

# Making sense of mouth ulceration: part five

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In the fifth part of the series, Crispian Scully looks at the issue of gastrointestinal disorders and mouth ulceration.

The clinical appearance of an oral ulcer on its own is rarely diagnostic. Any ulceration with other orofacial or extraoral lesions may be suspect.

In the light of multiple causes, some systematic way of dealing with ulceration is needed, such as my system of splitting causes into:

- Systemic
- Malignancy
- Local
- Aphthae
- Drugs.

## Gastrointestinal disorders

This article discusses the third of the systemic causes – gastrointestinal disorders.

The main gastrointestinal disorders that may present with mouth ulceration include coeliac disease, and Crohn's and related diseases.

## Coeliac disease

Coeliac disease (gluten sensitive enteropathy) is usually an inherited disorder. People with the disease have sensitivity to gluten, a protein found mainly in wheat, and patients suffer small intestinal disease leading to malabsorption. This manifests in many ways, especially:

- Haematinic deficiency
- Failure to thrive
- Infertility.

Oral lesions may include mouth ulceration (ulcers mimic aphthae) and enamel hypoplasia in early onset coeliac disease.

Coeliac disease is frequently under-diagnosed and we still see older people (even in their 60s and 70s) whose diagnosis has been missed. Diagnosis is typically confirmed by:

- Anti-endomysial antibodies
- Transglutaminase
- Small bowel (jejunal) biopsy.

Management is by antigen exclusion – a gluten-free diet.

## Crohn's disease

Crohn's disease is a heterogeneous group of chronic inflammatory disorders mainly causing regional enteritis (ileitis).

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Figure 1: Lip swelling.



Figure 2: Ulceration.



Figure 3: Gingival swelling.

Seen mainly in Caucasians, it is increased in Ashkenazi Jews and 20% of people with Crohn's disease have a blood relative with inflammatory bowel disease (IBD).

The cause is unclear but the inflammatory response is probably mediated by factors such as tumour necrosis factor alpha (TNF $\alpha$ ) and there are non-caseating granulomas in submucosa and lymph nodes.

Microorganisms have been implicated but some may simply take advantage of damaged mucosa and inability to clear bacteria from the intestine.

Crohn's disease can affect any part of the digestive tract, from mouth to anus – as well as producing extraintestinal disease in some patients.

Manifestations depend on the severity and sites affected, but typical features include:

- Abdominal pain
- Anaemia
- Arthralgia
- Diarrhoea (repeated episodes)
- Non-specific constitutional signs and symptoms
- Weight loss.

Orofacial involvement is common and can precede intestinal symptoms. It includes:

- Lip or face swelling (Figure 1)
- Ulceration (may be linear) (Figure 2)
- Gingival swelling (Figure 3)
- Mucosal 'cobblestoning' and tags
- Angular cheilitis (stomatitis) and split lips (Figure 4).

However, because of vague and protean manifestations, Crohn's disease is often under-diagnosed. There are no specific assays or diagnostic analyses – it is a diagnosis by exclusion. Tests include:

- Faecal calprotectin (often raised)
- Blood count (anaemia common)
- Serum potassium, zinc and albumin (often reduced)
- Erythrocyte sedimentation rate (ESR), C-reactive protein

(CRP), anti-Saccharomyces cerevisiae antibodies, antineutrophil cytoplasmic antibody (ANCA) and seromucoid (often raised)

- Small bowel MRI or CT; plain-film and contrast radiography
- Endoscopy (sigmoidoscopy, colonoscopy)
- Ultrasound
- Mucosal biopsy (for granulomas).

Diagnosis of intestinal Crohn's disease can be fraught – not least because of patchy distribution, and is sometimes only confirmed after intestinal resection and histopathological examination of specimen late in the course of disease. Repeated evaluations (including sequential colonoscopies) may be required to establish the diagnosis.

Treatment is by specialists with a high-fibre diet and sometimes:

- Aminosalicylates (ASA), or newer 5-aminosalicylates (mesalazine, olsalazine)
- Antimicrobials (metronidazole, ampicillin, ciprofloxacin, others)
- Immune modifiers: corticosteroids locally (prednisolone, budesonide) or systemic corticosteroids, azathioprine, 6-mercaptopurine (6-MP), or methotrexate and biologics (anti-TNF $\alpha$  agents [adalimumab, certolizumab pegol or infliximab])
- Thiopurines (eg, 6-MP, azathioprine) can increase risk of non-Hodgkin's lymphoma.

Up to 60% of patients with Crohn's disease require surgery at some point.

### Orofacial granulomatosis

Some patients with clinical evidence consistent with oral Crohn's disease have no intestinal symptoms of the disease and, while some may have evidence of Crohn's disease in the intestine, others do not. Orofacial granulomatosis (OFG) is the term coined for those with no detectable gastrointestinal involvement.



Figure 4: Split, swollen lip and palatal lesions.



Figure 5: OFG facial swelling.

Orofacial lesions mimic those in Crohn's disease and may include:

- Facial or labial swelling (Figure 5)
- 'Cobblestone' proliferation of mucosa or mucosal tags
- Ulcers.

Variants include:

- Miescher, or granulomatous cheilitis
  - Lip swelling alone
- Melkerson-Rosenthal syndrome
  - Lip swelling
  - Fissured tongue
  - Facial palsy.

OFG may sometimes result from reactions to foods or additives – most commonly:

- Cinnamaldehyde
- Benzoates.

Like Crohn's disease, OFG is often under-diagnosed because of vague and protean manifestations. Again, it is a diagnosis by exclusion – there are no specific diagnostic tests. Reactions to foods should be excluded by antigen exclusion/allergy tests. Gastrointestinal and other investigations are often indicated to exclude Crohn's disease and other conditions that can produce granulomas (notably tuberculosis and sarcoidosis).

If systemic Crohn's disease can be excluded, patients still need to be kept under observation for possible Crohn's disease development later.

Management is challenging. Exclusion of offending

substances may help facial swelling resolve. Topical or intralesional triamcinolone acetonide alone or in combination with topical pimecrolimus or tacrolimus may be trialled but systemic clofazimine, dapsone, methotrexate, tacrolimus, thalidomide, other immunosuppressants or anti-TNF biologics (under physician guidance) may be needed.

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