) or other serious disease, but not all patients who complain of soreness have discernible organic disease. Even in those with detectable lesions, the level of complaint can vary enormously – some patients with large ulcers experience little; others with minimal ulceration complain bitterly of discomfort. Sometimes there is a psychogenic or cultural influence.

Specialist referral may be indicated if the Practitioner feels:
- The diagnosis is unclear;
- A serious diagnosis is possible;
- Systemic disease may be present;
- Unclear as to investigations indicated;
- Complex investigations unavailable in primary care are indicated;
- Unclear as to treatment indicated;
- Treatment is complex;
- Treatment requires agents not readily available;
- Unclear as to the prognosis;
- The patient wishes this.

Terminology

Epithelial thinning or breaches may be seen in:
- Mucosal atrophy or desquamation – terms often used for thinning of the epithelium which assumes a red appearance since the underlying lamina propria containing blood vessels shows through. Most commonly seen in desquamative gingivitis (usually related to lichen planus, or less commonly to pemphigoid) and in geographic tongue (erythema migrans, benign migratory glossitis), a similar process may also be seen in systemic disorders such as deficiency states (of iron, folic acid or B vitamins).
- Mucosal inflammation (mucositis, stomatitis) can cause soreness. Viral stomatitis, candidosis, radiation mucositis, chemotherapy-related mucositis and graft-versus-host-disease are examples.
- Erosion is the term used for superficial breaches of the epithelium. These often initially have a red appearance, since there is little damage to the underlying lamina propria, but it typically becomes covered by a fibrinous exudate and then has a yellowish appearance (Figure 1). Erosions are common in vesiculobullous disorders such as pemphigoid.
- Ulcer is the term used usually where there is damage both to epithelium and lamina propria. An inflammatory halo, if present, also highlights the ulcer with a red halo, around the yellow or grey ulcer (Figure 2). Most ulcers are due to local causes such as trauma or burns but recurrent aphthous stomatitis must always be considered.

Causes of oral ulceration

Ulcers and erosions can also be the final common manifestation of a spectrum of conditions, ranging from epithelial damage resulting from trauma, to an immunological attack as in lichen planus, pemphigoid or pemphigus, to damage because of an immune defect, as in HIV disease and leukaemia, infections as in herpesviruses, tuberculosis and syphilis, or nutritional defects such as in...
Oral Medicine: Update for the Dental Team

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Dental local anaesthesia. Ulceration of the upper labial frenum, especially in a child with bruised and swollen lips, or subluxed teeth or fractured jaw can represent non-accidental injury. At any age, trauma, hard foods, or appliances may also cause ulceration. The lingual frenum may be traumatized by repeated rubbing over the lower incisor teeth in cunnilingus or in recurrent coughing.

Table 1. Main causes of oral ulceration.

<table>
<thead>
<tr>
<th>Causes</th>
<th>Mnemonic</th>
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<tbody>
<tr>
<td>Systemic diseases</td>
<td>So</td>
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<td>Malignant disease</td>
<td>Many</td>
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<td>Local causes</td>
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<td>And</td>
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<td>Drugs</td>
<td>Directives</td>
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Systemic disease
Blood (Haematological) disorders
- Anaemia
- Gammopathies
- Haematonic deficiencies
- Leukaemia and myelodysplastic syndrome
- Neutropenia and other white cell dyscrasias

Infections
- Acute necrotizing gingivitis
- Chickenpox
- Deep mycoses
- Hand, foot and mouth disease
- Herpangina
- Herpes simplex virus
- HIV
- Infectious mononucleosis
- Syphilis
- Tuberculosis

Gastrointestinal disease
- Coeliac disease
- Crohn disease
- Ulcerative colitis

Skin (Mucocutaneous) disease
- Behcet syndrome
- Chronic ulcerative stomatitis
- Epidermolysis bullosa
- Erythema multiforme
- Lichen planus
- Pemphigus vulgaris
- Sub-epithelial immune blistering diseases (pemphigoid and variants, dermatitis herpetiformis linear IgA disease),

Malignant neoplasms
- Oral
- Encroaching from antrum

Local causes
- Trauma
- Appliances
- Iatrogenic
- Non-accidental injury
- Self-inflicted
- Sharp teeth or restorations
- Burns
- Chemical
- Cold
- Electric
- Heat
- Radiation

Aphthae

Drugs
- Cytotoxic drugs
- Nicorandil
- NSAIDs

Miscellaneous uncommon diseases
- Eosinophilic ulcer
- Giant cell arteritis
- Hypereosinophilic syndrome
- Lupus erythematosus
- Necrotizing sialometaplasia
- Periarteritis nodosa
- Reiter syndrome
- Sweet syndrome
- Wegener granulomatosis

Table 2. Main causes of mouth ulcers

Vitamin deficiencies and some gastrointestinal disease (Tables 1 and 2).

Ulcers of local causes
At any age, there may be burns from chemicals of various kinds, heat, cold, or ionizing radiation or factitious ulceration, especially of the maxillary gingivae (Figures 3 and 4). Children may develop ulceration of the lower lip by accidental biting following...
as in whooping cough or in self-mutilating conditions.

Most ulcers of local cause have an obvious aetiology, are acute, usually single ulcers, last less than 3 weeks and heal spontaneously. Chronic trauma may produce an ulcer with a keratotic margin (Figure 5).

Recurrent aphthous stomatitis (RAS; aphthae; canker sores)

RAS is a very common condition which typically starts in childhood or adolescence and presents with multiple recurrent small, round or ovoid ulcers with circumscribed margins, erythematous haloes, and yellow or grey base (Figures 6 and 7).

RAS affects at least 20% of the population, with the highest prevalence in higher socio-economic classes. Virtually all dentists will see patients with aphthae.

Aetiopathogenesis

Immune mechanisms appear at play in a person with a genetic predisposition to oral ulceration. A genetic predisposition is present, and there is a positive family history in about one third of patients with RAS. Immunological factors are also involved, with T helper cells predominating in the RAS lesions early on, along with some natural killer (NK) cells. Cytotoxic cells then appear in the lesions and there is evidence for an antibody dependent cellular cytotoxicity (ADCC) reaction. It now seems likely therefore that a minor degree of immunological dysregulation underlies aphthae.

RAS may be a group of disorders of different pathogenesis. Cross-reacting antigens between the oral mucosa and microorganisms may be the initiators, but attempts to implicate a variety of bacteria or viruses have failed.

Predisposing factors

Most people who suffer RAS are otherwise apparently completely well. In a few, predisposing factors may be identifiable, or suspected. These include:

- Stress: underlies RAS in many cases. RAS is typically worse at examination times;
- Trauma: biting the mucosa, and dental appliances may lead to some ulcers;
- Haematinic deficiency (deficiencies of iron, folic acid (folate) or vitamin B₁₂) in up to 20% of patients;
- Sodium lauryl sulphate (SLS), a detergent in some oral healthcare products, may produce oral ulceration;
- Cessation of smoking: may precipitate or aggravate RAS;
- Gastrointestinal disorders particularly coeliac disease (gluten-sensitive enteropathy) and Crohn’s disease in about 3% of patients;
- Endocrine factors in some women whose RAS is clearly related to the fall in progesterone level in the luteal phase of their menstrual cycle;
- Immune deficiency: ulcers of a similar appearance to RAS may be seen in HIV and other immune defects, although clearly the aetiopathogenesis is different;
- Food allergies: in some studies hypersensitivity to various food additives has been shown to be important, although this is not a universal finding.

- Drugs (see below), Behcet syndrome, HIV, Epstein-Barr virus, auto-inflammatory states (periodic fevers) and skin diseases, such as erythema multiforme, may occasionally produce aphthous-like lesions.

Keypoints: aphthous ulcers

- They are so common that all the dental team will see them;
- It is important to rule out predisposing causes (sodium lauryl sulphate, certain foods/drinks, stopping smoking or vitamin or other deficiencies) or conditions such as Behcet syndrome that can cause aphthous-like lesions;
- It is necessary therefore to enquire about eye, genital, gastrointestinal or skin lesions and fever;
- Topical corticosteroids are the main treatment.

Clinical features

There are three main clinical types of RAS, though the significance of these distinctions is unclear and it is conceivable that they may represent three different diseases.

1. Minor aphthous ulcers (MiAU; Mikulicz Ulcer)
   - Occur mainly in the 10–40 year age group;
   - Often cause minimal symptoms;
   - Are small round or ovoid ulcers 2–4 mm in diameter in most situations but often more linear when in the buccal sulcus, a common site. The ulcer base is initially yellowish but assumes a greyish hue as healing and epithelialization proceeds. They are surrounded by an erythematous halo and some oedema;
   - Are found mainly on the non-keratinized mobile mucosa of the lips, cheeks, floor of the mouth, sulci or ventrum of the tongue.

   They are only uncommonly seen on the keratinized mucosa of the palate or dorsum of the tongue;
   - Occur in groups of only a few ulcers (1–6) at a time;
   - Heal in 7–10 days;
   - Recur at intervals of 1–4 months;
   - Leave little or no evidence of scarring

2. Major aphthous ulcers (MjAU; Sutton’s Ulcers; Periadenitis Mucosa Necrotica Recurrents (PMNR) (Figures 8, 9, 10)
   - Are larger, of longer duration, of more frequent recurrence, and often more painful than minor ulcers;
   - MjAUs are round or ovoid like minor ulcers, but they are larger and associated with surrounding oedema;
   - Reach a large size, usually about 1 cm in diameter or even larger;
   - Are found on any area of the oral mucosa, including the keratinized dorsum of the tongue or palate;
   - Occur in groups of only a few ulcers (1–6) at one time;
   - Heal slowly over 10–40 days;
   - Recur extremely frequently;
Table 3. Investigation of aphthae.

- Full blood count;
- Haematinsics;
  - Ferritin;
  - Folate;
  - Vitamin B₁₂;
- Serological screen for coeliac disease (tissue transglutaminase antibody or anti-endomysial antibody).

Table 4. Examples of readily available topical corticosteroids.

<table>
<thead>
<tr>
<th>Steroid</th>
<th>UK trade name</th>
<th>Dosage every 6 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium potency</td>
<td>Betnesol</td>
<td>0.5 mg; use as mouthwash</td>
</tr>
<tr>
<td>Betamethasone phosphate tablets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High potency</td>
<td>Clenil modulite</td>
<td>1 puff (200 mg) to lesions</td>
</tr>
<tr>
<td>Beclometasone (Beclomethasone)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dipropionate spray</td>
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</tr>
</tbody>
</table>

May heal with scarring;
Occasionally found with a raised erythrocyte sedimentation rate or plasma viscosity.

3. Herpetiform ulceration (HU)

- Are found in a slightly older age group than the other forms of RAS;
- Are found mainly in females;
- Begins with vesiculation which passes rapidly into multiple minute pinhead-sized discrete ulcers (Figure 11);
- Involve any oral site including the keratinized mucosa, increase in size and coalesce to leave large round ragged ulcers;
- Heal in 10 days or longer;
- Are often extremely painful;
- Recur so frequently that ulceration may be virtually continuous;
- Despite the name they have nothing to do with herpes infection.

Diagnosis

There are no specific tests, so the diagnosis must be made on history and clinical features alone. However, to exclude the systemic disorders discussed above, it is often useful to undertake the investigations shown in Table 3.

Biopsy is rarely indicated, usually where a different diagnosis is suspected.

Management

Other similar disorders, such as Behcet syndrome, must be ruled out (Article 2). Predisposing factors should then be corrected. Fortunately, the natural history of RAS is one of eventual remission in most cases. However, few patients have spontaneous remission until after several years and, although there is no curative treatment, measures should be taken to relieve symptoms and reduce ulcer duration.

- Good oral hygiene should be maintained. Chlorhexidine or triclosan mouthwashes may help.
- There is a spectrum of topical anti-inflammatory agents that may help in the management of RAS.
- Topical corticosteroids can usually control symptoms. Common preparations used include four times daily:
  - Medium potency topical betamethasone sodium phosphate (eg Betnesol), or
  - Higher potency topical corticosteroids (eg beclometasone – Clenil modulite) (Table 4).

   The major concern is of adrenal suppression with long-term and/or repeated application but there is no evidence that these cause this problem.

   Topical tetracycline (eg doxycycline), or tetracycline plus nicotinamide may provide relief and reduce ulcer duration, but should be avoided in children under 12 who might ingest the tetracycline and develop tooth staining.

   If RAS fails to respond to these measures, systemic immunomodulators may be required, under specialist supervision.

Keypoints for patients: aphthous ulcers

- These are common;
- They are not thought to be infectious;
- Children may inherit ulcers from parents;
- The cause is not known but some follow...
use of toothpaste with sodium lauryl sulphate, certain foods/drinks, or stopping smoking; 
- Some vitamin or other deficiencies or conditions may predispose to ulcers; 
- Ulcers can be controlled but rarely cured; 
- No long-term consequences are known.

Websites and patient information
http://www.doctorsofusc.com/condition/document/11983
http://www.cks.nhs.uk/patient_information_leaflet/mouth_ulcer

Infections
Infections that cause mouth ulcers are mainly viral, especially the herpesviruses, Coxsackie, ECHO and HIV viruses. Bacterial causes of mouth ulcers, apart from acute necrotizing ulcerative gingivitis, are less common. Syphils and tuberculous are uncommon but increasing, especially in people with HIV/AIDS. Fungal and protozoal causes of ulcers are also uncommon, but increasingly seen in immunocompromised persons, and travellers from the developing world.

Herpes simplex virus (HSV)
The term ‘herpes’ is often used loosely to refer to infections with herpes simplex virus (HSV), a ubiquitous virus which commonly produces lesions in the mouth and oropharynx. HSV is contracted by close contact with infected individuals from infected saliva or other body fluids after an incubation period of approximately 4–7 days.

Primary infection is often subclinical between the ages of 2–4 years. This is usually caused by HSV-1 and is commonly attributed to ‘teething’, particularly if there is a fever. However, primary infection can occur at any age and present with stomatitis (gingivostomatitis).

In teenagers or older, this may be due to HSV-2 transmitted sexually.

Generally speaking, HSV infections above the belt (oral or oropharyngeal) are caused by HSV-1 but below the belt (genital or anal) are caused by HSV-2.

The mouth or oropharynx is sore (herpetic stomatitis or gingivostomatitis): there is a single episode of oral vesicles which may be widespread, and break down to leave oral ulcers that are initially pin-point but fuse to produce irregular painful ulcers (Figure 12). Gingival oedema, erythema and ulceration are prominent and the cervical lymph nodes may be enlarged and tender, and there is sometimes fever and/or malaise. Patients with immune defects are liable to severe and/or protracted infections.

HSV is neuroinvasive and neurotoxic and infects neurones of the dorsal root and autonomic ganglia. HSV remains latent thereafter in those ganglia, usually the trigeminal ganglion, but can be re-activated to result in clinical recrudescence (see below).

Diagnosis
Diagnosis is largely clinical. Viral studies are used occasionally and can include:
- Culture – this takes days to give a result;
- Electron microscopy – this is not always available;
- Polymerase chain reaction (PCR) detection of HSV-DNA – this is sensitive but expensive;
- Immunodetection – detection of HSV antigens is of some value.

Management
Although patients have spontaneous healing within 10–14 days, treatment is indicated particularly to reduce fever and control pain. Adequate fluid intake is important, especially in children, and antipyretics/analgesics, such as paracetamol/acetaminophen elixir, help. A soft bland diet may be needed, as the mouth can be very sore. Aciclovir orally or parenterally is useful mainly in immunocompromised patients or in the otherwise apparently healthy patient, if seen early in the course of the disease, but do not reduce the frequency of subsequent recurrences.

Recurrent HSV infections
Up to 15% of the population have recurrent HSV-1 infections, typically on the lips (herpes labialis; cold sores), from re-activation of HSV latent in the trigeminal ganglion. The virus is periodically shed into saliva, and there may be clinical recrudescence. Re-activating factors include fever such as caused by upper respiratory tract infection (hence herpes labialis is often termed ‘cold’ sores), sunlight, menstruation, trauma and immunosuppression.

Lip lesions at the mucocutaneous junction may be preceded by pain, burning, tingling or itching. Lesions begin as macules that rapidly become papular, then vesicular for about 48 hours, then become pustular, and finally scab within 72–96 hours and heal without scarring (Figure 13).

Recurrent intra-oral herpes in apparently healthy patients tend to affect the hard palate or gingivae with a small crop of ulcers which heals within 1–2 weeks. Lesions are usually over the greater palatine foramen, following a palatal local anaesthetic injection, presumably because of the trauma.

Recurrent intra-oral herpes in immunocompromised patients may appear as chronic, often dendritic, ulcers, often on the tongue.

Diagnosis
Diagnosis is largely clinical; viral studies are used occasionally.
Management

Most patients will have spontaneous remission within one week to 10 days, but the condition is both uncomfortable and unsightly, and thus treatment is indicated. Antivirals will achieve maximum benefit only if given early in the disease, but may be indicated in patients who have severe, widespread or persistent lesions and in the immunocompromised. Lip lesions in healthy patients may be minimized with penciclovir 1% cream or aciclovir 5% cream applied in the prodrome. In severe cases where recurrences are frequent, systemic aciclovir may be indicated. Lip lesions in immunocompromised patients require systemic aciclovir or other antivirals such as valaciclovir (the precursor of penciclovir).

Keypoints for patients: cold sores

- These are common;
- They are caused by a virus (*Herpes simplex*) which lives in nerves forever;
- They are infectious and the virus can be transmitted by kissing;
- They may be precipitated by sun-exposure, stress, injury or immune problems;
- They have no long-term consequences;
- They may be controlled by antiviral creams or tablets, best used early on.

Websites and patient information
http://www.cks.nhs.uk/patient_information_leaflet/cold_sore
http://www.nlm.nih.gov/medlineplus/tutorials/coldsores/htm/_no_50_no_0.htm

Drug-induced ulceration

Drugs may induce ulcers by producing a local burn, or by a variety of mechanisms, such as the induction of lichenoid lesions (Figure 14). Cytotoxic drugs (eg methotrexate) commonly produce ulcers, but non-steroidal anti-inflammatory drugs (NSAIDs), including rofecoxib, alendronate (a bisphosphonate), nicorandil (a cardiac drug) and a range of other drugs, may also cause ulcers.

A drug history is important to elicit such uncommon reactions, and then the offending drug should be avoided.

Patients to refer:

- Patients with ulceration unresponsive to topical therapy;
- Malignancy;
- HIV-related ulceration;
- Syphilis;
- TB;
- Drug-related ulceration;
- Systemic disease;
- Mucocutaneous disorders.

Technique Tips - Management of a De-bonded, Fixed-fixed, Resin-bonded Bridge

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