

## Medi-Vision™ Film Transcript Programme 54

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### Oral Medicine 4: Aphthous and related Mouth Ulcers

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*Introduced by*  
David C Anderson

#### Learning Objectives

**Professor David Anderson.** This is the one of a comprehensive series of MediVision Programmes on the fascinating subject of Oral Medicine. We are fortunate here to draw on the expertise of Professor Steven Challacombe and his staff in the Department of Oral Medicine in Guys Hospital in London, and here we see five patients with aphthous, and other forms of oral ulceration.

Through viewing this film you should achieve the following learning objectives:

- Be able to recognize and define aphthous ulceration, and its three principal variants
- Appreciate the role of quitting cigarette smoking in sometimes exacerbating aphthous ulcers
- Understand the principles of treatment of aphthous ulceration using topical steroid mouthwashes
- You should have a clear idea when a patient with minor or major aphthous ulceration should be referred to a Specialist Oral Medicine Clinic
- You should be able to distinguish an aphthous ulcer from a persistent traumatic ulcer
- You should recognise Acute Necrotising Ulcerative Gingivitis (ANUG), appreciate its association with HIV and with cigarette smoking, and the principles of treatment
- Recognise and describe the erythematous form of candidiasis, and distinguish it from other causes of depapillation of the tongue
- Appreciate the presentation of different forms of mouth ulcers in association with agranulocytosis, and other systemic diseases
- And be able to discuss the causes of ulceration of the hard palate

## Introduction

**DA** Steve, on these films we are going to see a lot of patients with different types of ulceration. What are the general principles that a clinician should apply in deciding 'is this an important condition which I should refer, or is it something I can manage myself?'

**SC** Yes, I think this is a key question. The differentiation of mouth ulcers sounds more complex, perhaps, than it actually is. In our view the key question is whether the ulcers are recurrent, or persistent, or a single episode. If they are recurrent they are likely to be recurrent aphthous stomatitis, and the clinician can make a decision whether to treat or refer. If they are persistent, they are more likely to be an oral manifestation of systemic disease, like one of the dermatological diseases or a gut disease, or an autoimmune disease. If it is a single episode they are more likely to be infectious, such as herpes or even some less common disease such as syphilis or gonorrhoea. So that decision of when to refer and when to treat and when to ignore can really be broken down to : 'are these ulcers, are they persistent, or is this a single episode?'

**DA** So if they are recurrent it depends on how severe they are clinically...

**SC** Yes...

**DA** And if it's a single episode which is self-limiting that's fine, but if they're persistent they should be referred..

**SC** Yes, if they are recurrent it's unlikely to be sinister such as a carcinoma. But even if they are recurrent and severe they will need referral.

## Patient 1 Aphthous Ulceration

**PS** Here we have Stella who is in her late thirties, and she has recurrent mouth ulcers. How many ulcers do you get in one go, Stella?

**S** At least 11 or 12, something like that

**PS** And where do you get these ulcers?

**S** Mainly on my tongue and in the front of my mouth

**PS** Okay. And how long does each individual ulcer last do you think?

**S** About six weeks. I can't really tell whether one's gone away and another's come back. Because they are there constantly.

**PS** So you don't get any ulcer-free days at all?

**S** No, no

**PS** Okay. And do these little ulcers all join up to form one big one?

**S** Sometimes they do, sometimes yes.

**PS** How big would you say your biggest ulcer's been? About the size of half a finger nail?

**S** Yes, yes.

**PS** Right. Are you a smoker?

**S** I used to be.

**PS** When did you give up?

**S** Approximately four years ago

**PS** And was there any relation between giving up smoking and your ulcers starting?

- S** Yes. I think since I gave up smoking my ulcers then appeared.
- PS** Any gastric problems?
- S** I have endometriosis. I so have a stomach problem of such, but nothing else.
- PS** And you don't have any bouts of diarrhoea or constipation, no problems with your bowel?
- S** No
- PS** And are you on any medicines for your endometriosis?
- S** I'm on Microgynon.
- PS** Does that make any difference to your ulcers. Do you find that being on the pill or not being on the pill made any difference to your ulcers at all?
- S** It's hard to tell really... no it didn't really... no

### Examination

**PS** Stella has got several ulcers today, and you can see that she has got an ulcer in the middle of her lower lip. This is really quite small – it's one to two millimeters in diameter, and there's a circle of erythema around it. This isn't particularly typical of a minor aphthous ulcer, because the erythema is very, very broad. Whereas the ulcer that she has on the side of her lip here is much more typical of minor aphthae. It's slightly more circular, slightly bigger and it's got a much smaller rim of peri-ulcer erythema. Can you stick your tongue out?.... When Stella sticks out her tongue you can see that she has got several very small ulcers on the tip. She has one here, here, here, and if you lift the tip up there's one here.... Either this is coming or going, it's a bit difficult to tell. These are very small, about 1 mm in diameter, with not much peri-ulcer erythema., probably more suggestive of a **herpetiform** (ulcer) because they are very small.

**PS** It's obviously very sore when you are pulling patients around with ulcers on their lips, so we have to be quite careful where we put our mirrors. And the patient's also very good at telling us where they've got other ulcers. We've seen those on your tongue and those on your lips... any more today?

**S** Yes I've got some right at the very back underneath my tongue, but I don't know if you'll be able to see it because it's right far at the back.

**PS** And does it make it hurt to swallow

**S** Yes it does

**PS** Let's see if we can see ulcers on the posterior pharyngeal wall or inside the tonsillar fossa. Say 'Ah'.

**S** Ah

**PS** No I can't see them, so they are obviously further back.

**PS** We've seen Stella has some ulcers on her lips, tongue,.... All these little ulcers will be painful. Which are your sorest ulcers today, Stella>

**S** This one at the side of my mouth actually, because it seems to keep catching .... It's right on the edge of my lip.

**PS** Site is often very important in how uncomfortable the ulcers are. Have you tried tetracycline mouth washes?

**S** Yes, I have

**PS** What happened?

**S** It didn't make any difference

**PS** Have any of the other things that we've given you helped you?

**S** No

**PS** What have you tried so far?

**S** I've tried Betnazol tablets used as a mouthwash...

**PS** Betnazol is a topical steroid, it's betamethasone, and although it's designed to be swallowed by asthmatics when they need a systemic dose of steroid we use it topically, and it's a very effective way of providing a topical steroid to the oral mucosa. What else have we given you?

**S** Basically I use the asthma inhaler as well, to spray onto the ulcers that are quite severe

**PS** We actually use budesonide – it gives you less of a problem with oral candidiasis.

**PS** Stella has a mixture of herpetiform aphthae and smoking-related aphthae. The evidence for this is that the ulcers came on soon after she gave up smoking, and that she hasn't responded very well to tetracycline mouthwashes which is the treatment of choice for herpetiform ulcers. She also hasn't responded very well to treatment for minor aphthae, a common occurrence in patients who have smoking-related aphthae. She didn't respond very well to topical steroids. She has also had **colchicine**, as well as the tetracycline mouthwashes. We started treating her with **azathioprine** – she's been on 50 mg for about 6 weeks. If she doesn't respond to azathioprine, then we will consider **thalidomide**. Thalidomide is only really used for patients who have failed to respond to conventional therapy, and we would be worried prescribing this to a female of child-bearing age, and we would also be worrying about peripheral neuropathy. So this won't be a decision we'll take lightly.

**PS** **Minor ulcers** tend to start in the first and second decade. You tend to get one to five ulcers that are about 5 millimetres in diameter, that will last for up to two weeks. **Major aphthae** again occurring in the first or second decade for their onset are larger ulcers, one centimeter or more, lasting for anything up to three, 4, 5 up to 6 weeks in some patients. And these ulcers are much deeper and heal with scarring. The third type of ulcer, **herpetiform aphthae**, tend to have an onset in the third decade. With these type of ulcers you get many more ulcers – nine or ten, 15, 20 ulcers at any one crop. Often these ulcers are small, and they will coalesce to form a larger ulcer, but each individual ulcer will only be 2 to 3 mm in diameter. These again last from 10 days to 2 weeks. And a particular feature of these clinically is that they have much more erythema around them, and they tend to be in slightly different sites from the minor and major (ones). They tend to

be either in the anterior portion of the mouth, or around the soft palate and tonsillar fauces.

## Patient 2

### Severe major aphthae

**PS** This is Deborah, who had very severe oral ulceration. So let's look at her mouth and see the extent of her scarring following her major aphthous stomatitis episodes since the age of 19. Pop your head back for me..... Okay... when Deborah is breathing through her nose and relaxing, the uvula and soft palate drop down showing that she has a very narrow orifice to her nasopharynx. And then say 'ah'.

**D** Ahhh

**PS** And then you can see it rises up and the shape changes. In fact what we see all around is white banding. Open as wide as you can Deborah.. that's absolutely fantastic... you can see there's a big white band that comes down on the left hand side and another band that comes down on the right hand side. And she's even got more scarring that extends from the retromolar region through to the base of the sulcus. She actually does not have any scarring of her tongue... stick your tongue out at me... showing that it's unlikely that any of her large ulcers were around her tongue. Close up for me. ... And neither does she have any scarring on her lower lip, again suggesting that her really large ulcers have always been on her soft palate and tonsillar fossa region.

**PS** Deborah has had ulcers since she was 19, and because she has only had two episodes of genital ulcers, no skin lesions and no problems with uveitis she doesn't fulfil the criteria of Behçets (disease). She has had a couple of children. So what were your ulcers like during pregnancy?

**D** Better when I was pregnant, and breast feeding, and then they got worse again when I stopped.

**PS** The thing to note with Deborah is that because of her hormone levels she has had altered ulcers, but they didn't disappear completely. This is something that we find quite commonly. And the other thing that is of interest with Deborah is that her voice quality has changed because the shape of her soft palate has changed, and her pharyngeal seal has also changed. So have you noticed your voice.. when did it change?

**D** I think it's been since probably the last major ulcer I had which was about three years ago, when I had that really massive ulcer... I think since then... I noticed that I can't sing, and I used to be able to sing.

**PS** And the last large ulcer was actually even more distal than we can see with the camera. It was really quite low down wasn't it?

**D** Yes

**PS** And you've also had ulcers on the posterior pharyngeal wall as well as around your tonsils. Have you ever had any ulcers elsewhere... in your stomach?

**D** No

**PS** You haven't had ulcers as low down as that, or oesophageal either?

**D** Well I don't know. Sometimes they feel that like are, because they are so far down.

**PS** Is it difficult to swallow?

**D** Yes and no. I find that I drink quite a lot of water with food as a way of kind of getting it down. Anything that's very dry I might find difficult

**PS** Well, the hole is smaller, so I'm not surprised it's more difficult to swallow dry things. And lubricating will help. Tell me some of the things that you have used to help with your ulceration.

**D** In terms of medication?

**PS** Yes

**D** Well, prednisolone was the first thing that really worked for me. Because they were so far back, all of the kind of topical things don't tend to really work if it's a bad ulcer. Betnazole I have used, which sometimes it will stop something progressing. And azathioprine, which has worked really well for me. I've used that ... I've had two courses of that now, 6 or 7 month courses.

**PS** You've had no side-effects from azathioprine?

**D** No. Oh, actually I've had sometimes a week or so of feeling quite sick.

**PS** And you had a little blip when you had hepatitis in the middle, and we wondered whether it was azathioprine.

**D** Yes, that was a bit of bad luck

**PS** But it came via your father in law, didn't it. You'd all been on holiday and picked it up from somewhere. But you recovered quite quickly and in fact there were no long-term effects on your liver from that and we were able to resume the azathioprine therapy quite quickly.

## Discussion

**DA** Steve, these two patients are obviously at the extreme end of the problem that is aphthous ulceration. What's the definition of an aphthous ulcer first of all.

**SC** We define recurrent aphthous stomatitis as a condition in which you get more than two spontaneously arising episodes of ulceration a year I should mention first of all that it is probably the most common oral mucosal disease. And we believe it affects between 8 and 10% of the population. There are the **three major types. Major** aphthous ulceration, **minor RAS and herpetiform**. Of those, the majority of the population would suffer from minor, and perhaps up to 90%, and perhaps 6 or 7 % would be Major, and a few percent herpetiform. In a specialized Oral Medicine Clinic the ratios would be slightly different but in General Practice it would probably be of that order. I think the majority of cases which have let's say three episodes of ulceration a year and are minor may not need treatment and may not need referral at all. But as we've seen with our cases today at the severe end they require systemic therapy. And it's important that **all cases of Major (RAS) are referred**.

**DA** Major being principally defined by the size of the ulcers?

**SC** Yes, in what we define as major recurrent aphthous stomatitis, or Major RAS, the patient is capable of getting ulcers at least a centimeter in diameter, and they can affect both the **keratinised mucosa** - that's the dorsum of the tongue and the palate - as well as all the non-keratinised areas - around the mouth, which minor normally affects. It's important to investigate the severe cases, because haematological abnormalities can play an exacerbating role. So we have a standardized protocol, where we would look at haematinics - that's folate, B12, iron - particularly iron as well as a full blood picture. And certainly a proportion of patients presenting with RAS will have an underlying haematological abnormality which is contributing to that. So that's an easy way that the practitioner can check if there is something that can be done. After that the treatment depends on severity. At the very severe end we would use systemic therapy and those really ought to be referred for diagnosis and ought to be done in a Specialised Clinic. However symptomatically, many patients can be helped by local topical therapy, and the best forms of these are local steroid therapy. And the favourite for us is Betnazol tablet used as a mouth wash - where you dissolve a tablet in 10 ml of water, rinse it round the mouth, hold it in the mouth for 2 minutes, and then spit out. And we do that four times a day when the ulcers are present, but twice a day when they are not. So the steroid is there before the ulcers arrive. And if you do that you can reduce the frequency of attacks as well as the severity.

**DA** And what's known about the pathology?

**SC** Quite a lot, but in essence it's a non-specific pathology. We believe it to be a variant of an autoimmune disease, and that is a lymphocyte-mediated disease, but the pathology itself is not specific to RAS, so we would get back after biopsy a non-specific histological report of an ulcer.

### **Patient 3 Traumatic ulcer**

#### **Dr Richie Yeung**

**RY** Mr Woo is a 67-year old gentleman who had problems on the right hand side of the tongue. He feels pain and discomfort. And it only started a few days ago, and the condition is more or less the same - no improvement, no worse. He is working in a hair salon, and dined out a lot, and he has problems with eating, because whenever he eats he has pain, so he has to swallow his food. He is taking antihypertensive drugs and at the same time his hypertension is controlled. Now we turn to Mr Woo's oral cavity.

#### **...Mr Woo, put out your tongue**

Now we look at the lateral border of the tongue. You can see there's a 5 millimetre ulcer. On the lateral border, and he also has a lot of scarring - there's a white line on the lateral border of the tongue. Mr Woo has a removable type of denture. When we look at the upper jaw he also has a removable denture and his teeth are in very poor condition. Most likely the patient may have chronic irritation from biting, and so create this traumatic line.. maybe due to poor dentition, maybe due to poor nutrition. Our treatment recommended to him is

topical steroid combined with hot saline mouth bath. With the above treatment the ulcer will heal very quickly.

### Discussion

**DA** Now this elderly gentleman has got a single ulcer. What's the cause of it in his case do you think?

**SC** I think the most likely cause is trauma, and there are a couple of reasons for that. One is there is scarring associated with it, and he has a sharp tooth in the vicinity. And the third thing is his age. It raises the question of how important it is to distinguish recurrent ulceration from persistent because of the many different types of mouth ulcers. The key distinguishing feature is whether they are recurrent or not.

**DA** Right. But this might be helped by local steroids do you think?

**SC** Yes, short-term local steroids should help to treat this. But obviously the removal of the cause, like the sharp tooth would be even better.

### Patient 4 Acute necrotizing ulcerative Gingivitis

**PS** Here we have a patient who has very painful gingivae. Tell us what it's been like

**Pt** It's quite a numb pain – it's there all the time – it's difficult to eat and drink, and is quite unpleasant

**PS** How many days has it been present?

**Pt** About a week now progressing

**PS** Have you ever had this before?

**Pt** I remember having it once before probably about 18 months ago

**PS** Are you a smoker?

**Pt** No

**PS** And are the gums actually bleeding?

**Pt** Yes

**PS** And what's the most painful? Is it eating or brushing your teeth?

**Pt** Brushing the teeth.

**PS** All right. Let's have a look at your mouth.. What we can see is some inflammation around the gingivae, particularly in this lower anterior section, with some very small ulceration, and blunting of the papilla between the two teeth, whereas on the other side there is no inflammation and no ulceration. When we look in the upper arch there is more ulceration and erythema. The particular feature of this is the blunting off of usual the triangular gingival papilla, and there's a necrotic ulcer there with erythema across that anterior section, whereas in the posterior portion the gingivae are nice and healthy, oral hygiene is good, and we have no ulceration and no swelling.

**PS** When we examine the rest of his oral cavity... open for me... stick your tongue out. You can see here that we've got a central depapillated area. The

area on this side and this side is the normal papillated area, and this horseshoe-shaped area is depapillated and erythematous. This is a hallmark of erythematous candidiasis. These two clinical signs are oral manifestations of HIV disease. This patient has been HIV positive for about four years and is generally well. His CD4 count is over 300

**PS** Have you been on any anti-HIV treatment at all?

**Pt** No

**PS** Have you had any other problems associated with HIV?

**Pt** No, just the gums

**PS** Just the gums. The episode he had about 18 months ago probably represented another episode of Acute Necrotising Ulcerative Gingivitis (ANUG). It's always more common in smokers, and now we are finding its more common in those that are HIV infected. What he doesn't have is any Hairy Leukoplakia. There are no corrugated white patches down the sides of his tongue. The hairy leukoplakia does indicate those patients who untreated are likely to progress to a Pneumocystic carinii infection. But this patient clearly does not have a hairy leukoplakia, and therefore we would not make any predictions regarding his HIV progress. He merely has two common manifestations of HIV disease, the oral candidiasis being the most common.

**PS** Concurrently he has very enlarged tonsils with deep pits and scarring. I am sure that recurrent tonsillitis has been a great problem for him over a number of years irrespective of his HIV. If we palpate his submandibular regions, we'd expect to find that he does have submandibular lymphadenopathy – cervical chain lymphadenopathy – which he does.

**PS** We are going to treat his Acute Necrotising Ulcerative Gingivitis with metronidazole, in order to combat the gram negative bacteria that are responsible for this infection, and we also need to do some local measures. He needs to have the gingival pockets irrigated with chlorhexidine, and any plaque and calculus removed. We would expect this episode of ANUG to respond very quickly to metronidazole, but unfortunately for some HIV patients it is quite a recurring problem.

### Discussion

**DA** Steve, this patient's got two lesions. A peculiar form of candidiasis, and then this condition of necrotizing gingivitis. What's the significance, first of all, of him being HIV positive?

**SC** In this case very significant. Those two lesions – that's erythematous candidiasis – a red form of candidiasis, and necrotizing ulcerative gingivitis are two of the sentinel oral signs of HIV infection. So we would expect to see these lesions in somebody who was HIV positive, and conversely if we saw these lesions, especially as a pair, we would expect some underlying immunodeficiency – in this case HIV

**DA** So why the difference in response to candidiasis in somebody who is HIV positive

**SC** An interesting question – there is recent evidence that the epithelial cells themselves are altered. Actually we do have another form of red candida under dentures. And we believe that to be a contact lesion. WE are not sure this is the analogous situation, but we believe that's worth pursuing further.

**DA** But you can, presumably, get the normal candidiasis in somebody who is HIV positive?

**SC** Absolutely. In fact there is a very strong correlation between getting the thrush-type, that's pseudomembranous candidiasis, with decreasing CD4 counts. And it may well change – somebody who has got candidiasis – the erythematous type – and who gets profoundly immunodeficient will almost certainly develop pseudomembranous candidiasis.

**DA** Right. And the gingivitis? Is this bacterial in origin?

**SC** That's bacterial. These are Gram-negative anaerobes. In addition to HIV it is strongly associated with smoking. I have to say that 30 years ago it used to be quite common. We rarely see it nowadays, and even less commonly in non-smokers.

#### **Patient 5 Palatal ulcers & agranulocytosis**

**DA** Steve, I just want to show you footage that I got recently of a woman in her late thirties who had one episode of thyrotoxicosis, was treated with carbimazole, and then because she had an allergic reaction with Propylthiouracil. Upon relapse about a year or a year and a half later very quickly within about 2 or 3 weeks she became unwell, thought she had a virus infection, and then got what she thought was a gland in the right side of her neck, and then pain in the mouth. And this is the lesion two or three days later when I saw her..... the mouth lesion. At this time she had a profound neutropenia, I mean no granulocytes at all and she required quite dramatic antibiotic therapy. But what are the features of these two ulcers in the top of the mouth that interest you?

**SC** Well, firstly they are not aphthous – they are not recurrent. I have to say they are slightly unusual ulcers even for agranulocytosis. Because those usually appear either on the dorsum of the tongue or posterior pharyngeal wall. These ulcers that we are seeing here – the main one in the centre of the palate is about a centimeter, with a rolled ridge, slightly hyperplastic around it, and very little effect on the rest of the mucosa. Whereas most of the agranulocytosis we expect to appear with quite a lot of atrophy or erythema around the oral cavity. So that's an unusual appearance, but the timing is such to make the linkage very strong. There's one here in her right side, again in the hard palate – its definitely hard palatte and not soft palate, which is more like an erosion. And one wonders whether they might have been triggered by some trauma. In the middle of the palate, to account for that site, in the presence of an otherwise healthy palate.

**DA** And then if we move on to have a look at her two and a half weeks later...

**SC** Well this is very impressive response just in two and a half weeks. They are both essentially healed. One has not quite finished re-epithelialising. When you've got agranulocytosis you do expect to see more lesions around the gingivae, and where there are lots of bacteria and normally lots of polymorphs. And certainly the healing of the one nearer the teeth, and the one in the centre of the palate are impressive.

**DA** Yes, the drug was withdrawn, she was put onto meropenim and ultimately vancomycin, and the white count after the a few days started to come up, and by the time this had been taken it was back to normal

**SC** I do wonder though whether this might have been a reaction to the drug itself as opposed to agranulocytosis.

**DA** Right. This is an unusual site, the hard palate, is it

**SC** If I see ulcers on the hard palate, yes I would always be looking for another cause. It is unusual to see ulcers in that site. In fact I sometimes set my students questions about what ulcers appear on the hard palate, because out of these many types there are very few that do appear there, but virus-induced ones are some of those... trauma of course, and then the dermatoses, lichen planus and pemphigus and pemphigoid can all appear at that site.

**DA** Well, the patient herself was convinced that it had started with a virus infection, so maybe she was right, and maybe that was compounded by a drug-induced neutropenia. Do you think that's possible?

**SC** Well I think it is. The fact that she complained of pain in the lymph nodes first before she was aware of ulceration in the mouth, may be significant, because that would indicate that the virus was there and perhaps the lesion at that time was quite small, and it's become secondarily infected by the time we saw it clinically.

## Summary and Conclusions

### DA

- So in summary, we started with a discussion of general principles and Professor Challacombe emphasized the importance of distinguishing whether ulcers are recurrent or persistent or a single episode
- The first patient, Stella, had a mixture of minor aphthae and herpetiform aphthae; you should now be able to distinguish these two forms of aphthous ulceration. Because she is severely affected she needs azathioprine, and also colchicine
- The second patient, Deborah had severe scarring around the fauces from recurrent major aphthae
- We then saw a Chinese gentleman with a single ulcer related to trauma from a decayed and loose tooth
- The fourth case was a young man with HIV infection who showed two of its oral manifestations, namely acute necrotizing ulcerative gingivitis, or ANUG; and erythematous candidiasis, and we heard about the treatment of these two conditions.

- Finally I discussed a patient of mine with Professor Challacombe. She was thyrotoxic and had developed agranulocytosis while on propylthiouracil and apparently following a viral type of illness. She presented with two ulcers on the hard palate, which we heard is an unusual site for patients with agranulocytosis.

So turning back to our original learning objectives, you should now:

- Be able to recognize and aphthous ulceration, and its three principle variants
- You should appreciate that quitting cigarette smoking can sometimes exacerbate aphthous ulceration
- You should understand the principles of treatment by using topical steroid mouthwashes
- Have a clear idea when a patient should be referred to a Specialist Oral Medicine Clinic
- You should be able to distinguish an aphthae from a persistent traumatic ulcer
- Recognise acute necrotising ulcerative gingivitis (ANUG), appreciate its association with HIV and smoking, and know how to treat it
- You should recognise and describe erythematous candidiasis, and be able to distinguish it from other causes of depapillation
- You should now appreciate mouth ulcers in association with agranulocytosis, and other systemic diseases
- And finally you should be able to discuss the causes of ulceration of the hard palate