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Saturday, August 10, 2019

(Room 2)

11:00 - 11:55 WS #89: Ulcers in the Mouth

12:05 - 13:00 WS #99: Ulcers in the Mouth (Repeated)

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Ulcers in the Mouth

South GP CME 2019



Objectives

- Recognise common causes of oral ulceration
- Initiate management by controlling pain and devising an ongoing treatment plan
- Recognise sinister signs that require specialist management



Oral Ulceration

- Common and painful – hence presentation
- An ulcer is a **breach in the oral epithelium** and results in **pain** or soreness, especially when eating spicy foods or citrus foods
- Patients vary enormously in their symptoms and there are a diverse number of causes of oral ulcers
- The aim is to discuss mainly history and clinical presentation rather than clinical or pathological classifications

Main Causes of Mouth Ulcers

- Trauma
- Recurrent Aphthous Stomatitis
- Infectious causes
- Dermatological / Immunological (includes allergy)
- Malignancy

The history

Some types of oral ulcers are recurring, so often no ulcers on the day

Some key aspects of history may help to distinguish between various types of oral ulcers

Importance of History in Oral Ulceration

- Age of patient
- Has the patients had previous ulcers and are they cyclical or persistent
- Site of ulcers...?on keratinised or non-keratinised mucosa
- Has the patient had herpes in the past?
- Does the patient have a history of allergies?

Age

- **Recurrent Aphthous Stomatitis** usually occurs 10-40 year olds
- **Dermatological:** OLP & vesiculobullous will usually occur in middle-aged and beyond
- **Primary Herpes:** usually children, but if adult it will be accompanied by flu-like illness
- **Malignancy:** All ages. SCC will usually be older adults. Haematological malignancies occur in children and adults

Importance of History in Oral Ulceration

- Age of patient
- Has the patients had previous ulcers and are they cyclical or persistent?
- Site of ulcers...on keratinised (hard palate) or non-keratinised mucosa?
- Has the patient had herpes in the past?
- Does the patient have a history of allergies, atopic?

History

- Single v multiple
- Does it involve other mucosal sites e.g. eyes
- Has the patient started drugs recently or are they on nicorandil?
- Has the patient stopped smoking recently?
- Is the patient generally in good health?

Main Causes of Mouth Ulcers

- Trauma
- Recurrent Aphthous Stomatitis
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Traumatic

- Mechanical (toothbrush, dentures)
- Chemical (aspirin burn)
- Thermal (pipe smoking, hot food)





Management of traumatic oral ulceration

- Try to identify and remove cause
- Review in 2 weeks
- If not healed, reconsider diagnosis e.g. if it is a solitary ulcer, consider carcinoma and biopsy

Recurrent Aphthous Stomatitis

Minor RAS (80% of all RAS)

- 1-3mm “regular” outline oral or oval ulcers
- Occur in crops, with variable ulcer-free periods
- Last up to 10 days & heal without scarring
- Never occur on keratinised mucosa i.e. never on hard palate or attached gingiva
- Painful







Recurrent Aphthous Stomatitis

- Mainly “Minor Aphthous Stomatitis”(80%)
- Also “Major” & “Herpetiform” (20%) stomatitis

Major Aphthous Stomatitis



Recurrent Aphthous Stomatitis

- *“No known cause and no know cure?”*
- It is known that about 20% of people get aphthae
- Much is known about what triggers ulcers in these people
- Therefore, the aim is to avoid triggers



RAS.....known triggers

- Haematinic deficiency in 20% of sufferers
- Iron, B12 & Folic Acid
- 60% positive response following appropriate supplementation

RAS triggers

- Psychological factors
- Allergies / Drugs (SLS free toothpaste may help)
- Systemic causes e.g. cyclic neutropenia, Crohn's or Coeliac disease

SLS free toothpaste



- Most toothpastes contain sodium lauryl sulphate
- Small studies looking at SLS free toothpaste in RAS
- Herlofson (1994) RCT of 10 patients showed mean reduction of 70% in numbers of ulcers in RAS patients
- Suggested SLS denatures the oral epithelium making it more susceptible to ulceration

Oral Ulceration as a manifestations of Crohns disease

- Manifestations may arise as specific lesions that may be due to the same disease process as in CD
- Oral manifestations may be secondary to malabsorption or blood loss







More triggers in RAS

- Trauma (penetrating)
- Cessation of smoking as less keratinisation of mucosa
- Family history
- Endocrine factors
- Immunological factors..T helper cells predominate with some NK cells early on in lesion, followed later by cytotoxic cells & evidence of antibody dependent cellular cytotoxicity

RAS management

- Pain relief - Difflam, Hyaluronic Acid
- Address precipitating factors e.g. replacement therapy & investigation of underlying cause
- B vitamins
- SLS free toothpaste
- Avoidance of sharp foods **Topical & systemic agents**

Topical steroids..

- 0.1% Triamcinalone acetanide paste (Oracort, Kenalog in Orabase) use 4 times daily on **dried** mucosa
- Redipred 5mg prednisolone / ml...suggest mouthwash diluted in 20mls
- Betamethasone (becotide) 50 or 100 inhaler 2 puffs 4 times daily or cream. Potent and off-license
- Flixonase spray

Topical Hyaluronic Acid (Aftamed in NZ)

- Good pain control of OLP over 4 hour period
- Some enhanced healing
- No contraindications for use and no adverse events. Generally easy and pleasant to use

Infectious Oral Ulceration

Viral

- Tends to be all over mouth, including keratinised epithelium.
- Usually extensive ulceration
- If secondary HSV, should be history of cold sores

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Management

- Often children
- Advice that child is infectious (eyes and others..school & family)
Will be better in 7-10 days
- Fluids & **Symptomatic** relief
- Never steroids
- Perhaps anti-virals



Bacterial Causes of Oral Ulceration

Syphilis

- Incidence lowered in 1980s due to contact tracing, but rose again from mid-1990s and continues to rise
- Worldwide trend
- Oral lesions in each stage are quite different and generally pass unnoticed
- Secondary syphilis – a possible cause of oral ulceration

Secondary Syphilis

- 6/52 after primary lesion or 2-4 months after exposure
- Mild fever, malaise, headache, generalised lymphadenopathy
- Followed by skin rash & oral lesions
- Rash is variable..pinkish symmetrical macules that start on trunk

Oral Lesions (Secondary syphilis)

- Tonsils, lateral border of tongue and lips
- May be flat ulcers covered by greyish membrane (snail tract lesions)
- Or ulcers that coalesce – very marked lymphadenopathy
- Discharge from ulcers contains spirochaetes and saliva is very infectious
- Serology positive & diagnostic. Biopsy unhelpful

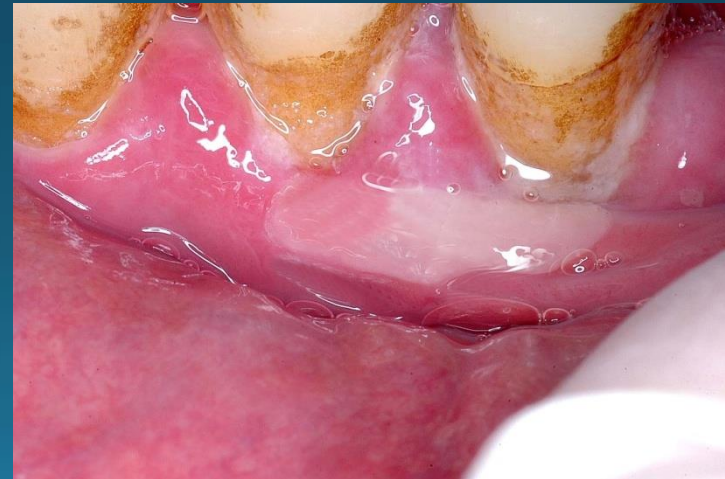


Vesiculobullous Disorders

- Pemphigus
- Pemphigoid
- Erythema Multiforme (also under allergy)

Vesicles and bullae

- A vesicle is a small fluid-filled blister affecting the skin or mucosa.
- Bullae are larger fluid filled lesions
- Oral bullae are caused by:
 - Viral infections
 - Drug reactions
 - Genetic disorders
 - Autoimmune disorders



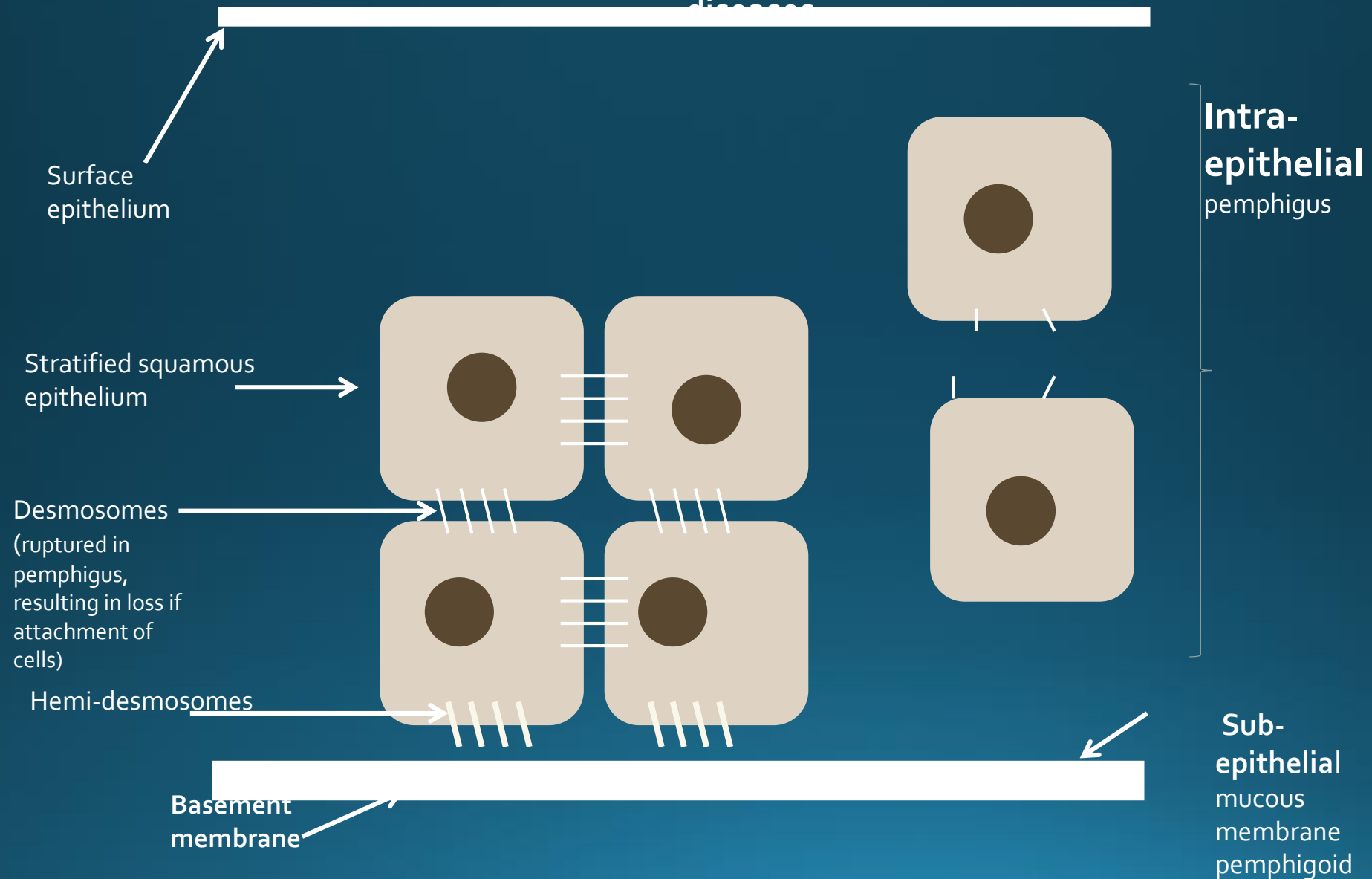
Clinical Presentation

- Blisters are rarely seen
- Usually non-healing ulcers with tags
- Occur on areas of pressure
- Direct extension to oesophagus, pharynx & larynx
- May present as sore throat, swelling or pain & difficulty in swallowing



Splits in the mucosa of vesiculobullous diseases

Splits in the mucosa of vesiculobullous



Pemphigus (Greek *pemphix* = *bubble or blister*)

- Term for group of potentially *life threatening*, chronic, autoimmune disorders
- Characterized by epithelial blistering
- Affects mucocutaneous surfaces
- Autoantibodies are directed against desmosomes i.e. the anchoring complexes that link epithelial cells to each other
- Several variants (depending on which desmosome component autoantibody is directed)

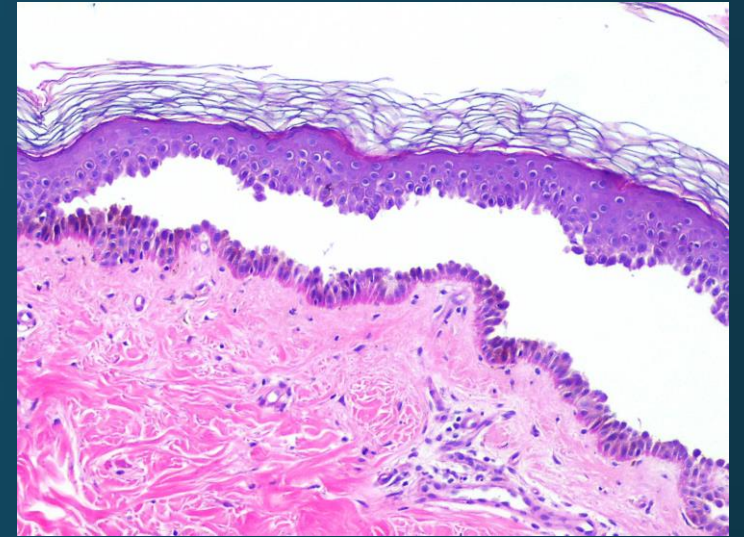
Pemphigus vulgaris

- Life threatening, organ specific human autoimmune disease
- 70% of pemphigus cases
- Wide range of incidence across the world (0.76-16 cases per million, per year)
- More common in Jewish populations (Ashkenazi origin) and in Eastern countries (India, Malaysia, China, Japan)
- Affects males and females equally
- Mean age 40-60 years

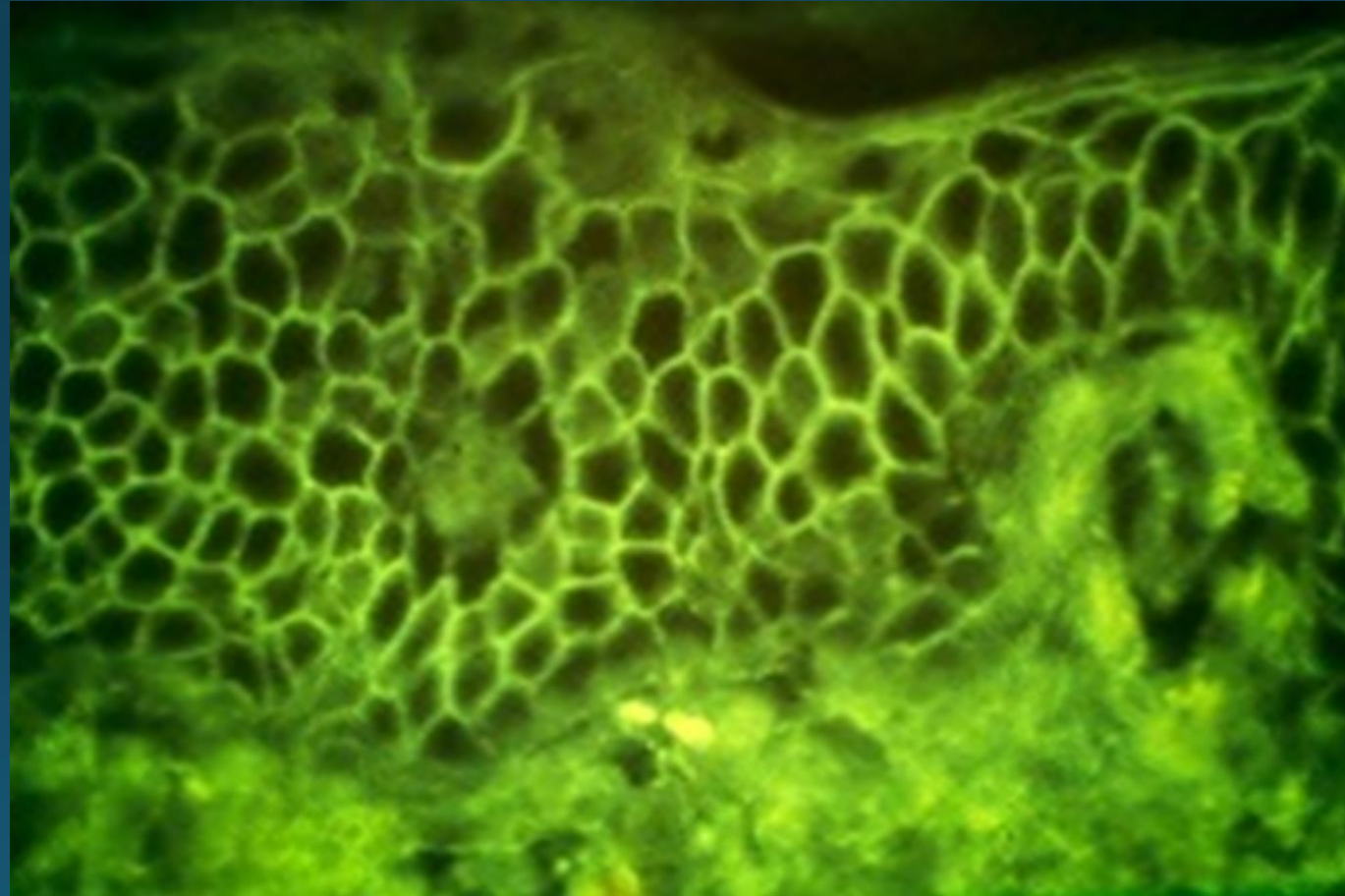


Histopathological Features

- Intraepithelial bullae
- Cleft like spaces
- Secondary acanthosis occurs between stratum spinosum & basal cells
- Basal cells project into bullae..”tombstones”
- Little inflammatory cell infiltration until rupture
- Small rounded cells with dark nuclei may occur in clumps “Tzanck cells”



Direct Immunofluorescence on biopsy sample



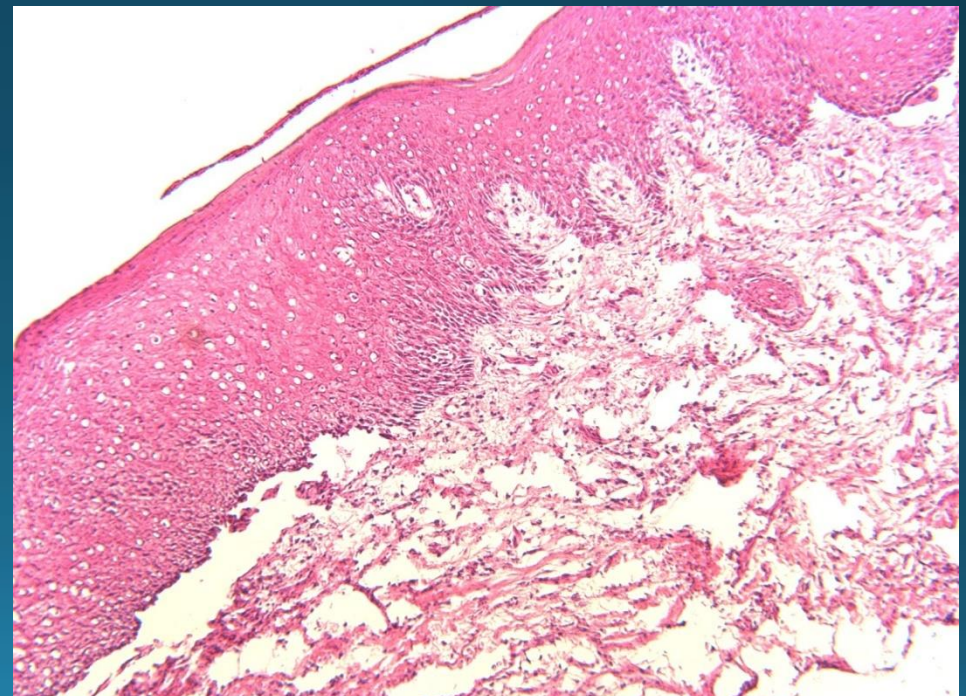
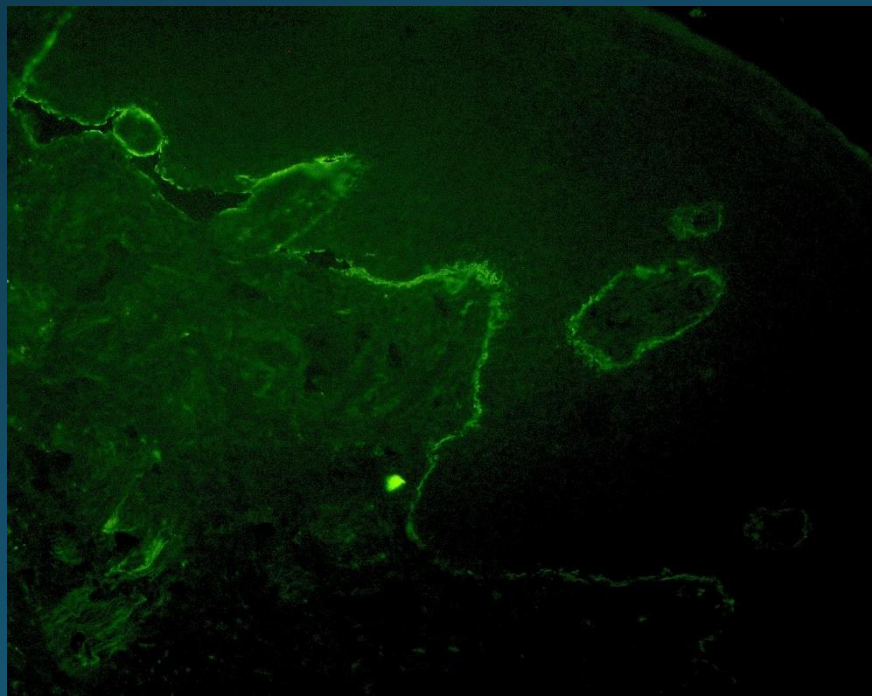


Management

- A challenge
- Use of glucocorticoids alone or in combination with immunomodulant drugs may control disease activity – difficult to determine which is superior
- Need to monitor
- Once remission is achieved, reduce dose

Pemphigoid

- A family of chronic sub-epithelial blistering disorders
- Can affect the oral, nasal and conjunctival mucous membranes
- F>M
- Bullous & Mucous membrane pemphigoid
- Genetic predisposition but may be drug induced



Management

- Usually topical steroids
- Sometimes systemic steroids
- Occasionally dapsone



Recurring Erythema Multiforme

- An acute, reactive, immune mediated disorder of the skin and mucosal membranes
- A spectrum from mild to Stevens-Johnson syndrome (mortality 5%)
- EM affects healthy young adults, peak being 20-40 years
- Lesions occur as a result of body reactivity to a number of antigens, often herpes simplex (23-70%), but may be drugs, mycoplasma (children), alcohol, NSAIDS, anti-epileptics
- No specific diagnostic test (exclude a viral cause)
- Recurring – generally better with each episode
- Supportive care – topical steroids



Drugs causing Oral Uceration

- Cytotoxics e.g. Methotexate
- NSAIDS
- Nicorandil
- Others e.g. captopril

Drugs causing oral ulceration

Nicorandil

- Potassium channel activator for angina pectoris
- Causes severe persistent malignant looking oral ulceration within 9 months of starting and resolves with 1 month of stopping Scully C, OS OM OP OR & Endo 2001;91(2):189-193



Oral Lichen Planus

Know your lichens

Oakmoss (*Evernia prunastri*)

Usually found in Britain growing on the branches of oak trees, oakmoss is sensitive to nitrogen pollution, so can be used as a useful indicator of air purity. During the Bosnian war, it was one of a number of lichens used by isolated enclaves as an emergency food



Horsehair (*Bryoria* sp)

Horsehair species festoon the branches of both pine and spruce in the boreal forest. This lichen is used as fodder for reindeer during periods when reindeer moss is hard for them to reach. It can be cooked as an emergency food and, when dried, makes an excellent tinder for fire lighting

Oral Lichen Planus

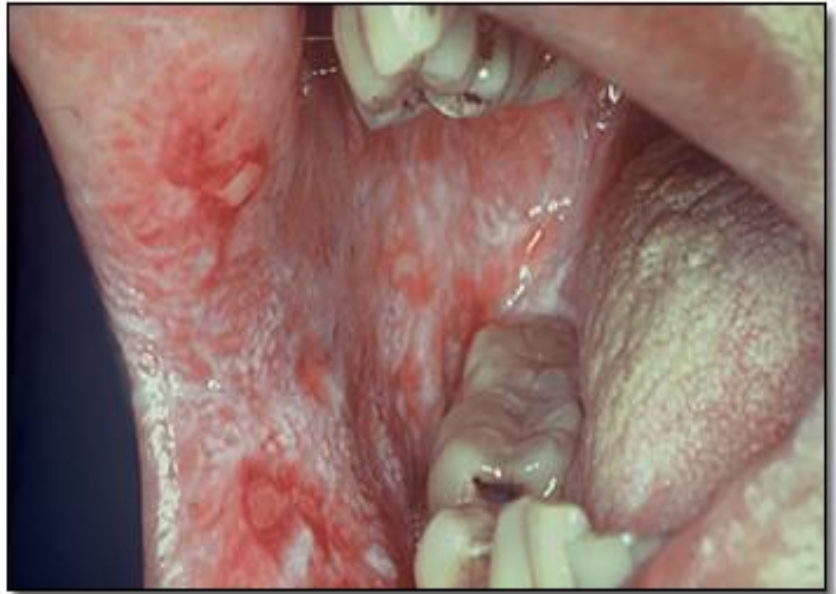
- A common chronic inflammatory mucocutaneous disorder that typically affects mucous membranes (mainly the mouth) and skin
- It occurs in 1-2% of the population
- It typically occurs in middle-ages females, but also affects males
- As yet no particular ethnic groups have been identified as being at particular risk

Aetiology of OLP

- Remains unclear
- It is believed that OLP represents a cell-mediated immunological reaction within the affected tissues, although the precise trigger is unknown
- Associations with Hepatitis C virus
- **Stress** exacerbates the condition

Clinical presentation

- **Reticular**..often symptoms of roughness rather than pain
- **Papular**..white raised areas of 1-2 mm in diameter
- **Plaques**..homogenous leukoplakia, more usually in smokers
- **Atrophic**..thin mucosa, red but not ulcerated and often painful
- **Erosive**..frank painful ulcers
- **Bullous**..vesicles or small blisters within white patches







Other LP sites

- Skin..purple / silver pruritic papules, often involving wrists and shins
- May involve nails (longitudinal ridging)
- Can cause alopecia
- Frequently genital involvement



Oral Lichenoid reaction

- This refers to LP which is thought to be an allergic reaction to drugs, amalgam etc and is more likely to be asymmetrical and in unusual sites like the palate
- Drugs e.g. NSAIDS, anti-diabetics, anti-hypertensives, anti-malarials, anti-microbials etc.
- Dental restorations, particularly amalgam



An Oral Potentially Malignant Disorder

- Current evidence based on follow-up studies and retrospective studies, reporting approximately 1% over 10 years
- Risk possibly 3-5% over 10 years (IAOO 2011)
- Possibly oral lichenoid are most at risk (*van de Meij 2003*)
- Theoretically, immunosuppressant therapy could increase the risk, but Gandolfo (2004) suggested that this was not the case
- Traditional risk factors for squamous cell carcinoma (scc) do not appear to play a role



Aspects of treatment

EAOM guidelines



- 1. Asymptomatic , non-ulcerative. Explanation, good OH and general advice
- 2. Symptomatic, non-ulcerative. Topical anaesthetic or barrier agents, with reduction of provoking factors
Topical Hyaluronic acid

- 3. Erythematous / ulcerative OLP. Topical corticosteroids with antifungals if required.
- Attend hygienist, perhaps replacement of amalgams. Long term review.
- 4. Severe symptomatic, ulcerative OLP. Systemic steroids (reducing dose) and anti-fungals
- 5. Recalcitrant OLP. Low dose, short term corticosteroids, Azathioprine, topical ciclosporin, topical tacrolimus, mycophenolate mofetil is not established.

Corticosteroids in OLP

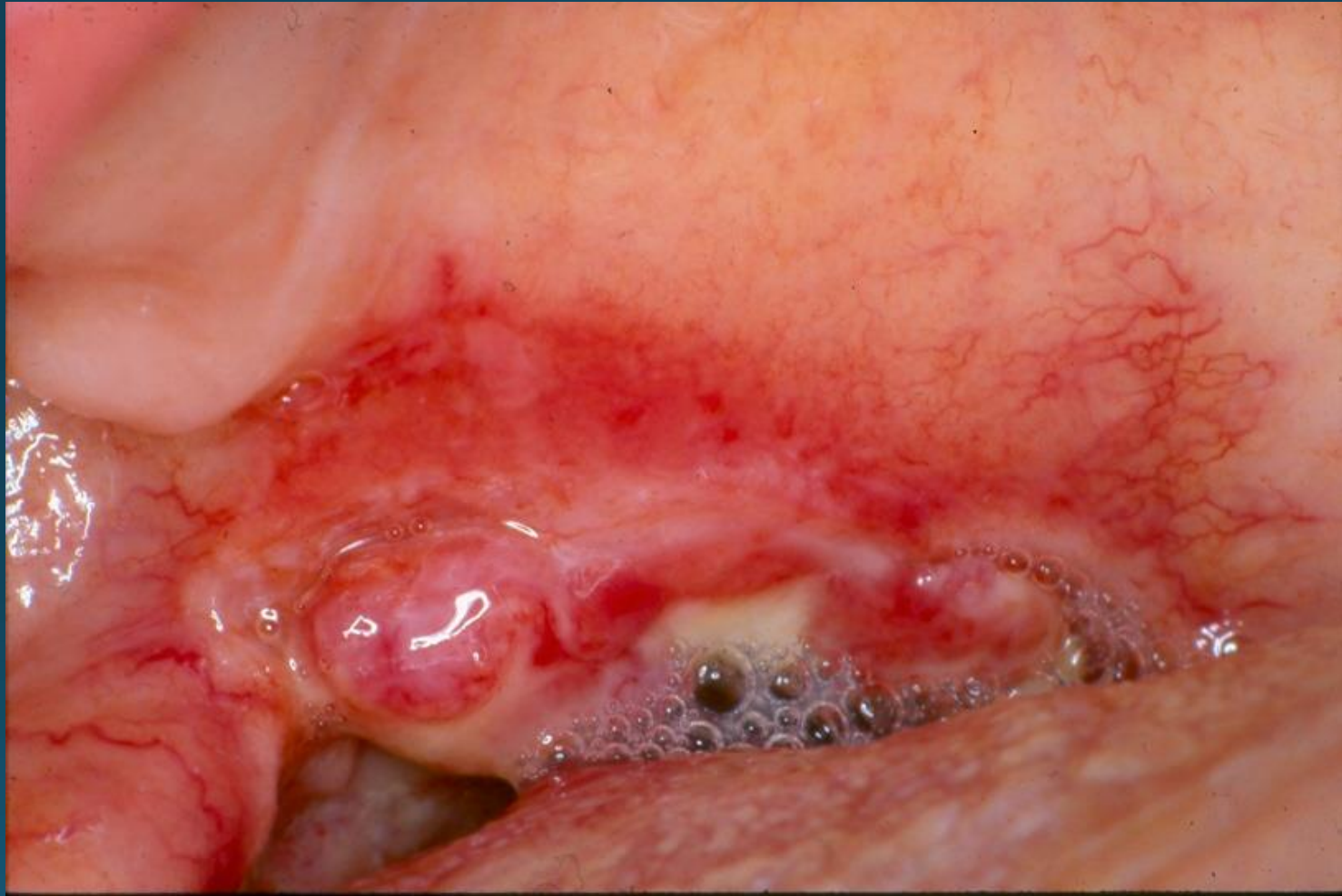
- Twelve studies identified in systematic review (*Al-Hashimi 2007*), although rarely high levels of evidence
- Vincent (1990) looked at systemic prednisone, but not found to be more effective than triamcinolone acetonide paste
- Evidence for topical agents showed Class 1 (useful & effective) for this alone, with clobetasol propionate 0.05% & 0.025% at next level.
- Intra-lesional corticosteroids were not more effective, were painful and associated with mucosal atrophy, may increase malignant risk

Prognosis of OLP

- Lasts 15-25 years
- Increased risk of malignant change
- Patients should therefore be kept under review
- Worrying changes in clinical appearance requires referral and biopsy

Malignant oral ulcers





A 55 year old lady presented to casualty with a mouth ulcer of many months...40 units of alcohol per week, ex-smoker



Oral Cancer

- Despite advances in treatment, the 5-year survival has remained approximately 50% for the last 50 years (higher survival for overall head & neck cancer, 62%)
- “Shift”, with greater increase in oropharyngeal cancer, but intra-oral cancers are still the most common and are the greatest cause of morbidity and mortality (Warnakulasuriya 2009)

Oral Cancer

Should be easy to address as:

- Risk Factors
- Oral Potentially Malignant Disorders
- Oral cavity is easily visible

Oral Cancer

- A disease of older age associated with lifestyle risk factors, notably alcohol, tobacco and betel. (Users of both tobacco and alcohol have a 50-fold (or greater) increased risk of developing head and neck cancer*)
- Increasing involvement of HPV in some tumours and a younger age
- Mortality & morbidity remain high, mainly through late diagnosis

* Maier et al 1992 Tobacco and alcohol and the risk of head and neck cancer. *Clinical Investigator*, 70, 320-327.

Known Risk factors

- Smoking (60% all, 80% FOM)
- Alcohol (24% all, 41% FOM)
- Betel nut
- Social deprivation and older age (“non- dental attenders”)
- Radiation
- Previous oral cancer
- Nutrition & sunlight
- Viruses, especially HPV (also EBV)
- Poor OH , trauma

Factors influencing early diagnosis of cancer in the oral cavity

JM Elwood et al. 1985 Can Med Assoc J;133:651-656

- Looked at 160 consecutive patients with diagnosed oral cancer. Compared factors that differed according to staging at presentation
- 55% of these oral cancer patients had Stage 1 or 11 disease at presentation
- Socioeconomic status determined by “best job”
- Regular dental attendance defined as visit the dentist at least one visit in the last 5 years

Significant factors affecting staging at presentation

- Visit to dentist in last 5 years (p value 0.0002). Visible but asymptomatic lesion in 81% of Stage 1 & 11 patients. Symptoms in 42% of Stage 11 & 1v patients. Dental attenders tended to be within higher socioeconomic groups. Diagnostic process starts with somebody looking for a lesion
- Socioeconomic status (p value 0.04)
- Alcohol consumption (p value 0.03) > 17 drinks a week was a less favourable factor

Malignant oral ulcers in general practice

- Greater risk with smoking, alcohol and immunosuppression
- Have they attended a dentist or hygienist – someone checking their mouths
- Persistent ulcer as opposed to multiple or recurring in different sites

Ulcers in the mouth

Main Causes of Mouth Ulcers

- Trauma
- Recurrent Aphthous Stomatitis
- Infectious causes
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Importance of History in Oral Ulceration

- Age of patient
- Has the patients had previous ulcers and are they cyclical or persistent
- Site of ulcers...?on keratinised or non-keratinised mucosa
- Has the patient had herpes in the past?
- Does the patient have a history of allergies?

History

- Single v multiple
- Does it involve other mucosal sites e.g. eyes
- Has the patient started drugs recently or are they on nicorandil?
- Has the patient stopped smoking recently?
- Is the patient generally in good health?

Management

- Pain relief and reduction of inflammation
- Investigation of cause
- Awareness of more less common, but serious causes of oral ulceration

Objectives

- Recognise common causes of oral ulceration
- Initiate management by controlling pain and devising an ongoing treatment plan
- Recognise sinister signs that require specialist management

