



Fifteen-minute consultation: a structured approach to the management of recurrent oral ulceration in a child

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ABSTRACT

Objective To present a structured approach for an outpatient consultation of a child with recurrent mouth ulcers.

Method Review of literature and description of approach followed in our unit.

Conclusions The literature emphasises the need to consider local and systemic causes for oral ulceration in a child. Focused history and examination are key in establishing the cause and in order to ensure appropriate management.

BACKGROUND

A 12-year-old girl is referred to the general paediatrician with recurrent mouth ulcers. She has had three episodes in as many months, each lasting about a week, greatly limiting her intake of food and fluids for days and causing her to be so miserable that she cannot attend school or her favourite sporting and social activities. There is no apparent response to oral aciclovir therapy. Her parents are concerned as to the cause and about her falling behind at school should the episodes continue to recur.

TERMINOLOGY TAUTOLOGY?

The term 'aphthous ulcer' is somewhat of a tautology: 'aphtha' originates from the Greek for eruption or ulcer; medical texts define them as 'canker sores' (not very illuminating in this day and age); Webster definitions dictionary descriptively states they are 'roundish pearl-coloured specks or flakes in the mouth, lips etc, terminating in a white slough',¹ describing thrush. Better then to use the terms recurrent aphthous stomatitis (RAS) or recurrent oral/mouth ulceration to signify what we recognise as a

roundish breach in the integrity of the oral or lip mucosa.

WHAT SHOULD YOU COVER IN THE HISTORY?

Recurrent mouth ulceration is common, said to occur in between 1% and 10% of children.² Most troublesome is usually the associated pain, such that oral intake may be so reduced that the child becomes dehydrated, but otherwise, there is typically little by way of systemic upset. While the majority of cases are idiopathic, they can be associated with an underlying systemic disease, including nutritional deficiencies and inflammatory conditions; so generalised complaints will be a clue. A focused history and examination are therefore crucial in order to reach a working differential diagnosis and to plan appropriate management.

The following points should be covered in the history.

Onset, prodrome and disease pattern

Detailing the onset, progression and duration of individual lesions is important because it helps to distinguish localised aphthous ulcers from systemic causes of oral ulceration. In the absence of additional clinical features, recurrent ulcers that resolve with complete healing are suggestive of an idiopathic cause.

Age at first onset is important diagnostically; recurrent herpetiform ulcers are rare in children under the age of 5 years,³ while RAS associated with periodic fever syndromes such as periodic fever with aphthous ulcers pharyngitis and adenitis (PFAPA) tend to start before the age of 5 years.

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Timing of ulcers emerging in relation to other symptoms can also be a guide to diagnosis. Ulcers appearing following a prodromal tingling and additional features such as generalised malaise may help in differentiating idiopathic or herpetic from non-herpetic lesions. Other prodromal features such as fever, coryza or lethargy before ulcers appear may indicate viral causes.

Systemic features

When systemic features accompany RAS, the priority is to exclude serious underlying disease because mouth ulcers may be the sentinel feature of more sinister serious pathology.

- ▶ Haematological disorders, such as leukaemia and cyclical neutropenia may present with RAS.
- ▶ Immunodeficiency (primary or secondary immunodeficiency) may present with RAS, accompanied by recurrent or unusual infections, failure to thrive, dysmorphic features or poor skin condition.
- ▶ RAS with cyclical fever with periods of recovery in an otherwise well child may indicate one of the periodic fever syndromes.
- ▶ In the context of anorexia, weight loss, change in bowel habit or chronic diarrhoea, RAS may point to a protein-losing enteropathy or inflammatory bowel disease.
- ▶ RAS in the context of recurrent orogenital ulcers may represent autoimmune conditions such as Behcet's disease although these are rare in childhood.

Table 1 offers an overview of causes and proposed investigations for oral ulceration.

Dietary symptoms

History of pica or fussy eating could point towards dietary deficiency as the potential cause.³

FOCUSED EXAMINATION IN A CHILD WITH RAS

Assessment for aetiological factors: Examination of skin, joints and assessment of growth should be undertaken with care to exclude serious underlying conditions such as autoimmune disease, malignancy and immunodeficiencies.

Lesions around the urethral opening may indicate Behcet's disease if infective causes (viral or bacterial) are excluded.

Idiopathic and herpetic ulceration: Once you have excluded systemic causes for recurrent aphthous ulceration, then it is important to make the distinction between idiopathic ulceration and herpetic ulcers.

Classification of ulceration by morphology: Lesions can be classified according to size, number, location, healing time and healing completeness; the categories are minor, major or herpetiform. Table 2 describes the features of each type of ulceration. Presence of clusters of intensely painful tiny lesions is suggestive of herpetic stomatitis. figures 1–3 demonstrate different ulcer types.

WHAT INVESTIGATIONS MIGHT YOU CONSIDER?

In the absence of systemic features, extensive investigation is rarely warranted; the child and parents can be reassured that the episodes are likely to be self-limiting. If episodes are severe, it might be helpful to substantiate your reassurance with basic tests, such as full blood count and blood film to exclude malignancy, neutropenia and infection, and viral swabs for culture or molecular diagnostics.

Where further investigation is warranted due to systemic features you may consider:

Table 1 Causes of oral ulceration and suggested first-line investigations

	Causative agent	Associated features	Initial investigations
Infection			
Recurrent ulcers	Hand foot and mouth disease: Coxsackie A virus or enterovirus 71, Herpes Simplex 1 and 2, HIV	Tingling prodrome, systemic features such as fever, lethargy, weight loss and recurrent illnesses.	Full blood count, swab for viral diagnostics, serology for HIV and virology. TB testing where appropriate.
Persistent ulcers	HHV 6, Varicella /Herpes Zoster, CMV, EBV, Syphilis, Tuberculosis		
Autoimmune disorders	Crohn's disease, Behcet's disease, Systemic Lupus Erythematosus, Coeliac disease, PFAPA syndrome, MAGIC syndrome	Systemic features such as weight loss, bleeding, lethargy, cycles of fever, diarrhoea, myalgia, arthralgia	Full blood count, inflammatory markers, ESR, autoantibodies, IgA, tissue transglutaminase.
Immune disorders	Immunodeficiency syndromes	Recurrent infections, failure to thrive	Full blood count, immunoglobulins, lymphocyte subsets, serology for HIV.
Trauma	Teething, dental appliances	History of trauma	
Vitamin deficiencies	Iron, B12, folate, vitamin C, magnesium, zinc	Poor diet, weight loss, skin and hair changes, pallor, tongue depapillation	Full blood count, haematinics, zinc, magnesium, Vitamin C levels
Neoplastic/haematological	Anaemia, leukaemia, agranulocytosis, cyclical neutropenia	Lethargy, fevers, pallor, tongue depapillation	Full blood count, LDH, urate, blood film
Idiopathic recurrent aphthous stomatitis	Normal haematology	Recurrent and healing completely between episodes	Full blood count, blood film, haematinics, viral swab for diagnostics

MAGIC syndrome, mouth and genital ulcers with inflamed cartilage; PFAPA syndrome, periodic fever, aphthous ulcers, pharyngitis and adenitis; TB, tuberculosis; ESR, erythrocyte sedimentation rate; HHV, human herpes virus; CMV, cytomegalovirus; EBV, Epstein–Barr virus; LDH, lactate dehydrogenase

Table 2 Classification of oral aphthae by morphology⁴

Class	Features
Minor Aphthae (80%) MiRAS Figure 2	<ul style="list-style-type: none"> ▶ Single to few ulcers ▶ <1 cm diameter ▶ Spontaneous resolution within 7–10 days ▶ No scarring ▶ Occur predominantly on non-keratinised mucosa
Major Aphthae (10%) MaRAS Figures 1 and 3	<ul style="list-style-type: none"> ▶ Single to few ulcers ▶ Deep and >1 cm in diameter ▶ Prolonged healing >2 weeks ▶ Scarring ▶ Occur on non-keratinised but also keratinised mucosa
Herpetiform Aphthae (10%) –	<ul style="list-style-type: none"> ▶ 10–100 ulcers ▶ Very small (1–3 mm, often grouped) ▶ Spontaneous healing in days to weeks ▶ May scar ▶ Often occur on ventral surface of tongue

RAS, recurrent aphthous stomatitis

1. **Haematological tests:** Beyond the full blood count, haematinics may be useful to rule out nutritional deficiencies (iron, ferritin, folate, total iron-binding capacity, B vitamins, zinc and magnesium). Where there is suspicion of immunodeficiency, plasma immunoglobulins and lymphocyte subsets should be checked.
2. **Serological testing:** With systemic features, there should be a low threshold for excluding HIV infection (ensuring that both parent and child—as age/cognitively-appropriate—are advised of the intention to test beforehand). Additional tests such as erythrocyte sedimentation rate, antinuclear antibody and antineutrophil cytoplasmic antibodies should be considered to investigate autoimmune conditions. IgA anti-endomysial antibodies and IgA and IgG tissue transglutaminase antibodies may be useful if there is a history of poor weight gain or other clues such as diarrhoea, lethargy or abdominal distension that might point to inflammatory bowel disease.

**Figure 1** Major recurrent aphthous stomatitis on buccal mucosa.**Figure 2** Minor recurrent aphthous stomatitis.

3. **Local infection tests:** Swabs from the ulcer base (as tolerated) should be sent for bacterial and viral diagnostics (PCR, cultures etc.) where there is a suspicion of infectious aetiology: herpes simplex virus (HSV), tuberculosis, enteroviruses etc, although the yield is low. However, serology for Epstein–Barr virus and cytomegalovirus is rarely useful in determining the cause of RAS.
4. **Histology:** There is rarely need to biopsy ulcers, but unusual, persistent and recalcitrant lesions might warrant this, especially where there is suspicion of granulomatous conditions such as orofacial granulomatosis, tuberculosis or malignancy. Similarly, for typical but severe herpetiform ulcers, which are negative on infection screening, biopsy for tissue culture may be considered to confirm the diagnosis if the lesions are unresponsive to treatment.

WHAT ARE THE TREATMENT OPTIONS?

While the long-term management of recurrent ulceration depends on the diagnosis, acutely the principal goals are threefold:

1. to adequately manage any pain,
2. to ensure adequate hydration and
3. to promote healing.

Especially for infants and small children, careful assessment for decreased feeding, short-term weight loss and poor urine output are important. Dehydration can

**Figure 3** Recurrent aphthous stomatitis on palate.

result insidiously, especially where reduced fluid intake is coupled with increased insensible losses from mouth breathing and drooling, particularly if the need for effective symptomatic relief is not appreciated.

Where an underlying cause is found, measures to prevent recurrence are considered where applicable, such as for herpes simplex ulceration or nutritional deficiencies.⁵

Local agents

Local anaesthetics: Topical local anaesthetics (washes, gels, sprays, lozenges etc.) are widely used to provide some short-term symptomatic relief, which also help improve oral intake.

Antimicrobials: Antimicrobial mouthwash such as chlorhexidine help to reduce duration of ulceration by preventing superinfection, although this can be at the cost of short-term brown staining of the teeth and tongue.

Tetracycline mouthwash, for example, doxycycline (100 mg dissolved in water and held in mouth for 3 min before discarding) is very useful in reducing pain and duration of ulcers.⁶

Topical Steroids: Topical steroid preparations are helpful for promoting ulcer healing and preventing recurrence.⁷ These include corlan pellets (that can be placed adjacent to the ulcer), sprays (eg, fluticasone spray) and mouthwashes (eg, betamethasone tablets dissolved to make a mouth rinse).

Systemic agents

Acute therapy: For likely or proven herpetic ulcers, early administration of aciclovir/valaciclovir, intravenously or, if tolerable, orally, is appropriate for reducing the viral load and to accelerate healing. The typical course required is 7–10 days, longer in severe cases. After an episode, advise that prompt and intense treatment of any future episodes may be of benefit; recognise prodromes such as the prevesicle

tingle of HSV ulcers as the prompt to commence treatment as this may abort or abrogate an episode.

Preventative therapies: In cases where recurrences are frequent, preventative strategies should be considered that are proportionate to the severity and frequency of recurrences. However, evidence of efficacy is limited. A Cochrane review found only two trials of aciclovir treatment for herpes stomatitis with weak evidence of benefit.⁸ However, it has been demonstrated that valaciclovir may reduce frequency of recurrences if given as prophylaxis for proven HSV stomatitis in adults and children.^{5 9 10}

Steroid treatment should only be considered for severe recurrent aphthous ulceration and only when underlying infective or malignant causes have been excluded. If steroid treatment is considered, prednisolone is typically prescribed in dose of 1 mg/kg (maximum 60 mg) for 7 days to be tapered over next few days, started within a week of onset (ideally within 72 h) provided there is no contraindication. Referral to a specialist Oral Medicine unit in severe, recalcitrant cases is often warranted.

Colchicine 1–2 mg/day may decrease severity and duration of ulcers. Although this is rarely used in children, it is worth considering in severe, recalcitrant cases.

EVALUATING SEVERITY AND RESPONSE TO TREATMENT

Disease severity scoring can be helpful to assess severity and response to treatment, and a recently devised system for ulcer severity scoring includes number, size, duration, ulcer-free period, site and associated pain.¹¹ The reference has a useful clinical scoring tool for assessment of the disease course over time, such that the effectiveness of acute therapies, the need for prophylactic measures and its effect on the disease course can be evaluated with some objectivity over

Table 3 Overview—a structured approach to the management of RAS

History	Examination	Investigations	Management
To EXCLUDE systemic features that may indicate other causes and differentiate between herpetic and non-herpetic RAS:			Continued monitoring of pain, dehydration, healing and treatment response
<ul style="list-style-type: none"> ▶ Age at first onset ▶ Prodrome ▶ Onset ▶ Duration (days) ▶ Pain Severity ▶ Ulcer-free period (weeks) 	<ul style="list-style-type: none"> ▶ Site ▶ Number ▶ Size and depth (mm) ▶ Scarring ▶ EXCLUDE involvement of other systems (skin, eyes, joints) ▶ Growth 	<ul style="list-style-type: none"> Full blood count, blood film, haematinics, viral swab for diagnostics 	<ol style="list-style-type: none"> 1. <i>Pain management:</i> <ul style="list-style-type: none"> ▶ Topical anaesthetics 2. <i>Manage dehydration:</i> <ul style="list-style-type: none"> ▶ Advice on feeding ▶ Promote healing 3. <i>Promote healing:</i> <ul style="list-style-type: none"> ▶ Antimicrobial mouthwash ▶ Topical steroids ▶ Oral aciclovir if likely herpetic ulcers 4. <i>Preventative treatment:</i> <ul style="list-style-type: none"> ▶ Oral valaciclovir ▶ Consider steroids and colchicine (rare)

RAS, recurrent aphthous stomatitis

time. In younger children, where examination is difficult and a meaningful grading score is not achievable, observation of additional skin lesions and level of pain are important. Table 3 summarises the approach to children with RAS.

CONCLUSIONS

RAS is common in childhood and causes are usually benign and self-limiting, so we highlight when and how to investigate for rare but important aetiologies and summarise treatment options for common causes, recognising that the evidence base is limited. Treatment needs to be individualised and attempts made to evaluate the effect of interventions on the clinical course over time. As the majority of ulcers without systemic features are idiopathic, effective symptom control may be the mainstay of care once the child and family are assured of the benign clinical course.

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