CLINICAL ORAL MEDICINE

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Second edition

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Preface

Since the appearance of the first edition there have been developments of some significance in the understanding and management of oral ulceration and temporomandibular joint dysfunction which have necessitated rewriting those sections. A new chapter on the tongue has been added and there has been updating and revision of most chapters.

At a more personal level Dr Gayford has taken up a career in psychiatry so the revisions for this edition have been left to me. I would like to record my thanks to Professor R. A. Cawson, Dr W. H. Binnie and Dr M. Wilton for discussions over the past few years which have illuminated my understanding of many topics, which I hope is reflected in the text.

There are moves afoot to introduce a separate examination in Oral Medicine and Pathology in London University BDS finals. This I deplore since dental surgery (or stomatology) is neither sufficiently large nor complex to require this interminable subdivision. It is, however, a reflection of the growing recognition of oral medicine in undergraduate education—a beneficial change.

1979

R.H.

Errata

p. 132, line 10. *For* Stomatisis *read* Stomatitis.

pp. 266, 267. The illustrations for *Figs.* 11 and 12 should be transposed.

List of Plates Omit

(*Following* p. 276)

Foreword

It is a relatively short time since the first chair in Oral Medicine was established in a British University. The increase of knowledge both in basic medical science and its clinical application has unavoidably encouraged specialisation; this makes it essential that the busy clinician should have access to these developments in a convenient form so that he can assess their significance in his own field.

The second edition of this deservedly successful textbook will enable him to do this. Clinical experience has enabled the authors to give appropriate emphasis to what is important and to refer only briefly to conditions which are seen infrequently. Some measure of condensation has been unavoidable if a proper balance was to be ensured. There is an excellent bibliography at the end of each chapter.

Good wine needs no bush but this is undoubtedly the best work of its kind that I have read. I can recommend it to students for whom it will provide a sound foundation and to clinicians as a comprehensive survey and a most useful source of reference.

Introduction

To both doctors and dentists alike, the mouth represents an important part of the body which suffers diseases peculiar to it and is also frequently involved in many systemic disorders. Oral medicine may be defined as the diagnosis and treatment of 'medical' conditions of the mouth and associated structures. However, the practice of oral medicine, as defined above, is divided between the medical and dental professions, sometimes to the detriment of the patient. No plea is being made for the recognition of oral medicine as a separate speciality spanning medicine and dentistry, yet there is a place for practitioners with a sound knowledge of the subject. For teaching purposes and research, specialization in particular subjects, including oral medicine, is required.

The mouth and face cannot be divorced from the patient as a whole and one of the fascinations of oral medicine is that it may lead the clinician into all the branches of medicine and dentistry. Often it is difficult to know when to call a halt but any clinician must have the humility to refer a case, however interesting, to a colleague better equipped to continue the patient's treatment. This is easier if colleagues have an understanding of each others' speciality, so that a study of oral medicine should lead to better cooperation between medical and dental practitioners.

This book is hopefully directed to a wide audience; firstly to medical and dental practitioners. We also hope that specialists in medicine, surgery and dentistry will feel richer for an understanding of oral medicine, especially as they are so often called upon to practise this subject — generally unaware that they have departed from their own sphere of activity. Secondly, the needs of postgraduate dental students have been considered since experience of teaching them has emphasized the need for a text to cover their requirements. Doctors are asked to bear with thumbnail sketches of systemic disorders which are intended for dental surgeons whose indulgence is likewise craved while dental conditions are described for medical readers.

Very little pathology has been included which in no way reflects our estimation of that subject but rather the fact that there are several excellent texts of oral pathology, so we have confined ourselves to clinical features. For the same reason, purely dental diseases have been largely ignored.

Acknowledgements

We wish to thank Professor Sir Robert V. Bradlaw, CBE, MDS, FRCS, late Dean of the Institute of Dental Surgery and Director of the Eastman Dental Hospital, for allowing us to reproduce Plates 21, 23, 29, 30 and 31, and for information related to cases under his care.

Dr W. Gooddy, MD, FRCP, consultant neurologist to the National Hospital, Queen's Square and University College Hospital, London, kindly read the chapters related to neurology and offered helpful advice. We would also like to thank all our colleagues, medical and dental, for helpful discussion and criticism. Illustrations have been kindly prepared by the Photographic Department of the Eastman Dental Hospital and some by a colleague, Dr Philip Merdin, MB, CHB.

Finally, we record our deep indebtedness to the secretaries who have prepared the manuscript, in particular Mrs B. Rayiru and Miss N. Valère.

January 1971 J. J. G. R. H.

Contents

Chapter 1

Oral Ulceration

Introduction. In this chapter will be considered the major causes of oral ulceration (excluding neoplastic disease) which are not preceded by vesiculobullous lesions.

They will be considered under the following main headings:

1. Recurrent aphthous ulceration.
2. Behçet's syndrome.
3. Reiter's syndrome.
   (digression) Human lymphatic antigen system and oral ulceration.
4. Necrotizing sialometaplasia.
5. Agranulocytosis and neutropenia.

Recurrent Aphthous Ulceration

Aphthous ulcers are persistently recurrent, painful ulcers of the oral mucosa, of unknown aetiology. It seems probable that presently grouped together are a heterogenous collection of clinical entities.

Synonyms

There is much confusion caused by the large number of names that have been used to describe this condition: such terms as aphthous stomatitis, canker sore, dyspeptic ulcers, habitual ulcers, mucosal ulcers, Mikulicz's ulcers, ulcer necroticum mucosae oris and ulcers neuroticum mucosae oris are to be seen in the literature.

Variants of aphthous ulcers

Not all aphthous ulcers have the same clinical features. There is considerable variation in size, depth and length of persistence. Where the ulcers are large, penetrating into the deeper tissues with associated submandibular lymphadenopathy, the term 'major aphthae' may be used, or

alternatively, 'periadenitis mucosa necrotica recurrens'. This type of ulcer lasts much longer and heals with a scar.

Patients presenting with multiple small ulcers the size of a pinhead have been described under the term 'herpetiform aphthous ulcers'. Not all agree that this type of ulcer should be regarded as a variant of aphthous ulcer but should be regarded as a viral-induced ulcer. Attractive though this view may be, there is no proof to substantiate it.

Incidence

This varies according to the section of the population sampled. No figures less than 10 per cent have been quoted for any population survey. Of patients who are attending hospital outpatient departments for any condition, the incidence is 20 per cent and in selected groups figures as high as 60 per cent have been recorded. Females are more commonly affected than males, probably in the ratio 3:2. Ulcers may start in childhood, but do so more usually in the teenager. In most cases they become less frequent as the patient enters the fourth decade and may fade in the fifth and sixth decades of life. Women seem to persist with their ulcers longer than men and may start at an earlier age.

Aetiology and pathogenesis

As stated above, the aetiology is unknown. Many interesting hypotheses have been put forward with their associated groups of supporters, each is held enthusiastically for a time and then fades to be replaced by a new theory which reflects current research.

It is proposed to mention briefly some of the aetiological factors that have been cited.

1. *Heredity:* About 50 per cent of patients have a history of one parent having aphthous ulcers; it is much rarer for both parents to have the condition. Siblings are not always affected and it would be very rare indeed to find a large family suffering in this way. Sircus was of the opinion that where two parents were involved there could be anticipation in the age of occurrence with some of their children.

2. *Trauma:* This is supported by the clinical observation that some patients develop a crop of ulcers following minor trauma to the oral mucosa. Commonly this follows routine dental treatment, where even the presence of a cotton-wool roll in the mouth or the injection of a local

anaesthetic may produce ulceration. Many cases occur with no history of previous trauma.

3. *Infection:* This may be divided into (a) bacterial and (b) viral.

a. Bacterial: the recent isolation of transitional L-form bacteria from aphthous ulcers has revived this idea. Transitional L-form bacteria may be classified as mycoplasma but have many features in common with streptococci. Hopeful though this theory may have seemed to some workers, the finding of these organisms is not persistent, nor is their presence confined to aphthous ulcers. Koch's postulates have in no way been demonstrated.

b. Viral: this theory was more in vogue before the appropriate techniques were available for the investigation of viruses. Although it has not been possible constantly to isolate any virus, much work has been done assuming that *Herpes simplex* is the causative agent. The outcome of this has been slightly surprising in that patients with recurrent aphthous ulceration have been shown to have a lower incidence of *Herpes simplex* antibodies than the control sample of subjects with no history of aphthous ulceration. Nevertheless, claims have been made for the isolation of *Herpes simplex* antibodies in recurrent herpetiform ulceration and even giant cells have been found. There is a great deal more evidence and constant results needed before these theories can be accepted.

4. *Association with gastrointestinal disturbances:* About 30 per cent of patients with aphthous ulcers have an associated history of dyspepsia, but the incidence of proven peptic ulceration is no higher than in the general public. Aphthous ulcers are extremely frequent in patients with ulcerative colitis. Oral ulceration of 'aphthous' type is not uncommon in coeliac disease and a prominent and early feature of tropical sprue.

An extremely interesting observation was reported in 1976 by Ferguson et al. that of 33 patients with severe recurrent oral ulceration 8 had jejunal mucosal biopsy specimens with typical histological features of coeliac disease (none of these patients had evidence of malabsorption or clinical features of coeliac disease). Furthermore, treatment with a gluten-free diet produced considerable improvement in the oral ulceration. Unfortunately these observations have not been confirmed (Cawson and Lehner, personal communication).

Tropical sprue is a malabsorption syndrome of unknown aetiology occurring in Asia and the Caribbean, often with acute enteritic onset, associated with folate deficiency and malabsorption of vitamin B_{12},

D-xylose, fat and nutrients. It may be considerably helped by folic acid but far better results occur if that is supplemented by broad-spectrum antibiotics, while vitamin B_{12} is also required if tissue stores are lowered by chronic disease. The aetiology remains unknown. The oral ulceration accompanying sprue may well be associated with the folate and vitamin B_{12} deficiency (*see below*), due to malabsorption or be related in an entirely different way to the aetiological agent. By all accounts extensive oral ulceration clinically similar to aphthous ulceration is a prominent feature.

5. *Association with atopy:* Twenty per cent of patients with aphthous ulcers have a history of asthma, eczema or hay fever.

6. *Hormonal influence:* In women a crop of aphthous ulcers is often noted premenstrually and many more women have a cyclic occurrence of ulcers. Other observers have reported that the incidence of aphthous ulceration falls during pregnancy. Bishop et al. claim that there is a group of female patients in whom there would appear to be an endocrine factor. Many of these patients suffered from associated dysmenorrhoea.

7. *Emotional factors:* Fifty per cent of females and 33 per cent of males show a clear emotional factor which may precipitate crops of ulcers. The high incidence found in some groups of young girls preparing for examinations is a clear pointer. Other factors which have already been cited could be indirectly due to emotional factors, e.g. association with dyspepsia and premenstrual tension. Many other patients relate crops of ulcers to periods of stress in their professional or domestic life. Just over 30 per cent of patients in one series investigated showed established features of neuroses. Most commonly this was a mild anxiety state, but obsessional features were not unusual. Depressive features are seen on rare occasions.

8. *The question of auto-immunity:* It is currently very fashionable to claim that diseases of previously unknown aetiology are due to auto-immunity. Aphthous ulceration is no exception to this. Lehner makes a strong case for auto-immunity being an aetiological factor, he claims that in a high proportion of patients with recurrent aphthous ulceration it is possible to demonstrate antibodies to fetal oral mucosa by haemagglutination, complement-fixation and precipitation techniques. Immunofluorescent histochemical techniques were used to show cell-bound antibodies in the tissue surrounding aphthous ulcers. He admits

that this fulfils only two of Witebsky's criteria for auto-immunity, but there are very few conditions that are accepted as auto-immune disease which fulfil all these criteria.

Nevertheless, it is possible to demonstrate auto-antibodies in many cases where there is chronic tissue destruction. The antibodies are caused by the tissue damage and are not the cause of the lesion.

Immediately before ulceration occurs there is an accumulation of lymphocytes which *may* indicate that these cells are of prime significance in causing destruction of the epithelium. Why the lymphocytes accumulate is not clear—either in response to altered epithelium or extrinsic antigenic assault.

Dolby has shown that *in vitro* oral epithelium in tissue culture may be damaged by lymphocytes from patients with aphthous ulceration and that this cytopathogenic action is inhibited by antilymphocytic serum. Similar damage to epithelial cells could not be produced by serum containing antimucosal antibodies from aphthous ulcer patients and the lymphocytic action was not enhanced by serum.

Thus lymphocytes may play a role in the pathogenesis of aphthous ulcers.

9. *Haematological factors:* Wray et al. have shown that investigation to exclude iron, vitamin-B_{12} and folate deficiency is essential since in many cases such deficiency may be associated with aphthous ulceration. In practice it is sufficient to carry out haemoglobin and red cell estimations (including film) to exclude macrocytic anaemia but a serum iron is essential as it is very common to find recurrent 'aphthous' ulceration associated with iron deficiency without anaemia (sideropenia). It is also true, however, that many people with iron deficiency, even if anaemic, do not develop recurrent oral ulceration. Equally anaemia (or iron deficiency) may predispose to candidal infection and to *erosive* episodes in lichen planus.

Important figures from the Glasgow work include the following (130 patients):

a. 17·7 per cent of patients had Fe^{++}, folate or vitamin-B_{12} deficiency as compared with 8·5 per cent of controls.

b. Of 15 iron-deficient patients only 4 were anaemic.

c. Five patients were shown to have gluten-sensitive enteropathy of whom 4 had folate-deficiency anaemia.

d. Five patients were vitamin-B_{12} deficient of whom 3 had anaemia while 2 had no evidence of the deficiency in the peripheral blood.

All patients responded beneficially to treatment of the deficiency —two-thirds of them showing complete remission of oral ulceration.

This work has been confirmed but Lehner has interpreted the findings as indicating a progressive iron deficiency *resulting* from recurrent aphthous ulceration.

Clinical features

The clinical picture of minor aphthous ulcers will be described separately from the two variants, major and herpetiform aphthous ulcers, although they may be seen in the same patient. All occur at the same sites in the mouth, i.e. on the non-keratinized mucosa. On rare occasions aphthous ulcers may be seen on the dorsum of the tongue when they appear as the small type of lesion.

Minor Aphthous ulcers: The patient is aware of pain or soreness in an area of the mouth. He may notice that the mucosa is nodular. If the lateral margin of the tongue is involved, there may be hyperaesthesia. At this stage the only physical sign is an area of erythematous mucous membrane. Within 24 hours the mucous membrane breaks down to form a small ulcer which increases in size for the next few days. A typical ulcer is oval and about 3–4 mm in diameter, but some may be up to 2 cm in diameter. Its edge may be slightly raised and surrounded by erythematous tissue. The ulcer is shallow with a grey sloughing floor. Pain from the ulcer may make eating and even speaking difficult, often making the patient miserable. As the patient finds difficulty in cleaning his teeth there may be foetor oris.

The ulcers vary a great deal in shape, according to their site. On the cheeks and lips they tend to have a regular outline, but on the under surface of the tongue and the floor of the mouth they are far more irregular in outline, while in the vestibular sulci they tend to be serpiginous. Ulcers may occur singly or three to four at the same time. Generally there is some overlap, so that as one ulcer heals another may start. A spate of ulcers may occur associated with one of the precipitating factors, following which the patient may be free from ulcers for weeks or months. Alternatively the patient may never be free from ulcers.

Healing may start after five days, but can be delayed for up to two weeks, especially if the ulcer is persistently traumatized. Once healing starts, the ulcer usually becomes less painful. There may be some associated submandibular lymph-node tenderness, but rarely frank,

palpable lymphadenopathy. The ulcer heals by epithelization from the margins and leaves a small erythematous area of new mucosa which fades in a few days. No scar remains after an aphthous ulcer has healed, provided the ulcer remains superficial and is not aggravated by trauma, medicaments or infection.

Major aphthous ulcers (often called a periadenitis-type ulcer): Ulcers are usually single and protracted in their course. In most cases there is a history of this type of ulceration, but isolated ulcers do occur in patients with a history of aphthous type ulceration. A large, deep ulcer slowly develops with raised margins which are erythematous and shiny, indicating that there is considerable oedema. The floor of the ulcer is covered with a grey slough and an indurated base may be palpated. Usually there is a definite submandibular lymphadenopathy and the patient may feel ill, with slight fever. The ulcer is extremely painful and may persist for as long as six weeks. When the ulcer eventually heals, it does so with scar formation. A cobblestone appearance may be seen in the mucosa of the lip, due to multiple ulcers healing with scar formation.

Herpetiform aphthous ulcers: A large number of small ulcers the size of a pinhead may occur in crops. As many as thirty ulcers may be seen in the mouth at the same time. At first the ulcers are discrete, surrounded by small haloes of erythema, but they may eventually coalesce into clusters. It is this similarity to herpetic lesions which has led to the use of the term 'herpetiform'.

In spite of their small size, these ulcers can be painful and can make the patient's mouth very uncomfortable, due to their large number. Healing is much quicker than with the other type of ulcer and the whole cycle may take only three to four days, but by the time this has happened there are many new ulcers. It is a very persistent condition which can be most depressing to patients in its resistance to treatment.

Differential diagnosis and investigation

Usually there is little difficulty in arriving at a diagnosis from the history, even if the ulcers have healed by the time the patient presents. Cyclical neutropenia may produce a single ulcer of the oral mucosa; this can quickly be excluded by the white cell count. Herpangina produces ulcers on the soft palate and pharynx. The Coxsackie group A viruses can often be isolated from throat washings and serological tests for the virus confirm the diagnosis. There seems little value in investigating for herpes