Surgical pathology of the mouth and jaws

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8. Diseases of the oral mucous membranes

Mucosal, particularly ulcerative, diseases include both surgically treatable conditions and non-surgical conditions, though they are not always easy to differentiate. Nevertheless, some of them, such as lupus erythematosus, are important indicators of severe underlying systemic disease. Of current concern is the prevalence of HIV infection, in which any of a great variety of oral mucosal lesions may be seen. If, therefore, stomatitis has unusual features, a resolute attempt should be made to make a firm diagnosis from the history, clinical features, biopsy and, if necessary, other laboratory investigations. Particular attention should be given to the medical and drug history, and whether other mucous membranes or the skin are affected.

Biopsy is mandatory, particularly in the bullous diseases. In such cases, the diagnosis can frequenly only be confirmed by microscopy. In other cases, microscopic findings can be less definite, but often (as in the cases of major aphthae, for example) serve to exclude more serious diseases.

Frequently, a critical factor is the adequacy of the specimen and it has never ceased to be a source of wonder to the authors that some surgeons, who may have carried out commando operations leaving little remaining between the eyes and larynx, sometimes produce soft tissue biopsies so small as often (without exaggeration) to be difficult to find in the specimen bottle.

Though the subject of biopsies has been discussed earlier, it must be emphasized again that a mucosal specimen must be at least 1 cm long. In many mucosal diseases, such as lichen planus, the specimen needs to be no more than 5 mm deep, but in others such as Crohn's disease it should be as deep as can safely be made.

Infections

Primary herpetic stomatitis

Primary infection is caused by the herpes simplex virus, usually type 1, which, in the non-immune, results in an acute vesiculating stomatitis. Thereafter, recurrent (reactivation) infections usually take the form of *herpes labialis* (cold sores or fever blisters).

Transmission of herpes is by close contact and where there are large, poor, urban communities, up to 90% develop antibodies to herpesvirus during early childhood. In more affluent countries, the incidence of herpetic stomatitis has declined and it is seen in adolescents or adults, rather than children, and is more commom in the immunocompromised such as in HIV infection. In many British and US cities, by contrast, approximately 70% of 20 years olds may be non-immune, as a result of lack of exposure to the virus.

Clinical features

The early lesions are vesicles which can affect any part of the oral mucosa, but the hard palate and dorsum of the tongue are characteristic sites. The vesicles are dome shaped and usually 2-3 mm in diameter. Recently ruptured vesicles leave flat, yellowish, disc-shaped lesions which progress to circular, sharply defined, shallow ulcers with yellowish or greyish floors and red margins. The ulcers are painful and may interfere with eating.

The gingival margins are frequently swollen and red, particularly in children, and the regional lymph nodes are enlarged and tender. There is often fever and systemic upset, sometimes severe, particularly in adults.

Oral lesions usually resolve within a week to 10 days, but malaise can persist so that an adult may not recover fully for several weeks.

Microscopy

The vesicle is sharply defined and forms in the upper epithelium; the roof is several cells thick and is therefore sufficiently strong that intact vesicles are often seen. Viral-damaged epithelial cells are seen in the floor of the vesicle. Direct smears from an early lesion show viral-damaged cells with ballooning degeneration of the nuclei or multinucleate cells. Later, the full thickness of the epithelium is replaced by viral-damaged cells and is destroyed to produce a sharply delimited ulcer.

A rising titre of antibodies, reaching a peak after 2-3 weeks, provides absolute but retrospective confirmation of the diagnosis.

Differential diagnosis

Teething. An infant who develops an acutely sore mouth usually has herpetic stomatitis. Acute generalized soreness of the mouth, especially with lymphadenopathy, does not result from teething.

Acute ulcerative gingivitis (AUG). Herpetic ulcers can sometimes affect the tips of the interdental papillae and adjacent gingiva and be mistaken for acute ulcerative gingivitis. However, vesicles and ulcers elsewhere in the mouth, and the lymphadenopathy or fever of herpes, readily distinguish the conditions. Acute gingival ulceration in children in the Western world is usually herpetic, but acute ulcerative gingivitis may be seen if they are immunocompromised.

Herpes zoster. The first symptom is usually pain which may resemble toothache. The lesions have a characteristic distribution on one side of the skin of the face and mucosa supplied by the trigeminal nerve, as discussed below.

Recurrent aphthae. Individual ulcers may resemble those of herpetic infection. However, there is usually a history of recurrences, no systemic upset and the regional lymph nodes are rarely enlarged. Usually only two or three aphthae appear in any one crop, are not

preceded by vesicles and also, unlike herpes, do not affect the hard palate or gingival margins and rarely the dorsum of the tongue.

Hand-foot-and-mouth disease. The infection is usually very much milder than herpetic stomatitis with only one or two small scattered oral ulcers. Intact vesicles are rarely seen, regional lymph nodes are not involved and there is no associated gingivitis. The vesicles on the extremities are distinctive and frequently there is a cluster of cases.

Treatment

Acyclovir is a potent antiherpetic drug. It is of low toxicity and is effective even for potentially lethal herpetic encephalitis or disseminated infection. Acyclovir suspension used as a rinse and then swallowed should accelerate healing of severe herpetic stomatitis if used sufficiently early. In AIDS or other immunodeficient patients, systemic acyclovir (tablets or intravenous injection) may be required.

In mild cases, topical tetracycline suspension, rinsed round the mouth several times a day, relieves soreness and may hasten healing by controlling secondary infection.

Patients who are unwell should preferably be kept in bed and given a soft diet. Young infants readily become dehydrated during the painful stomatitis and may rarely require intravenous rehydration.

Unusually prolonged or severe infections or failure to respond to acyclovir (200-40 mg five times daily by mouth for 7 days) suggest HIV infection. Herpetic ulceration persisting for more than a month is an AIDS-defining illness (Centers for Disease Control, 1987).

Herpes labialis

After the primary infection, the latent virus can be reactivated in 20-30% of patients to cause cold sores (fever blisters). Triggering factors include the common cold and other febrile infections, exposure to strong sunshine, menstruation or occasionally, emotional upsets or local irritation, such as dental treatment. Neutralizing antibodies produced in response to the primary infection are not protective.

Clinically, changes follow a consistent course with prodromal paraesthesia or burning sensations, then erythema at the site of the attack. Vesicles form after an hour or two, usually in clusters along the mucocutaneous junction of the lips, but can extend onto the adjacent skin.

The vesicles enlarge, coalesce and weep exudate. After 2 or 3 days they rupture, the raw area crusts over but new vesicles frequently appear for a day or two only to scab over and finally heal, usually without scarring. The whole cycle may take up to 10 days. Secondary bacterial infection may induce an impetiginous lesion which sometimes leaves scars.

Treatment

In view of the rapidity of the viral damage to the tissues, treatment must start as soon as the premonitory sensations are felt. Acyclovir cream may be effective if applied sufficiently early.

Herpetic cross-infections

Both primary and secondary herpetic infections are contagious. Herpetic whitlow is therefore a recognized though surprisingly uncommon hazard to dental surgeons and their assistants. Herpetic whitlows, in turn, can infect patients and have led to outbreaks of infection in hospitals and among patients in dental practice. In immunodeficient patients such infections can be dangerous, but acyclovir has dramatically improved the prognosis in such cases and is frequently given on suspicion.

Herpes zoster of the trigeminal area

Zoster (shingles) is characterized by pain, a vesicular rash and stomatitis in the related dermatome. The varicella zoster virus (VZV) causes chickenpox in the non-immune (mainly children), while reactivation of the latent virus causes zoster, mainly in the elderly. Unlike herpes labialis, repeated recurrences of zoster are very rare. Occasionally there is an underlying immunodeficiency. Herpes zoster is a hazard in organ transplant patients and can be an early complication of some tumours, particularly Hodgkin's disease or, increasingly, of AIDS where it is five times more common than in HIV-negative persons and potentially lethal.

Clinical features

Herpes zoster usually affects adults of middle age or over, but occasionally attacks even children. The first signs are pain and irritation or tenderness in the dermatome corresponding to the affected ganglion. The pain can be severe and may be felt by the patient as toothache. Prodromal toothache which led to extensive, unjustified dental treatment has been described by Goon and Jacobsen (1988) among others. Malaise and fever are usually associated.

Vesicles form on one side of the face and in the mouth up to the midline. The regional lymph nodes are enlarged and tender. The acute phase usually lasts about a week. Pain continues until the lesions crust over and start to heal, but secondary infection may cause suppuration and scarring of the skin.

The fact that patients are sometimes unable to distinguish the pain of trigeminal zoster from severe toothache has sometimes led to a demand for a tooth to be extracted. When this is done, the rash follows as a normal course of events, and this has given rise to the myth that dental extractions can precipitate facial zoster. Alternatively, the rash may be misinterpreted as an allergic reaction to a local anaesthetic.

Microscopically, the varicella zoster virus produces similar epithelial lesions to those of herpes simplex, but also inflammation of the related posterior root ganglion.

Management

Herpes zoster is an uncommon cause of stomatitis, but readily recognizable. It is distinguished from herpes simplex and other types of stomatitis by:

- pain (usually severe) preceding the rash

- facial rash accompanying the stomatitis

- localization of the lesions to one side, within the distribution of the second and third divisions of the trigeminal nerve.

According to the severity of the attack, oral acyclovir (200-800 mg, 5 times daily, usually for 7 days) should be given at the earliest possible moment, together with analgesics. In immunodeficient patients, intravenous acyclovir is required and may also be justified for this debilitating infection in the elderly.

Complications

Post-herpetic neuralgia mainly affects the elderly. The pain can resemble trigeminal neuralgia but is persistent rather than paroxysmal and unresponsive to carbamazepine. Analgesics may be of some help, but though antidepressants or other drugs such as amantadine have been tried, there is no consistently reliable treatment. However, transcutaneous electrical stimulation is sometimes effective. Whether very early and vigorous treatment with acyclovir reduces the risk of post-herpetic neuralgia developing remains unconfirmed.

A rare complication is maxillary osteomyelitis and spontaneous tooth exfoliation. Mintz and Anavi (1992), in reporting a case and reviewing earlier reports, managed the bone necrosis by closed nasal-vestibular drainage.

Hand-footh-and-mouth disease

This common, mild viral infection, which often causes minor epidemics among schoolchildren, is characterized by ulceration of the mouth and a vesicular rash on the extremities.

Hand-foot-and-mouth disease is usually caused by strains of Coxsackie A virus. It is highly infectious, frequently spreads through a classroom in schools and may infect a teacher or parent. The incubation period is probably between 3 and 10 days. It should not be confused with foot and mouth disease of cattle, a rhinovirus infection, which rarely affect humans.

Clinical features

The small, scattered oral ulcers usually cause little pain. Intact vesicles are rarely seen, and the gingivae are not affected. Regional lymph nodes are not enlarged except in unusually severe cases, and systemic upset is mild or absent.

The rash consists of vesicles, which are sometimes deep seated, or occasionally bullae. It is mainly seen around the base of fingers or toes, but any part of the limbs may be affected. The rash is often the main feature and such patients are unlikely to be seen by a dentist. In some outbreaks, either the mouth or the extremities alone may be affected. Serological confirmation of the diagnosis is possible but rarely required, as the history, especially of other cases, and clinical features are usually adequate. The disease usually resolves within a week. No specific treatment is available or needed, but myocarditis or encephalitis are rare complications.

Cytomegalovirus infection

Shallow, painful oral ulcers showing typical owl-eye inclusion bodies in the base have been seen in immunodeficient patients, particularly those with AIDS. Though it is not certain whether cytomegalovirus is the cause of the ulcers in these patients, the response of the ulcers to ganciclovir in 3 cases reported by French et al (1991) suggests that it was responsible.

The acute specific fevers

Fevers which cause oral lesions are rarely seen in dentistry. Those which cause vesicular rashes (smallpox and chickenpox) produce the same lesions in the mouth.

In the prodromal stage of measles, Koplik's spots may be seen on the buccal mucosa and soft palate and are pathognomonic. Palatal petechiae or ulceration, involving the fauces especially, are seen in glandular fever and are accompanied by the characteristic, usually widespread, lymphadenopathy.

Kawasaki's disease (mucocutaneous lymph node syndrome)

Kawasaki's disease is endemic in Japan, but though uncommon in Britain it is frequently unrecognized and the cause of a significant mortality.

Clinical features

Children are affected and have persistent fever, oral mucositis, ocular and cutaneous lesions, and acute cervical lymphadenopathy. Oral lesions consist of widespread mucosal erythema with swelling of the lingual papillae (strawberry tongue), but are of minor significance compared with the serious cardiac effects. Other features are discussed in Chapter 14.

Tuberculosis

The recrudescence of tuberculosis in the West is partly a consequence of the AIDS epidemic, and multiply-resistant mycobacteria are becoming widespread. Oral tuberculosis is rare as yet, but is a complication of open pulmonary disease with infected sputum. Elderly men or those with HIV infection are the main victims. The typical lesion is an ulcer on the mid-dorsum of the tongue; the lip or other parts of the mouth are less often affected. The ulcer is typically angular or stellate, with overhanging edges and a pale floor, but can be

ragged and irregular. It is painless in its early stages and the regional lymph nodes are usually unaffected.

The diagnosis is rarely suspected until biopsy has shown tubercle follicles in the floor of the ulcer. *Mycobacteria* can be demonstrated in the sputum (but rarely in the oral lesion) and chest radiographs show advanced infection.

Tuberculosis or non-tuberculous mycobacterial infection must be considered in patients with AIDS who develop oral ulceration with granuloma formation, microscopically.

No local treatment is needed; oral lesions clear up rapidly if there is effective chemotherapy for the pulmonary infection.

Tuberculous cervical lymphadenopathy (see Chapter 14)

Syphilis

Oral lesions in each stage of syphilis are clinically quite different from each other. Oral lesions are rarely seen or may pass unrecognized.

Primary syphilis

An oral chancre appears 3-4 weeks after infection and may form on the lip, tip of the tongue or, rarely, other oral sites. It consists initially of a firm nodule about 6 or 7 millimetres across. The surface breaks down after a few days, leaving a rounded ulcer with raised indurated edges, which may resemble a carcinoma, if on the lip. However, the appearances are variable. In the absence of secondary infection, the lesion is painless. The regional lymph nodes are enlarged, rubbery and discrete. A biopsy may only show non-specific inflammation but sometimes there is a conspicuous perivascular infiltrate.

Serological reactions are negative at first. Diagnosis therefore depends on finding *Treponema pallidum* which can be seen by dark-ground illumination of a smear from the chancre, but must be distinguished from other oral spirochaetes. Clinical recognition of oral chancres is difficult but important. They are highly infective, and treatment is most effective at this stage.

After 8 or 9 weeks the chancre heals, often without scarring.

Secondary syphilis

The secondary stage develops 1-4 months after infection. It typically causes mild fever with malaise, headache, sore throat and generalized lymphadenopathy, soon followed by a rash and stomatitis.

The rash is variable, but typically consists of pinkish (coppery) macules, symmetrically distributed and starting on the trunk. It is not irritating or painful and may last for a few hours or for a few weeks. The presence or history of such a rash is a useful aid to diagnosis. Oral lesions are rarely seen without the rash. The tonsils, lateral borders of the tongue and lips are

the main sites, and the usual findings are flat ulcers covered by greyish membrane. The lesions may be irregularly linear (snail's track ulcers) or may coalesce to form well-defined rounded areas (mucous patches).

The discharge from the ulcers contain many spirochaetes and saliva is highly infective. Serological reactions (see below) are positive and diagnostic at this stage, but biopsy is unlikely to be helpful.

Tertiary syphilis

The late stage of syphilis develops in many patients about 3 years or more after infection. The onset is insidious and during the latent period the patient may appear well. A characteristic lesion is the gumma.

Clinically, a gumma, which may affect the palate, tongue or tonsils, can vary from two to several centimetres in diameter. It begins as a swelling, sometimes with a yellowish centre which undergoes necrosis leaving a painless indolent deep ulcer. The ulcer is rounded, with soft, punched-out edges. The floor is depressed and pale (wash-leather) in appearance. It eventually heals with severe scarring which may distort the soft palate or tongue, or perforate the hard palate or destroy the uvula.

Microscopically, there may be no more than a predominance of plasma cells in the inflammatory infiltrate (a common finding in oral lesions) but associated with peri- or endarteritis. Granuloma formation may be seen but is rare; also rarely, there may be diffuse chronic inflammatory infiltration of the lingual muscles or coagulative necrosis mimicking caseation. However, even arteritis may be absent and the appearances can be completely non-specific. Diagnosis therefore depends on the serological findings.

Leucoplakia of the tongue may also develop during this late stage (Chapter 9), and other effects of syphilis such as aortitis, tabes or general paresis of the insane may be associated.

Serological diagnosis of syphilis

Tests are either specific, such as FTA-ABS, or non-specific, such as the VDRL (Table 8.1). The VDRL becomes positive 4-8 weeks after infection, and becomes negative only after effective treatment, but false positives can result from a variety of other causes. The FTA-ABS test acts as a check against false-positive or false-negative results, but remains positive despite effective treatment for the life of the individual.

Table 8.1 Interpretation of serological tests for syphilis

VDRL	*FTA-ABS*	*Usual interpretation*
+	-	False-positive
+	+	Active syphilis
-	+	Treated syphilis.

Treatment

Antibiotics, particularly penicillin, are the mainstay, but tetracycline and erythromycin are also effective. Treatment must be continued until non-specific serological reactions (VDRL) are persistently negative.

Candidosis

Candidal infection can cause the formation of whitish plaques or areas of erythema. These are discussed in Chapter 9.

Non-infective ulceration

Traumatic ulcers

Traumatic ulcers are usually caused by a denture and often in the buccal or lingual sulcus. They are tender, and have a yellowish floor and red margins; there is no induration. A similar ulcer, caused by the sharp edge of a broken-down tooth, is usually on the tongue or buccal mucosa.

A traumatic ulcer heals a few days after elimination of the cause, and thus confirms the diagnosis. If it persists for more than 7-10 days, or there is any other cause for suspicion, biopsy must be carried out.

Aphthous stomatitis (recurrent aphthae)

Recurrent aphthae are the most common disease of the oral mucosa and may affect 10-20% or more of the population. The distinctive feature is painful shallow ulcers which recur at more or less regular intervals. Ulcers resembling major aphthae can also be a feature of AIDS.

Aetiological aspects

Suggested factors have been extensively reviewed by Scully and Porter (1989) and include the following:

Infection. There is no evidence that herpes simplex or any other virus is the cause. *Streptococcus sanguis* and L-forms have been implicated in the past, but though microorganisms may secondarily infect aphthae there is no evidence that they are a direct cause or that cross-reacting microbial antigens play a significant role.

Immunological aspects. It has been fashionable to regard recurrent aphthae as an autoimmune disease. However, the enormous variety of immunological abnormalities reported over the years have been by no means consistently found. No convincing case for an immunopathogenesis has been made and Jonsson et al (1990), for example, do not include recurrent aphthae in their review of immunologically mediated oral diseases. The facts that the majority of patients are otherwise healthy and that there is no association with, or any other features of, any of the better substantiated autoimmune diseases make it difficult to

sustain an autoimmune hypothesis. The microscopic features are also not suggestive of an immunologically mediated reaction and, unlike autoimmune disease, recurrent aphthae are self-limiting in most cases.

Haematological and gastrointestinal disease. Between 10% and 15% of patients with recurrent aphthae may have haematological abnormalities, particularly iron or, less often, folate or vitamin B_{12} deficiency. Folate deficiency itself, though uncommon, is probably one of the few diagnosable and reliably treated causes of aphthous stomatitis. Typical aphthous stomatitis is occasionally the first overt manifestation of folate deficiency and resolves when folate is given. However, Porter et al (1988), in an investigation into the haematological status of 69 patients with recurrent aphthae, express doubts about the contribution to the oral ulceration of the deficiency states found in over 12% of them.

In the case of a possible association between ulcerative colitis, Crohn's disease or coeliac disease, it is difficult to exclude coincidence, since recurrent aphthae are very common in healthy persons. Nevertheless, intestinal disorders can cause folate or vitamin B_{12} deficiency and may promote aphthae indirectly.

In a minority of women, aphthae are worse premenstrually and may improve during pregnancy.

Clinical features

Patients with recurrent aphthae frequently show mild anxiety or obsessional traits. Extensive surveys, particularly that by Sircus et al (1957), have shown that they come almost exclusively from clerical, semi-professional or professional social groups, and the vast majority are non-smokers. Occasionally, the onset of a severe exacerbation of aphthous stomatitis follows cessation of smoking. Most patients with aphthous stomatitis have mouths that are well cared for and this suggests that local factors may be less important than has been suggested.

Recurrent aphthae often start in childhood or adolescence, peak in early adult life, then wane spontaneously. They usually resolve entirely before middle age and often much earlier.

The frequency, number and size of ulcers is very variable. Many patients have had sporadic small solitary ulcers for many years, but seek treatment because of increasing severity. Most such patients have ulcers at intervals of 2-4 weeks but, in severe cases, ulcers are continuously present - as some heal, others form. Quite commonly, there are remissions of a month or two and this makes the assessment of treatment difficult.

Aphthae appear singly, in crops of two or three or occasionally in much greater numbers. The first symptom is often a pricking sensation as if a toothbrush bristle had stabbed the mucous membrane. The ulcers soon become painful and tender and, in severe cases, may cause difficulties with eating or talking.

The ulcers are usually shallow, circular or elliptical and about 2-4 mm in diameter. The floor of an ulcer is yellowish, with a sharply defined red margin which is sometimes

raised by oedema to make the ulcer crater shaped. Pain usually persists for three or four days. Healing follows without scarring in about a week.

Recurrent aphthae have a characteristic distribution which is a useful guide to the diagnosis. Unlike those of herpetic stomatitis, for example, aphthae affect only non-keratinized areas and not the masticatory mucosa of the hard palate or gingival margins. Only patients with severe aphthous stomatitis occasionally have ulcers on the dorsum of the tongue. If ulcers are seen in the vault of the palate, they are unlikely to be aphthae.

Clinical variants

- *Minor aphthae (Mikulicz type)* are by far the most common and have the features already described.

- *Herpetiform aphthae* comprise only a small minority. They are small (2-3 mm) ulcers which may be innumerable and become confluent. There is widespread erythema of the mucous membrane. The term 'herpetiform' applies only to the appearance, not the aetiology. Unlike herpetic ulcers, herpetiform aphthae lack preceding vesicles, are much less sharply defined and are more irregular in size and shape.

- *Major aphthae* also form a minority but are a very severe type, with ulcers one to several centimetres in diameter. They can persist for at least 3 months but sometimes much longer. Healing may be followed by scarring.

Among HIV-positive patients, any of the variants of recurrent aphthae may be seen, but MacPhail et al (1991) report that herpetiform and major aphthae were more common in this group than in HIV-negative persons and also seemed to have coincided with development of immunodeficiency. Patients with major aphthae in particular tended to be more severely immunodeficient and to have lower CD4 counts.

Microscopically, aphthae show non-specific inflammation. Ulceration appears to start with infiltration of the epithelium by leucocytes associated with beads of exudate. A typical ulcer shows a mixed inflammatory infiltrate. In the early lesion, lymphocytes are said to predominate and neutrophils to replace them later, but such descriptions are based on arbitrary estimates of the duration of the lesion. Perivascular cuffing is also said to be characteristic, but in practice is rarely seen.

The main microscopic feature which may possibly distinguish aphthae from traumatic ulcers is that the inflammatory infiltrate may be more intense and extend more deeply.

Diagnosis

The most important feature is the history, often prolonged, of recurrence of ulcers at more or less regular intervals. Differentiation from herpetic stomatitis has been discussed earlier. However, the possibility should also be borne in mind of Behçet's syndrome, of which oral aphthae may be the first sign.

Exceptionally, major aphthae may mimic carcinoma. The history is an important guide, but patients with aphthous stomatitis are just as susceptible to cancer as anyone else. A clinical feature which helps to differentiate cancer from a major aphtha is that carcinomas of this size (one or more cm in diameter) are indurated, whereas a major aphtha remains relatively soft. Nevertheless, biopsy should be carried out where there is any doubt.

Management

Haematological investigation is important mainly in patients whose aphthae start or worsen late in life. Routine blood indices sometimes need to be supplemented with serum iron or ferritine, folic acid or vitamin B_{12} levels. In most cases, deficiency states are latent, and the haemoglobin is within normal limits. A depressed serum ferritin level (sideropenia) is the most common finding.

Any haematinic deficiency should be investigated and treated. However, as already mentioned, such treatment other than for folate deficiency may not improve aphthae significantly. Treatment is therefore largely empirical and often unsatisfactory. Possible measures include the following:

Corticosteroids. Some patients gain relief from Corlan (hydrocortisone sodium succinate 2.5 mg) pellets, allowed to dissolve in the mouth 3 times a day. Other favour the use of soluble betamethasone (Betnesol) tablets as a mouthwash. Alternatively, beclomethasone (Becotide) aerosol can be used to spray more potent corticosteroids on to the ulcers.

Corticosteroids are unlikely to hasten healing of an ulcer, hence patients should preferably take pellets continuously (whether or not ulcers are present) to allow the corticosteroid to act in the earliest stages of ulcer formation, before symptoms develop. This is only feasible for those who have frequent ulcers, that is to say at two- or three-week intervals. Such a regimen should be tried for 2 months, then stopped for a month to assess whether there has been any improvement and whether there is any deterioration without treatment.

There is no evidence that currently available topical oral corticosteroids cause any significant adrenal suppression. Even continuous use of Corlan pellets appears to be harmless, but interruption to assess the effect of treatment can also be regarded as a safety measure.

Tetracycline mouth rinses. Despite the absence of any obvious rationale, controlled trials both in Britain and the USA have shown that tetracycline rinses significantly reduce both the frequency and severity of aphthae. Tetracycline may be used in conjunction with an antifungal drug. Tetracycline mixture (250 mg of tetracycline in 10 mL of fluid) can be held in the mouth for 2-3 min, 3 times daily. This should be done as soon as the patient feels that ulcers are starting to develop, but some find it helpful to use this mouth bath regularly for 3 days each week if they have frequent ulcers.

Chlorhexidine. A 0.2% solution held in the mouth 3 times daily for at least 1 min after meals may sometimes lessen the duration and discomfort of aphthae to some degree. Zinc sulphate or zinc chloride solutions may also have some beneficial effect.

Topical salicylate preparations. Salicylates have an anti-inflammatory action, and choline salicylate in a gel can be applied to aphthae. These preparations, available over the counter, may help some patients with mild aphthae.

Cyclosporin. Eisen and Ellis (1990) have reported successful treatment of recurrent aphthae with cyclosporin, but not all cases responded.

Major aphthae remain a difficult therapeutic problem. Systemic corticosteroids may give short-lived relief, then lose their effectiveness. Thalidomide appears to be the drug most likely to give relief. Dapsone and azathioprine have also been claimed to be effective in some patients. Relief of major aphthae in patients with AIDS may follow treatment with zidovudine. All of these drugs have significant toxic effects, but their use may be justified for so severe a complaint. Scully and Porter (1989) have reviewed the agents used in the management of recurrent aphthae as well as the aetiology and pathogenesis.

Ultimately, topical local anaglesics, such as lignocaine gel, are often the only preparations that allow the patient to eat in relative comfort.

In view of the lack of reliably effective treatment of aphthae, it is important to point out to patients, first, that there is no certain cure; second, that it is probable that the condition can be palliated and made at least tolerable and, third, that the disease is self-limiting, and that sooner or later it will clear up spontaneously.

Behçet's syndrome

This disease, which is rare in Britain, is characterized by oral aphthae of any of the types described above, associated with eye lesions (particularly iridocyclitis), genital ulceration, thrombophlebitis, pyoderma, sometimes arthritis and other more or less severe systemic lesions. Young adult males aged between 20 and 40 years are chiefly affected. Diagnosis depends on recognizing the concurrence of the multi-site lesions: there are no definitive laboratory rests, so that, as Wechsler and Piette (1992) have pointed out, confirmation of the diagnosis is sometimes difficult. The aetiology is still speculative and treatment is largely symptomatic. When major oral aphthae are troublesome, thalidomide may be the most effective treatment.

Lichen planus

Lichen planus, a common chronic inflammatory mucocutaneous disease, can give rise to white lesions, atrophic areas or erosions.

Aetiology

In spite of histological changes, which can be highly characteristic and specific, the aetiology of lichen planus remains obscure.

The predominantly T-lymphocyte infiltrate suggests the possibility of cell-mediated immunological damage to the epithelium. Nevertheless, tests of cellular immune responses

to extracts of skin lesions of lichen planus have produced inconclusive results so far, and it has not been possible to demonstrate humoral or lymphocyto-toxic mechanisms.

The fact that a disease indistinguishable from lichen planus can be induced by various drugs also suggests involvement of an immunopathogenesis. Lichen planus is also a characteristic feature of graft-versus-host disease, but nevertheless is not causally associated with any of the recognized autoimmune diseases. Lichen planus responds to immunosuppressive drugs (though not when associated with graft-versus-host-disease), but the nature of any immunological mechanism remains unclear.

The belief that lichen planus may be associated with an unusually high incidence of glucose intolerance or diabetes mellitus or, alternatively, with rheumatoid arthritis has not been confirmed. The so-called Grinspan syndrome of lichen planus, diabetes mellitus and hypertension appears to be no more than a chance association of these common disorders or related to the drugs used.

The traditional view that lichen planus is associated with emotional stress is difficult to evaluate or substantiate.

Clinical features

The white lesions are frequently asymptomatic. Nevertheless, lichen planus is probably the only disease which, if untreated, can cause unrelieved soreness of the mouth for many years. Middle-aged or older people are predominantly affected and the disease is rarely seen before the age of 30 years. Women account for at least 65% of patients.

The lesions have characteristic clinical appearance and distribution. Both features should be taken into account in making the diagnosis.

Striae are sharply defined and form lacy, starry or annular patterns. They may occasionally be interspersed with minute, white papules: rarely, papules may predominate. Striae may be impalpable or felt to have a stringy texture. Less common types of white lesions are confluent plaques. The latter are more likely to be seen on the dorsum of the tongue or in other sites in long-standing disease.

Atrophic areas, with redness and thinning but not ulceration of the mucosa, are often combined with striae.

Erosions are widespread, shallow irregular areas of epithelial destruction, usually covered by a slightly raised yellowish layer of fibrin. This appearance often gives rise tot he idea that they are intact or recetnly ruptured bullae. However, bullous lichen planus is a rarity that is hardly ever authenticated.

The margins of erosions may be slightly sunken due to fibrosis and gradual healing at the periphery. Patterns of striae radiating from the margins of erosions may also be seen.

These three types of lesion have corresponding microscopic features.

Distribution

By far the most frequently affected sites are the buccal mucosa, particularly posteriorly, but the lesions may spread forward almost to the commissures. The next most common site is the tongue, either the edges or the lateralmargins of the dorsum or less frequently the centre of the dorsum. Atrophic lichen planus often involves the gingivae, but striae are rare there. The lips are sometimes involved, but the palate is rarely, and the floor of the mouth hardly ever affected.

Lesions are very often symmetrical, often strikingly so, but may be more prominent on one side than another. Rarely, erosions may be the only sign or may precede the appearance of striae.

On the tongue, the lesions frequently form a narrow whitish band of depapillation along each side of the dorsum, sometimes with elongated erosions ni the centre of each band. Occasionally, a dense snowy white (leucoplakia-like) plaque with irregular margins forms in the centre of the dorsum.

Gingival lichen planus

Gingival involvement may be the predominant feature, and needs to be distinguished from other types of gingivitis. Atrophic lesions are most common, the epithelium is then thin and appears almost transparent, shiny, red and smooth. Unlike marginal gingivitis, the inflammation can extend to the reflection of the mucosa, but may spare the gingival margin. Gingival lichen planus is often also patchily distributed and may involve the gingiva of only three or four teeth in one quadrant of the mouth. Also, it only affects the lingual and palatal gingivae uncommonly. Striae are rare on the gingivae, but may be present elsewhere in the mouth.

The soreness caused by these atrophic changes - often in the past labelled non-specifically as 'desquamative gingivitis' - makes toothbrushing difficult. Accumulation of plaque and associated inflammation seem to aggravate lichen planus, and a vicious circle is set up. The contribution of local irritation to gingival lichen planus is suggested by the fact that it disappears when the teeth are extracted. Lichen planus under a denture is virtually unknown.

Symptoms are variable. Striae may only be noticed by chance by a dentist. In others, striae may cause a sensation of roughness or slight stiffness of the mucous membrane. Atrophic lesions are sore and erosions may make eating difficult.

Skin lesions

Lichen planus is a common skin disease and 25-35% of patients with oral lichen planus may also have skin involvement. The skin lesions characteristically form purplish, 2-3 mm papules. They have a glistening surface marked by fine (Wickham's) striae which may only be visible with a magnifying glass. The rash is usually irritating and its appearance may be changed by scratching. Skin lesions should be looked for on the flexor surface of the forearms, especially on the wrists.

Microscopy

The classical features can be summarized as follows:

- a saw-tooth profile of the rete ridges

- liquefaction degeneration of the basal cell layer

- a band-like lymphohistiocytic infiltrate which hugs the epitheliomesenchymal junction.

Striae show parakeratosis or hyperorthokeratosis, sometimes with a prominent granular cell layer. The rete ridges tend to be pointed and saw-tooth in shape. Along the junction between the epithelium and connective tissue there may be degeneration and liquefaction, with beads of fluid accumulating along the basement membrane. The basal cell layer is not usually identifiabl as such but colloid (Civatte) bodies (prematurely keratinized basal keratinocytes) may be present in the depths of the epithelium or extruded into the immediately underlying connective tissue. Fibrinogen deposition along the basement membrane zone may be conspicuous and there is often pigmentary incontinence.

In the corium, the infiltrate consists mainly of T lymphocytes, packed beneath the epithelium in a band-like distribution. These inflammatory cells form a compact zone which hugs the epithelio-mesenchymal junction and has a well-defined lower border.

Atrophic lesions show severe thinning and flattening of the epithelium, but the inflammatory infiltrate often retains its characteristic distribution and may be more dense.

In erosions, destruction of the epithelium leaves only the granulating connective tissue floor of the lesion, so that the appearances are non-specific. The diagnosis must be confirmed by finding typical lesions elsewhere in the mouth.

In many cases the microscopic features are not absolutely distinctive and no more than 'consistent with' lichen planus or difficult to distinguish from lupus erythematosus. The diagnosis must then be made in conjunction with the clinical features and laboratory investigation to exclude lupus erythematosus.

Management

The diagnosis of lichen planus can usually be made on the history, appearance and distribution of the lesions. If there is any doubt, a biopsy should be taken, particularly when striae are ill-defined. A streaky appearance is occasionally produced by dysplastic leucoplakias.

Tetracycline mouth baths (used as described for recurrent aphthae) seem sometimes to encourage erosions to heal. Hydrocortisone pellets or betamethasone mouth rinses are sometimes useful, but more potent anti-inflammatory corticosteroids such beclomethasone aerosols sprayed into the mouth 4-6 times a day are probably more effective.

Thrush can be a side effect of the more potent topical corticosteroids, so that an antifungal drug such as miconazole may have to be given concurrently.

Gingival lichen planus is the most difficult to treat. The first essential is to maintain rigorous oral hygiene. If this cannot be maintained, the chances of improvement are small. Corticosteroids should be used in addition, as described above. In this site, triamcinolone dental paste may be relatively easy to apply.

In exceptionally severe cases and if topical oral treatment fails, systemic corticosteroids are effective. Alternatively, intralesional corticosteroids may be tried. Eisen et al (1990) reported cyclosporin mouth rinses to be effective in a small group of patients.

Prognosis

As indicated earlier, lichen planus can be remarkably persistent, if untreated. In the past, patients have been known to have the disease for 20 or even 30 years. However, current treatment with potent corticosteroids is likely to be effective and patients with such long-standing disease are rarely seen.

The potential of lichen planus for malignant change has for long been controversial. A study by Holsmtrup et al (1988) involved 611 patients followed for a mean period of 7.5 years and, in this group, malignant change developed in 9 patients (1.5%). All the latter, except one, were women and malignant change followed the initial diagnosis after a mean period of 10 years (range 5-24 years). Compared with the estimated cancer risk in the population of Denmark, lichen planus would thus appear to increase it approximately 50-fold. Voute et al (1992), in their follow-up study of 113 patients, concluded that the 3 cases of oral cancer found after an average period of 7 years provided 'some but not very strong support' for the belief that lichen planus was premalignant, because of doubt about the original diagnosis. However, Holmstrup (1992), on the basis of five previous studies reported since 1985, felt that there was no longer any doubt about this risk and that its magnitude was between 0.5% and 2.5%, but was unable to identify any predictive factors.

Drug-associated lichen planus

A great variety of drugs, notably methyldopa, gold and antimalarial agents, and contact with amalgam restorations, have been reported to cause disease indistinguishable from lichen planus. The treatment is, wherever possible, to change the drug or restoration for an appropriate alternative.

Lupus erythematosus

Lupus erythematosus is an uncommon connective tissue disease which as two main forms, namely systemic and discoid. Either can give rise to oral lesions which may appear similar to those of oral lichen planus. Systemic lupus erythematosus has protean effects. Arthralgias and rashes are most common, but virtually any organ system or serous surface can be affected. The most serious consequences are from renal or cerebral involvement. A great variety of autoantibodies is produced and, of these, antinuclear antibodies are the most characteristic and regularly detectable.

Discoid lupus is essentially a skin disease with mucocutaneous lesions indistinguishable clinically from those of systemic lupus. These may be associated with arthralgia but, rarely, significant autoantibody production.

Clinically, oral lesions are found in about 20% of cases of systemic lupus, in an unknown number of patients with discoid disease and can rarely be the presenting signs of this disease. Typical lesions are white, often striate, areas with irregular atrophic areas or shallow erosions, but the patterns, particularly those of the striae, are typically far less sharply defined than in lichen planus and in discoid disease in particular. They often involve only a small area of one side of the mouth and may be in the vault of the palate - an unlikely site for lichen planus.

Lesions can be widespread and form variable patterns of white and red areas. There may also be small slit-like ulcers just short of the gingival margins. In about 30% of cases, Sjögren's syndrome develops and, rarely, cervical lymphadenopathy (Chapter 14) is the first clinical sign.

Microscopically, the oral lesions of discoid and systemic lupus show an irregular pattern of epithelial atrophy and acanthosis. The down-growths of the latter may be flame-like in contour or long and slender, extending deeply into the corium. There may be surface keratinization which may rarely appear to be invaginating the epithelium (keratotic plugging), liquefaction degeneration of the basal cell layer and thickening of the basement membrane zone by deposition of antigen/antibody complexes, which also appear in blood vessel walls, as shown by PAS staining. In the corium there is oedema and often a hyaline appearance. The inflammatory infiltrate is highly variable in density, typically extends deeply into the connective tissue and may have a perivascular distribution, but is frequently scanty in the lamina propria.

Though the appearances can sometimes be suggestive of either lichen planus or lupus erythematosus, the latter is unlikely to show the regular patterns of acanthosis or, more particularly, the band-like distribution of lymphocytes in the papillary corium. Karjalainen and Tomich (1989), in a statistical analysis of a range of microscopic features seen in lichen planus and lupus erythematosus, found that distinguishing features of the latter were vacuolization of keratinocytes, thick patchy PAS-positive sub-epithelial deposits, oedema of the upper lamina propria, PAS-positive thickening of blood vessels walls and dense, deep or perivascular inflammatory infiltrate.

Using frozen sections, a band of immunoglobulins and complement (C3) with a granular texture deposited along the line of the basement memmmbrane may be shown by immunofluorescence. This deposit underlies the lesions alone in discoid disease, but also underlies normal epithelium in systemic disease. In paraffin sections, immunoglobulin deposits may be detectable using immunoperoxidase staining. The only other feature that distinguishes systemic from discoid lupus microscopically is the characteristic, but rare, finding of frank vasculitis in the former.

Diagnosis of discoid lupus depends on the clinical features and particularly, rashes, often of a photosensitivity type. The autoantibody findings are of little importance except to distinguish discoid from systemic disease.

Mild systemic lupus can be difficult to distinguish clinically from discoid disease, and rarely there can be transition from discoid to systemic disease. However, systemic lupus should be recognizable by the pattern of autoantibody production. The most specific is that to double-stranded (native) DNA (dsDNA, nDNA).

Haematological findings in active SLE include a raised ESR, anaemia and, often, leucopenia or thrombocytopenia. Renal involvement is indicated by haematuria, proteinuria and red and white cell casts.

Oral lesions of discoid and systemic lupus respond in some degree to topical corticosteroids. Mild systemic lupus may be treated with anti-inflammatory agents alone, but more severe disease requires systemic corticosteroid or other immunosuppressive treatment. However, oral lesions frequently do not respond to doses of corticosteroids adequate to control systemic effects of the disease. Under such circumstances, palliative treatment is needed until disease activity abates.

Prognosis

Systemic lupus was thought at one time to have a high mortality and though uncommon, cerebral disease or, to a lesser degree, renal disease can be life-threatening. However, very many cases are relatively mild and ultimately self-limiting. Under such circumstances, over-enthusiastic immunosuppressive treatment can cause more trouble than the disease. As with other connective tissue diseases, there is an increased risk of cancer, especially lymphomas.

Pemphigus vulgaris

Pemphigus is a rare disease characterized by formation of vesicles or bullae on skin and mucous membranes and is usually fatal if untreated.

Aetiology

An immunopathogenesis can more readily be demonstrated in pemphigus than in any other oral disease. The two main findings are, first, a raised titre of antibodies (predominantly IgG) to the intercellular substances of the epithelium and, second, antibodies demonstrable by immunofluorescence along the intercellular junctions of the epithelium. The antibodies are tissue-specific and react only to the intercellular substance of squamous epithelium.

Clinical features

Women usually in the fourth or fifth decade are predominantly affected. Lesions may be seen first in the mouth but later involve the skin, particularly the trunk.

The vesicles are fragile and rarely seen intact in the mouth. A common appearance is therefore that of several small irregular erosions. These often have ragged edges and are superficial, painful and tender. When the mucous membrane is gently stroked, a vesicle or bulla may appear (Nikolsky's sign). Fluid taken from a recently ruptured vesicle should show characteristic rounded acantholytic epithelial (Tzanck) cells in a stained smear.

The rate of progress of the disease is very variable. It may be fulminating, with rapid development of widespread ulceration of the mouth and spread to other sites such as the eye within a few days and very soon afterwards to the skin. Occasionally, lesions may remain localized to the mouth for months or longer before they involve the skin.

The cutaneous vesicles or bullae vary from a few millimetres to several centimetres across. They at first contain clear fluid which may then become purulent or haemorrhagic. Rupture of the vesicles leaves painful erosions, with ragged margins of loose epithelium, which gradually crust over.

Microscopy

The essential feature is the loss of attachment of epithelial cells to each other (acantholysis). The changes are intra-epithelial and first seen as clefts just superficial to the basal cell layer. These splits widen until clinically visible vesicles or bullae form and finally rupture. The separated (acantholytic) epithelial cells become rounded, with their cytoplasm contracted round the nucleus, and can often be seen in small groups within a vesicle. Direct immunofluorescence, showing binding of immunoglobulins to the intercellular substance of the epithelium, is confirmatory. Electron microscopy has confirmed that this is the antibody-binding site.

Management

The severity of the disease may sometimes be such that the diagnosis must be confirmed as quickly as possible. As lesions spread over the body, loss of protein, fluid and electrolytes from the raw areas becomes severe and they readily become secondarily infected. Without treatment, death usually follows from septicaemia, but immunosuppressive drugs are usually life-saving. However, some cases pursue an indolent course.

Biopsy is essential and the changes are usually sufficiently characteristic to make a diagnosis. Once the diagnosis has been confirmed, adequate immunosuppressive treatment is required. Systemic corticosteroids are the main standby but, to keep the dose within acceptable limits, azathioprine is usually also given. Treatment may have to be lifelong and withdrawal of treatment typically leads to relapse. However, immunosuppressive treatment can cause severe, even fatal, complications. Rarely, a patient may have non-progressive disease, as described by Lamey et al (1992) who reviewed the response and alternative treatments for pemphigus.

Darier's disease (keratosis follicularis)

Darier's disease is a rare dominantly inherited genodermatosis characterized by acantholysis but, unlike pemphigus vulgaris, does not cause intraoral vesiculobullous lesions.

Clinically, the cutaneous lesions of Darier's disease include keratotic papules mainly of the upper parts of the body, palmar pits and dystrophy of the nails. The frequency of oral lesions ranges from 15% to 50% of patients. The palate is predominantly affected; it appears pebbly or may resemble smoker's keratosis. Recurrent salivary gland swelling due to duct

obstruction was seen in 30% of 24 patients reported by Macleod and Munro (1991). Isolated oral lesions in the absence of skin disease have been termed *warty dyskeratoma.*

Microscopically, there is localized hyperkeratosis, acantholysis with suprabasal cleft formation and dyskeratosis. The last gives rise to large cells with eosinophilic cytoplasm *(corps ronds)* and pyknotic elongated nucleis *(grains).* Acantholysis appears to result from a defect of the tonofilament-desmosome complex.

Current treatment is with retinoids. Toxic effects limit their long-term tolerance, but even in the absence of treatment the disease is not disabling.

Epidermolysis bullosa

Epidermolysis bullosa (EB) is characterized by skin fragility and bulla formation. There are three main heritable types (dystrophic, junctional and simplex - each with several subtypes and different modes of inheritance), categorized according to the level of tissue cleavage. There is also an acquired type which appears to be immunologically mediated.

Wright et al (1991), in an analysis of the variants of hereditary EB in 216 patients, found oral lesions in up to 100% of the recessive and 81% of the dominant dystrophic types, respectively. Oral lesions were present in up to 92% of the junctional types and in up to 59% of the simplex types, and were more frequent in association with generalized disease.

Clinically, oral lesions range from intermittent blistering in simplex-type disease to almost continuous blistering in response to minimal trauma and severe scarring in the generalized recessive dystrophic type. Scarring can be such as to obliterate the sulci, tie down the tongue and lead to microstomia. Intra-oral bulla formation can be severe in the junctional type, but disabling scarring is rare. In addition to blistering, intra-oral milia (small intra-epithelial cysts) may be seen particularly in dominant dystrophic EB, and appear as small papular swellings.

Microscopically, the different types of epidermolysis bullosa are distinguished by the level of cleavage. Cleavage can be intra-epithelial (epidermolytic, simplex type), through the lamina lucida (junctional type) or sub-epithelial (dermolytic, dystrophic type). In the simplex type, the mechanism is unusual in that cleavage is through the cytoplasm of basal cells and may be the result of a defect in keratin filaments, causing them to be fragile. As described earlier, the dystrophic type most frequently affects the oral mucosa and leads to the most severe scarring. In the dominant dystrophic type, intra-oral milia may form, probably as the result of epithelial cells becoming entrapped during blister formation.

Management

If seen sufficiently early, rigorous preventive dentistry needs to be enforced in all patients with a tendency to intra-oral scarring. Extreme gentleness during dental treatment is necessary to minimize trauma and prevent further damage to the oral mucosa, particularly in recessive dystrophic disease. It is essential to preserve the natural dentition, as distortion of normal oral morphology by scarring can make the retention of dentures impossible even if they could be tolerated. Patients with junctional type EB may be able to tolerate normal dental

procedures once the potential for scarring has been assessed. In some patients, phenytoin lessens the frequency of cutaneous blistering and is worth giving prophylactically for detnal treatment in any patients with a tendency to intra-oral scarring. Wright (1990) has described the dental care and anaesthetic management of patients with hereditary EB.

In generalized recessive dystrophic EB there is an enhanced risk of malignant change, either extra- or intra-oral in the scarred tissue. In those who survive into their thirties, regular oral examination is necessary to detect any carcinomatous change as early as possible.

Mucous membrane pemphigoid

Mucous membrane pemphigoid is an uncommon chronic disease causing bullae, painful erosions and sometimes scarring, particularly of mucous membranes. There can be serious complications such as blindness, but the disease is not lethal.

Clinical features

Women are mainly affected, and are usually aged over 50 years. The oral mucosa is often first affected and frequently the only site. Other sites are the eyes or the mucous membranes of the nose, larynx or oesophagus. The skin is rarely affected or to only a minor degree. Lesions are rarely widespread and progress is typically indolent.

In the mouth, bullae can often be seen intact but are sometimes filled with blood. Rupture of bullae leaves raw areas with a well-defined margin. Individual erosions can persist for weeks or months before healing. Further erosions may develop nearby and the process can persist for years. Other mucous membranes may eventually be involved. Nevertheless, in many patients lesions may remain localized to the mouth for very long periods.

Microscopy

Bulla formation results from loss of attachment of the epithelium to the connective tissue and is in the region of the basal lamina. In contrast to pemphigus, there is no acantholysis, but subepithelial bulla formation with separation of the full thickness of the epithelium from the connective tissue. Epithelium forms the roof of a bulla while the floor is formed by the corium, infiltrated with inflammatory cells which may also be seen in the bulla cavity.

The disease appears to be immunologically mediated, but linear deposition of immunoglobulin along the basement membrane zone is less readily demonstrable than complement components. Circulating autoantibodies against basement membrane zone proteins are detectable in low titre if sufficiently sensitive techniques are used.

Bullous pemphigoid is a similar disease but affects the skin, rarely involves the mouth and circulating autoantibodies are more readily and frequently detectable. It is also more frequent in males.

Management

The diagnosis can usually be confirmed by biopsy and immunofluorescence microscopy, but it is essential to obtain an intact vesicle or bulla. Nikolsky's sign may be positive, as in pemphigus vulgaris, and a striking clinical finding is that the epithelium may slide away beneath the edge of the knife, however sharp, when biopsy is attempted.

When the diagnosis has been made, the patient should be referred for ophthalmological examination. Scarring leading to impairment or loss of sight is the most serious complication. Rarely, fibrosis can cause stenosis of the larynx or oesophagus.

When localized to the mouth, mucous membrane pemphigoid can often be controlled with topical corticosteroids for very long periods, if not entirely. This treatment is usually without significant side effects and delays the need for giving systemic steroids with their attendant complications. However, if there is any sign of spread of the disease, particularly to the eyes, systemic corticosteroids should be given and are effective.

Linear IgA disease

Linear IgA disease affects the skin more frequently than the mouth but can closely resemble mucous membrane pemphigoid for which it has frequently been mistaken. Both are characterized by subepithelial bulla formation, but linear IgA disease (as its name implies) shows linear deposition of IgA along the basement membrane zone by immunofluorescence microscopy, and low titres of circulating IgA antibodies to basement membrane zone antigen may be detectable (Chan et al, 1990; Porter et al, 1992).

Linear IgA disease tends to be unresponsive to topical corticosteroids but may be controlled with dapsone or a sulphonamide, although a systemic corticosteroid may also need to be given.

Dermatitis herpetiformis

Dermatitis herpetiformis is of unknown aetiology, but about 70% of patients have histological evidence of coeliac disease, although clinically evident malabsorption is uncommon.

Clinically, males are affected twice as frequently as females and an intensely itchy vesiculopapular rash mainly on the face, scalp, extremities and shoulders is typical. Oral involvement is rare but ranges from mild erythematous patches to painful erosions due to ruptured bullae.

Microscopically, IgA is deposited in the basement membrane zone of the tips of the papillary corium and associated with papillary tip micro-abscesses.

Management

The microscopic and immunofluorescence findings should enable a distinction to be made from linear IgA disease. If the lesions are troublesome, there is a typically dramatic

response to dapsone or sometimes to a gluten-free diet. The latter is safer but difficult to maintain.

'Desquamative gingivitis'

This is not a diagnosis but a clinical description of diseases which cause the gingivae to appear red or raw. Usually the attached gingiva of varying numbers of teeth is affected. Atrophic lichen planus is the most common cause: less frequent is mucous membrane pemphigoid where the gingivae are typical sites of bulla formation and erosions. Linear IgA disease is a rare cause.

Unlike simple marginal gingivitis, the gingival margins are frequently spared, but the diagnosis should be confirmed by biopsy.

Bullous erythema multiforme (Stevens-Johnson syndrome)

In this mucocutaneous disease the mouth is probably invariably affected, and is often the only site, particularly among patients coming to dental practice, as in 95 patients reported by Lozada-Nur et al (1989).

Aetiology

The cause is not clear, though the disease may be a reaction to a variety of triggering agents. The latter include some infections, notably herpes simplex or mycoplasmal pneumonia and drugs, particularly sulphonamides. Barbiturates and penicillamine have also been blamed, but it is very rare to obtain a positive drug history. Even when drugs are being taken, they are not necessarily the cause.

The disease is regarded by some as being immunologically mediated, but no convincing mechanism has been proposed and in many, if not the majority, of patients no precipitating cause can be found.

Clinical features

Teenagers or young adults, particularly males, are predominantly affected. The most conspicuous feature is often the grossly swollen, crusted and bleeding lips. Within the mouth there are usually widespread irregular erosions with ill-defined margins and widespread erythema.

The eyes are the next most frequently affected site and conjunctivitis of variable severity may be seen. Dermal lesions may consist of widespread erythema alone or characteristic target lesions. These are red macules, a centimetre or more in diameter with a bluish cyanotic centre. In severe cases, large bullae form. The attack usually lasts for three or four weeks, with new crops of lesions developing over a period of about 10 days. Recurrences, usually at intervals of several months, for a year or two are characteristic but occasionally the disease is chronic and persistent.

In the most severe cases the patient is acutely ill after prodromal fever and constitutional disturbance and the term *Stevens-Johnson syndrome* is applied to this type of disease. Ocular damage can impair sight and rarely cause blindness. Even more rarely, renal damage can be fatal.

Microscopy

The histological appearances are variable. Widespread necrosis with eosinophilic colloid change in the superficial epithelium may be an obvious feature. Though not specific, this may progress to intra-epithelial vesiculation. Vesicles or bullae can also be sub-epithelial and there is dense infiltration of the corium by inflammatory cells. These may have a perivascular distribution but true vasculitis is absent.

There is no specific treatment. Corticosteroids may give symptomatic relief. Antibiotics are frequently also given in severe cases, with the idea of preventing secondary infection. Lozada-Nur et al (1992) have reported a complete response to levamisole in 31 out of 39 patients.

Reiter's disease

Reiter's disease comprises urethritis, arthritis and conjunctivitis, though the last is present in only about 50% of patients, and many other organ systems can be affected.

The aetiology is unknown and, though often regarded as a sexually transmitted disease, very many cases (as in Reiter's original patient) have followed outbreaks of infective enteritis by a variety of Gram-negative bacilli. Reiter's disease, therefore, appears to be a post-infective reaction with a strong association with HLA B27.

Clinically, men are predominantly affected in the ratio of up to 50 to 1 and are usually aged between 20 and 40 years. Arthritis of the extremities, sometimes intensely painful and often polyarticular, is usually the chief complaint. Skin or mucosal lesions are common, the temporomandibular joint is occasionally involved and facial palsy may be another complication. Fever and loss of weight are associated.

Oral lesions may develop in 20% or more, but are usually so transient and painless as to pass unnoticed. They most typically form rounded red areas with a peripheral, white raised line and can closely resemble stomatitis areata migrans (see below).

Most cases resolve after a few months, but recurrences may follow. The mucosal lesions should not require treatment, but joint pain responds to anti-inflammatory agents.

Acanthosis nigricans

Acanthosis nigricans is so called because of the pigmentation of the skin lesions. It is a well-recognized marker of internal malignancy, but there are several variants either devlopmental or associated with other types of systemic disease such as insulin-resistant diabetes mellitus or other endocrinopathies. The condition has been extensively reviewed by Sedano and Gorlin (1987).

Clinically, most patients are over the age of 40 years. Approximately 40% of patients with the malignant type of acanthosis nigricans have oral lesions consisting of shaggy thickening or confluent papillomatous overgrowths, particularly of the labial or lingual mucosa. The buccal mucosa may be thickened and velvety in texture, and gingival enlargement may be gross. The oral lesions are not pigmented.

The cutaneous lesions consist of multiple pigmented papillomatous or verrucous overgrowths of many sites, particularly flexural surfaces such as the axillae, neck, groin or inner thighs, or umbilical or perianal areas. Palmar and plantar hyperkeratosis is present in approximately 25% of patients.

The neoplasms are mostly of the gastrointestinal tract or its appendages and are highly malignant. Carcinoma of the stomach is most common and found in 60% of patients. Other types of tumours such as lymphomas are occasionally associated.

In a minority, mucocutaneous lesions sometimes precede detection of internal cancers by many years, but more frequently follow it. They may wax or wane as the neoplasm spreads or regresses in response to treatment, only to flourish again as the tumour recurs. This suggests that the mucocutaneous lesions are the response to chemical mediators released by the tumours.

Microscopically, the buccal mucosa is greatly thickened with many vacuolated epithelial cells, giving it a basket-weave appearance resembling white sponge naevus but with a more shaggy surface (Mostofi et al, 1983).

Oral lesions appear to affect only a small minority of the non-neoplastic types of acanthosis nigricans and do not appear to have been fully categorized.

Management

When oral lesions of malignant acanthosis nigricans are the first manifestation, screening of the gastrointestinal tract in particular must be carried out and, if necessary, repeated at intervals to allow early treatment of tumours. The oral lesions respond only to treatment of the underlying malignant disease, but once the latter has developed the average period of survival is no more than 2 years.

Pyostomatitis vegetans

Pyostomatitis vegetans is a rare oral manifestation of inflammatory bowel disease, particularly ulcerative colitis. Thornhill et al (1992) could find only 32 reports since it was originally described in 1949, but added three more. However, Chan et al (1991) had described two other cases. In approximately 50%, cutaneous lesions (pyoderma vegetans) are associated.

Clinically, the age of those affected ranges from the third to sixth decades, but occasionally the disease has not been recognized until even later. Males predominate in a ratio of 3 to 1. Diarrhoea is usually the first complaint, but ulcerative colitis sometimes continues for several years before oral lesions appear. Occasionally, however, oral lesions are the first sign or diarrhoea may be insignificant.

In the mouth, there are multiple, yellowish miliary pustules typically in a thickened, erythematous mucosa which is sometimes folded or fissured. The pustules readily rupture to release purulent material and leave shallow ulcers. Large irregular, fibrin-covered ulcers may be associated and may extend on to the vermilion borders of the lips. Pustules appear in almost any site within the mouth, particularly the gingival, buccal and labial mucosa, but rarely on the dorsum of the tongue. Other mucous membranes such as those of the genitalia may be affected and pyoderma vegetans, with pustules particularly in flexural areas, may be associated.

Microscopically, the pustules show suprabasal clefting and intra-epithelial vesiculation or abscess formation, but typically lack true acantholysis. They contain many eosinophils and there is a mixed inflammatory infiltrate in the corium. Immunofluorescence sometimes shows intercellular immunoglobulin, usually IgG, in the epithelium. A significant peripheral eosinophilia is usually associated and may amount to 20% of the total leucocyte count.

Management

Pyostomatitis vegetans must be distinguished from pemphigus vulgaris by (a) the pustular oral lesions and, when present, the skin lesions; (b) the association with diarrhoea or frank ulcerative colitis; (c) peripheral eosinophilia; and (d) the benign course. Microscopically, the lack of true acantholysis and the eosinophil content of the intra-epithelial abscesses help to distinguish the oral lesions from pemphigus vulgaris, but may resemble those of pemphigus vegetans.

The main requirement is treatment of troublesome bowel disease. Sulphasalazine or sulphamethoxypyridoxazine may be effective and may cause resolution of the oral lesions. They are probably the treatment of choice. Chronic ulcerative colitis may have to be treated by colectomy and this may allow the oral lesions to heal. However, the latter do not always respond to drug treatment of associated bowel disease. They occasionally respond to topical corticosteroids, but more frequently to systemic prednisolone. Dapsone is frequently also effective but may have to be stopped if haemolysis develops.

'Allergic stomatitis'

Many otherwise harmless substances coming into contact with the skin cause hypersensitization in susceptible subjects. Further contact then causes an inflammatory reaction. A common example is the reaction to a wide variety of household detergents and industrial materials.

Some mucous membranes such as the eyes can also become sensitized in this way, but other parts of the body differ widely in their response. Sulphonamide ointments, for example, are potent skin sensitizers, but are widely used without trouble in the eyes.

The oral mucous membrane appears to show yet other differences and appears to be unable to mount reactions comparable with contact dermatitis and there is no oral counterpart to allergic eczema. Indeed, atopic disease has no oral mucosal manifestations in the 10% of the population who suffer from it. Even patients who are sensitized to a material such as nickel can tolerate it in the mouth; it may then cause a characteristic rash but no oral lesions.

Amalgam restorations cause no trouble in patients sensitized to mercury, provided that the unset material does not touch the skin. Similar considerations apply to methyl-methacrylate. Those few people who are sensitized to the monomer can wear acrylic dentures with impunity. Inflammation under acrylic dentures, often in the past described as 'acrylic allergy', is usually candidal infection and most so-called allergic reactions of the mouth are probably due to direct irritation.

The number of authenticated cases of contact hypersensitization of the oral mucous membrane is, therefore, so few as to make it questionable whether the oral mucosa can mount this type of reaction. If it does so, it must be phenomenally rare, but examples of what are frequently regarded as oral hypersensitivity reactions are cinnamon-related lesions and plasma cell gingivitis.

Cinnamon-related lesions

Cinnamon or cinnamonaldehyde is a common flavouring agent in foods and toothpastes. It has been incriminated in a variety of intra-oral lesions such as soft tissue swellings due to a granulomatous reaction (Patton et al, 1985), as well as gingivitis, glossitis, cheilitis, swelling or ulceration with non-specific inflammatory changes microscopically (Lamey et al, 1990). By contrast, Miller et al (1992) have reported white keratotic patches on the buccal mucosa in 13 out of 14 cases, and sometimes also in other sites but on the gingiva in only 2. Microscopically, there was ortho- or parakeratosis, acanthosis and a mainly lymphocytic inflammatory infiltrate. Plasma cells were not prominent, but there were dense perivascular infiltrates. Ten of the patients reported by Lamey et al (1990) gave positive delayed reactions on patch testing with cinnamon and the majority experienced recurrences on rechallenge after withdrawal of cinnamon-containing products. Eleven of the 14 patients reported by Miller et al (1992) achieved major or complete resolution of their oral lesions on withdrawal of cinnamon.

Despite the strong suggestion of the involvement of hypersensitivity in the production of these lesions, the disparate nature of the clinical and histological responses to the same substance is difficult to understand.

Plasma cell gingivitis and mucositis

This is another reaction where hypersensitivity mechanisms have been implicated. Sollecito and Greenberg (1992) found that approximately 50 cases of plasma cell gingivitis were reported between 1966 and 1977, mainly in the USA. The disease suddenly then seemed to disappear. Silverman and Lozada (1977) postulated that it had been a reaction to an unidentified allergen in chewing gum, dentifrice or other product.

Clinically, plasma cell gingivitis appears as intense erythema and oedema of the attached gingiva.

Microscopically, there is irregular acanthosis, often with spongiform pustules, and a subepithelial infiltrate predominantly of plasma cells extending deeply into the connective tissue. The density of this infiltrate is comparable to that seen in myeloma, but is clearly reactive rather than neoplastic.

Of the two patients reported by Sollecito and Greenberg (1992), one was subjected to skin testing for many common allergens and an exclusion diet. Neither showed objective resolution, but topical corticosteroids were palliative.

In sharp contrast tothe lesions of plasma cell gingivitis, White et al (1986) reported a case of *plasma cell orificial mucositis* in an edentulous woman with psoriasis. Despite the microscopic similarities to plasma cell gingivitis, this reaction consisted of a thickened, fissured and erythematous plaque encircling the entire oral orifice, fissuring of the tongue and diffuse irregular thickening of the free edge of the epiglottis. Patch tests to 25 common dental allergens were negative and treatment with corticosteroids was ineffective.

Oral mucosal reactions to drugs

Of the numerous possible mechanisms for oral drug reactions, few have been convincingly clarified. These reactions are not common overall, but may be important as early signs of a dangerous systemic reaction. Nevertheless, a drug being taken is not necessarily the cause of any oral symptoms and coincidence is often difficult to exclude, particularly with common diseases such as lichen planus. The problem is made difficult by multiple drug treatment, but a precise drug history is always essential, as it may be relevant to other aspects of dental treatment. An obvious example is a patient taking systemic corticosteroids who may, as a result, have oral candidosis but is also at risk when subjected to surgery under general anaesthesia.

Local reactions to drugs

Chemical burns. An aspirin tablet held against the mucosa close to an aching tooth is a well-known cause of superficial necrosis and a white patch. When the irritant is removed, the dead epithelium is shed and the mucosa heals. Other irritant chemicals are chromic acid, trichloracetic acid, or phenol.

Disturbance of the oral flora and superinfection. Prolonged topical use of antibiotics, particularly tetracycline, in the mouth allows resistant organisms, particularly *Candida albicans*, to proliferate, causing thrush. Inhaled corticosteroids can have a similar effect by affecting local immunity.

Systemically mediated reactions to drugs

Depression of marrow function

Anaemia. Few drugs significantly depress red cell production alone. The main example is prolonged use of phenytoin which can occasionally cause folate deficiency and macrocytic anaemia. This in turn can produce severe aphthous stomatitis, which responds promptly when folate is given.

Leucopenia. Drugs capable of having this effect include antibacterials (particularly co-trimoxazole and chloramphenicol), analgesics (particularly phenylbutazone), phenothiazines

and antithyroid agents. Agranulocytosis is characterized by necrotizing gingival and pharyngeal ulceration and can go on to a severe sometimes lethal prostrating illness.

When the main effect is neutropenia, low-grade oral pathogens are able to overcome local resistance and produce necrotizing ulceration, particularly of the gingival margins.

Purpura. Drugs may affect haemostasis by depressing platelet production. Drug-induced purpura is often also an early sign of aplastic anaemia caused by drugs which cause general marrow depression, as indicated above. Purpura can produce severe spontaneous gingival bleeding or blood blisters and widespread submucosal ecchymoses.

Clotting function is impaired by other drugs, notably anticoagulants such as the coumarins. In overdose these can cause severe bleeding after oral surgery, but do not otherwise cause abnormal oral signs.

Depression of cell mediated immunity

Immunosuppressive drugs such as corticosteroids and cytotoxic agents greatly enhance susceptibility to infections. Viral and fungal infections of the mouth are common in patients having organ trasplants and cytotoxic chemotherapy. Confluent vesiculation due to herpes may clinically be difficult to distinguish from the plaques of thrush, as may bacterial plaques. Recurrent infections such as measles, chickenpox or herpes zoster are also seen.

Many cytotoxic drugs, particularly methotrexate, are liable also to cause mucositis. The latter can range from soreness and erythema to ulceration severe enough to prevent eating.

Lichenoid reactions

As discussed earlier, many drugs, notably gold and antimalarials (both used in the treatment of rheumatoid arthritis or other collagen diseases), and the antihypertensive agents methyldopa and, occasionally, captopril, can produce a disease indistinguishable from lichen planus with characteristic oral signs or sometimes widespread erosions alone.

Bullous erythema multiforme (Stevens-Johnson syndrome)

As mentioned earlier, drugs can occasionally trigger this disease. Those most commonly implicated are long-acting sulphonamides and, rarely, barbiturates, but many cases have no recognizable triggering agent.

Fixed drug eruptions

These sharply circumscibed skin lesions recur in the same site or sites each time the drug is given. Among many drugs capable of causing this reaction, phenolphthalein, a component of purgative mixtures, is well recognized. Involvement of the oral mucous membrane is exceedingly rare.

Exfoliative stomatitis and dermatitis

Exfoliative dermatitis is one of the most dangerous and severe types of reaction to drugs. Comparable changes to those on the skin may develop in the mouth and are seen as widespread erosions due to destruction of the epithelium. Occasionally, oral changes precede or may initially be more severe than the dermal changes and may cause the patient to seek help for the soreness of the mouth. Early diagnosis and treatment is essential as the reaction can be lethal.

Metals are important causes, but gold is the only one at all widely used currently. Several other drugs, particularly phenylbutazone (now restricted), and barbiturates have also been incriminated.

Healing of oral lesions may leave a lichenoid pattern of striae.

Other drug effects

Hingival hyperplasia. Phenytoin and less frequently cyclosporin, nifedipine or its analogues can cause progressive fibrous hyperplasia of the interdental papillae.

Oral pigmentation. (see Chapter 9).

Dry mouth. This is a relatively common side effect of drugs, especially those with an atropine-like action, particularly tricyclic antidepressants (Chapter 11).

Tongue complaints

The tongue can be involved in a generalized stomatitis and develop lesions similar to those in other parts of the mouth, but it is also the site of lesions or a source of symptoms peculiar to itself and, for unknown reasons, can produce the earliest symptoms of latent defects of haemopoiesis. For white lesions of the tongue, see Chapter 9.

Glossitis is used to describe the red, smooth and sore tongue particularly characteristic of anaemia. However, this combination of signs (redness and smoothness) and a symptom (soreness) are by no means consistently associated. Tongues can be sore in the absence of visible changes or smooth but asymptomatic. Sore tongue is an only too common complaint and four clinical variants are recognizable.

Ulceration of the tongue

The tongue may be involved in, or even the main site of, various kinds of stomatitis such as herpes simplex or, more often, lichen planus. The tongue may also be the site of solitary ulcers, particularly carcinoma, which when far back may be difficult to see.

In general, definable lesions such as these, make the diagnosis straightforward by their clinical features and often biopsy.

Glossitis

The tongue is more or less uniformly red (inflamed), smooth (atrophy of the papillae) and sore. The main causes are:

- *Anaemia.* Iron deficiency and pernicious anaemia are the main causes, and women are more frequently affected. The red cell indices are important, as a fall in haemoglobin level may lag behind morphological changes in the red cells. There may, therefore, be glossitis, haematological signs of a deficiency state, but a haemoglobin level within normal limits. Early vitamin B_{12} deficiency can cause peculiar streaky red changes on the dorsum of the tongue (Moeller's glossitis).

- *Candidosis.* The tongue can be red, sore and oedematous due to candidal infection. This is particularly characteristic of acute antibiotic stomatitis and is often then associated with angular stomatitis and other features of candidosis. This condition is rarely seen now that antibiotics are used somewhat less irresponsibly.

- *Other vitamin B group deficiencies.* These are exceedingly rarely seen, but glossitis with angular stomatitis is characteristic of riboflavin and to some extent of nicotinic acid deficiency. The diagnosis of vitamin deficiency should not be made on oral signs alone in an otherwise healthy patient. The giving of B group vitamins is a common gesture in an attempt to deal with the complaint, but is almost invariably ineffective. However, the lack of response makes it clear that deficiency of these vitamins is not a cause.

- *Lichen planus.* A smooth tongue due to atrophy of the papillae, particularly in long-standing disease, may be seen, but there is then no soreness. There is often a bluish-white sheen to the surface of the tongue, and other signs of lichen planus are likely to be present in other parts of the mouth. Soreness of the tongue in lichen planus is due to atrophic lesions or erosions.

The sore, physically normal tongue

This is the most common and troublesome type, predominantly affects post-menopausal females. In the absence of visible signs, it is often tempting to assume the complaint to be psychogenic, but this is not always the case.

Deficiency states. It is essential to appreciate that pre-anaemic deficiency states can cause soreness of the tongue without any visible abnormality in colour or texture. Women in the age group where sore tongue is most common are also the main group susceptible to pernicious anaemia. The haemoglobin is usually within normal limits, but red cell abnormalities are apparent from routine indices, particularly the mean corpuscular volume (MCV) and may indicate the need for further investigation. Specific treatment for the deficiency will relieve the symptoms.

Psychogenic disorders. Sore tongue unassociated with organic disease is a psychogenic symptom and comparable to atypical facial pain. The great majority of patients are also women of middle age or over, but diagnosis can be difficult. Depression is sometimes the

underlying trouble, but is often effective disguised and replaced by complaint of this physical symptom. In such cases, adequate treatment with antidepressant drugs such as amitriptyline or dothiepin can sometimes abolish the tongue complaint and restore the patient's general sense of well-being.

In a few patients the underlying problem seems to be an anxiety state. This can occasionally be dealt with by reassurance, especially if there is an unfounded feat, particularly of cancer of the mouth. In other cases, the basis for the anxiety seems to be less specific. A short course of an anxiolytic such as diazepam may occasionally be helpful.

As with atypical facial pain, there seem also to be many patients who complain bitterly and persistently of sore tongue, in whom no organic disease can be found and who show no response to psychoactive drugs or any other form of treatment.

Geographical tongue (benign migratory glossitis)

This common condition is characterized by the recurrent appearance and disappearance of red areas, frequently with a white margin, on the tongue.

The cause is unknown, but in some the condition is familial and has been described in several succeeding generations. The abnormality can be seen even in infancy, though probably is often unnoticed, but many cases are seen in middle-aged patients.

Clinically, geographical tongue may appear as irregular, smooth, red areas, usually with sharply defined edges; they extend for a few days, then heal, only to appear again in another area. Alternatively, the areas can be annular with slightly raised whitish margins and can coalesce to form scalloped patterns. *Stomatitis areata migrans* is the term given to similar lesions which occasionally appear in other parts of the mouth. Microscopically, these lesions show a close resemblance to those of psoriasis (Chapter 9) with spongiform intra-epithelial micro-abscesses. Morris et al (1992) have confirmed that migratory glossitis is four times, and stomatitis areata migrans five times, more frequent in patients with psoriasis than controls. These lesions may therefore be an oral form of psoriasis.

Most patients with migratory glossitis have no symptoms, but some complain of soreness. Sometimes, perhaps, the patient has suddenly noticed the appearance and become anxious that cancer is the cause. Reassurance is then necessary and may be effective. In others, soreness may be due to a coincidental haematological deficiency and haematological investigation is therefore necessary. However, it would not be surprising if the thinning of the epithelium, together with the inflammatory changes seen histologically, caused symptoms.

Soreness in association with geographical tongue may also be psychogenic and may then respond to appropriate treatment. Some evidence has been produced to show an apparently significant association between geographical tongue and emotional disturbance. However, there remain many where no cause for the soreness can be found and no treatment seems to be effective.

Hairy tongue

This appearance is due to overgrowth of the filiform papillae which become elongated and hair like, forming a thick fur on the dorsum of the tongue. The filaments may be up to half a centimetre long and may be pale brown to black in colour. Adults are affected and heavy smoking, overuse of antiseptic mouthwashes or antibiotics, or a defective diet may be responsible, but the cause is often unclear. The discoloration is caused by pigment-producing bacteria.

Treatment is unsatisfactoy unless a cause can be found and eliminated. The measure most likely to succeed is probably that of persuading the patient to scrape off the hyperplastic papillae and vigorously cleanse the dorsum of the tongue using a firm toothbrush. This dislodges many microbes mechanically and, by removing the overgrown papillae, makes conditions less favourable for their proliferation.

Sometimes the dorsum of the tongue may become black without overgrowth of the papillae. This may merely be staining by drugs such as iron compounds used for the treatment of anaemia, but is then transient. Alternatively, it may have similar causes to black hairy tongue (see Chapter 9).

Furred tongue is a coating with desquamating cells and debris. It is a typical sign in systemic infections, when the mouth becomes dry and little food is taken. It is often seen in the childhood fevers, especially scarlet fever.

Median rhomboid glossitis

Median rhomboid glossitis is a lesion of the midline of the dorsum of the tongue at the junction of the anterior two-thirds with the posterior third, and for long it was believed to be the result of persistence of the tuberculum impar. However, this view is no longer widely accepted: the anomaly appears to be very rare in children, but is seen in adults.

Clinically, the appearance is variable. There is sometimes a red or pink rhomboid (lozenge-shaped) area of depapillation, the area may be white or pink and it may be lobulated. It is typically symptomless.

Microscopically, the appearances are also variable and include irregular (pseudo-epitheliomatous) hyperplasia, with an inflammatory infiltrate. There is sometimes candidal infection (the white variant), and occasionally the lesion proves to be a granular cell tumour.

The chief importance of median rhomboid glossitis is that it has been mistaken for a carcinoma both clinically and histologically and treated accordingly (Ogus and Bennett, 1978). Carcinoma hardly ever develops in this site, but competent histological assessment is necessary. The candidal variant can be treated with antifungal drugs; otherwise, reassurance is frequently all that is required.

Foliate papillitis

The foliate papillae are small lymphoid follicles separated by shallow crypts on the posterior lateral margins of the tongue. They may become mildly enlarged and red. They may then be noticed by and alarm patients who inspect their tongues. Reassurance that this is not a tumour can readily be provided by showing the patient the similar foliate papilla on the opposite side of the tongue.

Acute glossitis

Acute glossitis is rare, but there have been several reports between 1965 and 1984, as reviewed by Stoddard and Deshpande (1991). Most cases have been in infants or children. *Haemophilus influenzae* has been the most frequently identified cause, but with current immunization schedules, many such cases may be prevented. Typically, the tongue is red, swollen, oedematous and may protrude from the mouth. In severe cases the airway may be endangered. Some examples have been categorized as cellulitis of the tongue, while other have progressed to abscess formation.

Management

Prompt treatment is necessary because of the threat to the airway, and early intubation may be advisable. Exudate should if possible be obtained for culture and sensitivities, and empirical antimicrobial treatment given until sensitivity findings dictate a change. Intravenous cefotaxime may be a suitable choice in view of the possibility that *H. influenzae* may be responsible.

Ischaemic necrosis of the tongue

Despite its excellent blood supply, ischaemic necrosis of the tongue is a rare but recognized entity and Sofferman (1980) reported 3 cases. It is virtually diagnostic of giant cell arteritis, and Missen (1961), in autopsy examinations of 10 patients with giant cell arteritis, found bilateral involvement of the lingual arteries in 9 cases. Rarely also this disease can cause ischaemic necrosis of the lip, other parts of the face or the scalp.

Giant cell arteritis has been described in Chapter 7. In some cases, treatment of the headache of this disease with ergotamine may have worsened the ischaemia. Ischaemia of the tongue is heralded by severe pain and swelling and may be accompanied by other signs of temporal arteritis or polymyalgia. The tongue becomes blanched, cold and painful to move. It then may become cyanotic and undergo necrosis. The whole of the anterior half of the tongue may slough away or has to be excised once a line of demarcation has become clear.

Treatment with corticosteroids, if started before ischaemia is too far advanced, may possibly prevent further deterioration. They should in any case be given as soon as the diagnosis is suggested by the symptoms, a greatly raised erythrocyte sedimentation rate and inflamed scalp vessels. Dare et al (1981) report a case where the tongue had become blanched, swollen and painful but there was no early response to corticosteroids (prednisolone 120 mg/day). Resolution followed anticoagulation with intravenous heparin and Rheomacrodex but, because of previous reports where lingual ischaemia had not progressed

to gangrene, Dare and colleagues were uncertain whether their treatment had achieved the desired effect or whether the ischaemia was self-limiting.