NEW ORAL DISEASES*

PROFESSOR CRISPIAN SCULLY
PHD, MD, MDS, FDSRCPS, FFDRCSI, FDSRCS, FRCPath

Centre for the Study of Oral Disease
University Department of Oral Medicine, Surgery and Pathology
Bristol Dental Hospital and School
Lower Maudlin Street
Bristol BS1 2LY
United Kingdom

Immune defects, immunosuppressive and other iatrogenic diseases, immunologically-mediated disease, and infections account for most new oral mucosal entities and aetiologies. The major impacts increasing oral disease over the past decade have probably been the appearance of infection with human immunodeficiency viruses (HIV)[1, 2] and the increasing use of immunosuppressive agents [3, 4]. These will undoubtedly be of even more major significance in the future as the immunocompromised patient is liable to develop mucosal disorders rarely seen in immunocompetent persons, as well as some new diseases.

The increasing prevalence of immunocompromising conditions and iatrogenic disease and the greater awareness of the importance of oral health in these persons, means that this area of expertise must be developed as a matter of some priority[5, 6].

A: IMMUNOCOMPROMISED PATIENTS

Immunosuppressive treatment is commonly used to inhibit graft rejection (a predominantly T lymphocyte phenomenon), and autoantibody production. Immunosuppressive drugs currently include particularly corticosteroids, azathioprine, cyclophosphamide and cyclosporin and predispose to oral infections and neoplasia.

The most common complication of immunosuppressive therapy is infection, with viruses, fungi or mycobacteria [9]. Hairy leukoplakia has been described in various immunocompromised patients, especially those having organ or tissue transplants [10] and is caused by Epstein-Barr virus.

Immunosuppressive therapy may predispose to oral carcinoma[11] Kaposi's sarcoma[12], and lymphomas[13]. Immunosuppressed renal transplant patients may develop oral white lesions (keratoses) - though these are not known to be premalignant [14].

Cyclosporin is now well recognised to cause gingival hyperplasia [15] and facial hirsutism as well as soft tissue morphological changes leading to a coarse facies [16].

B. OTHER IATROGENIC DISEASE

(1) BONE MARROW TRANSPLANTATION

Bone-marrow transplantation is increasingly used[5], patients being prepared by immunosuppression with cyclophosphamide and total body irradiation. Oral effects include mucositis, dry mouth and parotitis, sinusitis and infections[17-20]. Hairy leukoplakia is a rare complication.

Following the transplant, graft lymphocytes may attack the recipient to produce "graft versus host disease" (GVHD), characteristics of which are lichenoid reactions and sometimes a sclerodermatous reaction with dry mouth [18] predisposing to rampant caries [19, 20]. Cyclosporin or methotrexate are used to ameliorate or prevent GVHD but themselves may produce adverse oral effects - gingival hyperlasia or oral ulcers respectively [21].

(2) LICHEN PLANUS AND LICHENOID REACTIONS

Most of lichen planus remains idiopathic[22] but graft versus host disease, drugs, and restorative materials are sometimes implicated. The reported association of lichen planus with autoimmune liver disease in Southern Europeans has now been disproved in Scandinavian and British patients [23-25].

Drugs implicated in producing lichenoid reactions include the non-steroidal anti-inflammatory agents, antihypertensive agents, antidiabetic drugs and antimalarials[22, 26].

Oral lichen planus may also appear in close relationship to restorative materials [22, 27, 28] and electrogalvanism[28] and contact allergy [29-33] have been suggested causes though recent studies have found no evidence of hypersensitivity[34]. Lichenoid reactions may appear also to some composite restorations[35].

*Paper presented at the 16th Asian Pacific Dental Congress held in Kuala Lumpur, 22–27 April, 1993

Table 1. Oral side effects that occasionally follow drug treatment (most are rare but the more common are in bold type)

CANDIDOSIS
Broad-spectrum antimicrobials
Corticosteriods
Drugs casuing xerostomia
Immunosuppressives

ERYTHEMA MULTIFORME
(and Stevens Johnson syndrome)
Barbiturates
Busulphan
Carbamazepine
Clindamycin
Codeine
Frusemide
Penicillin
Pheylbutazone
Pheytoin
Sulphonamides
Tetracycline

ANGIOEDEMA
Aspirin
Essential oils
Mianserin
Penicillin

GINGIVAL HYPERPLASIA
Contraceptive pill
Nifedipine
Nitrendipine
Cyclosporin
Phenobarbitone
Phenytoin
Diltiazem

PIGMENTATION
ACTH
Amodiaquine
Anticonvulsants
Busulphan
Chloroquine
Minocycline
Heavy metals
Mepacrine
Phenothiazines

FACIAL PAIN
Phenothiazines
Stilbamidine
Vinca alkaloids

SALIVARY GLAND SWELLING
Anti-thyroid agents
Chlorhexidine
Ganglion-blocking agents
Insulin
Iodides
Isoprenaline
Methyldopa
Oxyphenbutazone
Phenothiazines
Phenylbutazone
Sulphonamides

SALIVARY GLAND PAIN
Bethanidine
Cimetidine
Clonidine
Cytotoxics
Guanethidine
Interferon
Methyldopa

HYPERSALIVATION
Anticholinesterases
Buprenorphine
Ethionamide
Iodides
Ketamine
Mercurials
Niridazole

XEROSTOMIA
Amphetamines
Anti-Parkinsonians
Antihistamines
Atropinics
Benzhexol
Clinidine
L-dopa
Ganglion blocking agents
Lithium

LUPOID REACTIONS
Gold
Griseofulvin
Hydralazine
Isoniazid
Methyldopa
Para-aminosalicylate
Penicillin
Phenytoin
Procainamide
Streptomycin
Sulphonamides
Tetracylines

PEMPHIGUS-LIKE REACTIONS
Penicillamine
Rifampicin

PEMPHIGOID-LIKE
REACTIONS
Clonidine
Frusemide
Penicillamine
Psoralens

ULCERATION
Cytotoxis
Emepromium
Gold
Indomethacin
Pancratin
Penicillamine
Phenytoin
Phenylbutazone
Potassium chloride
Proguanil
Monoamine oxidase inhibitors
Phenothiazines
Propantheline
Tricyclics
Verapamil

DISTURBED TASTE
Acetazolamide
Anti-thyroids
Biguanides
Clofibrate
Ethionamide
Gold
Griseofulvin
Guanoclor
Lincomycin
Lithium
Metronidazole
Niridazole
Penicillamine
Phenindione
Prothionamide

BURNING MOUTH
SENSATION
Captopril
Mianserin

LICHENOID REACTIONS
Amiphenazole
Chloroquinine
Chlorpropamide
Dapsone
Gold
Labetalol
Mepacrine
Methyldopa
Non-steroidal anti-inflammatory drugs
Oxprenolol
Para-aminosalicylate
Penicilliamine
Phenothiazines
Practolol
Tetracycline
Thiazides
Tolbutamide
Triprolidine

The management of oral lichen planus is mainly with topical corticosteriods and new agents such as etretinate [36] have had only limited success.

(3) OTHER DRUG – INDUCED ORAL DISEASE

Gingival hyperplasia is now a recognised complication of cyclosporin, nifedipine, diltiazem and some other calcium channel blockers[37, 38].

C. IMMUNOLOGICALLY-MEDIATED AND OTHER DISORDERS

(1) OROFACIAL GRANULOMATOSIS

The group of disorders variously described as oral Crohn's disease or orofacial granulomatosis, and the related Melkersson-Rosenthal syndrome and Miescher's cheilitis (cheilitis granulomatosa) can also sometimes be difficult to differentiate from sarcoidosis[39].

Classic Crohn's disease can be complicated by oral ulceration and other lesions even when there are no gastrointestinal symptoms [40]. Manifestations that may also be seen include orofacial swelling, mucosal tags, gingival hyperplasia, mucosal cobblestoning, and angular stomatitis. Since these may also be seen in the total absence of detectable gastrointestinal disease, the alternative term orofacial granulomatosis has been suggested[72].

Such patients are also predisposed to atopic disorders[42]: in some there may be an allergic basis [43]. Some may respond to dietary manipulation and avoidance of putative precipitants such as various flavourings and other additives[44]. In others, intralesional corticosteroids may be required[45] though systemic drug therapy is rarely needed.

(2) ALLERGIC REACTIONS

Though proven allergic reactions in the mouth appear to be rare[5] it is likely that some manifestations have been overlooked and that food intolerances will be recognised to be of greater importance. There have, for example, been clear examples of reactions to various dentifrices and other materials. Gingival lesions that have been recognised for many years and a new association with supraglottic plasmacytosis has now been described, though an allergic basis remains unproven[46].

Allergic reactions manifesting as cheilitis and gingival changes have been with tartar-control and some other dentifrices [47, 48].

(3) VESICULOBULLOUS DISORDERS

The vesiculobullous disorders characterised by subepithelial blistering and formerly termed pemphigoid, are now known to be a heterogeneous group of disorders, some of immunological[49] and others of non-immunological aetiology. The diagnosis of mucous membrane pemphigoid is often not reliably confirmed with histological and immunological evidence[50] but it is important to differentiate bullous pemphigoid[51], dermatitis herpetiformis [49] and the linear IgA variant[52], and non-immunological disorders such as localised oral purpura (angina bullosa haemorrhagica: ABH[53, 54]).

New topical corticosteroids offer therapeutic promise in the vesiculobullous disorders [55].

Another recently described entity is that of superficial mucoceles. These produce small intra-epithelial vesicles and can, therefore, be misdiagnosed as pemphigus [56] though immunostaining shows no positive intercellular antibody deposits.

E. ORAL DISEASE RELATED TO USE OF SMOKELESS TOBACCO

Smokeless tobacco had been increasing in popularity in many western countries. Two main types are in common use: snuff, and chewing tobacco[57-60].

There is limited evidence for an association between the use of smokeless tobacco and oral cancer and neoplasms other than in the oral cavity eg. pancreas[57, 61], but smokeless tobacco can induce oral keratosis and gingival recession[62-66] and, as it contains carcinogens its use is to be deprecated[67, 68].

F. BURNING MOUTH SYNDROME

Burning mouth syndrome remains a common condition, often with a psychogenic background, but sometimes with other aetiologies[69]. Among the more recent suggested organic causes are deficiencies of zinc [70] or B vitamins [71] but the results of these latter studies have not been confirmed by others [72]. A few patients may have similar symptoms due to sensitivity to food stuffs [73, 74].

REFERENCES

1. Scully C, Porter SR. Orofacial manifestations of HIV infection (Leading article). Lancet 1988; i: 976-977.

2. Greenspan J, Greenspan D, Winkler JR. Diagnosis and management of oral manifestations of HIV infection and AIDS. Infect Disease Clinics N Amer 1988; 2: 373-385.

3. Porter SR. Scully C, Greenspan D. Secondary immunodeficiency. In: Jones JH, Mason DK. Oral manifestations of systemic disease. 2nd Edition. Balliere Tindall, London 1990; pp 162-182.

4. Scully C, Porter SR. Immunodeficiency In: Ivanyi L. (ed) Immunology of oral diseases. Lancester. MTP Press 1986; pp 235-256.

5. Scully C, Cawson RA. Medical problems in dentistry. 3rd Edition, Butterworths, Oxford, 1993.

6. Little JW. and Falace DA. Dental management of the medically compromised patient. 2nd Edition, Mosby, St Louis 1984.

7. Scully C, Laskaris G, Pindborg J, Porter SR, Reichart P. Oral manifestations of HIV infection and their management: 1. More common lesions. Oral Surg 1991; 71: 158-166.

8. Scully C, Laskaris G, Pindborg J, Porter SR, Reichart P. Oral manifestations of HIV infection and their management: 2. Less common lesions. Oral Surg 1991; 71: 167-171.

9. Scully C. Oral infections in the immunocompromised patient. Br Dent J 1992; 172: 401-407.

10. Scully C. Epstein. JB. Porter SR. Oral hairy leukoplakia (Leading article). Lancet 1989; ii: 1194.

11. Varga E, Tyldesley WR. Carcinoma arising in cyclosporin-induced gingival hyperplasia. Brit Dent J 1991; 171: 26-27.

12. Manui H, Molengraft, F. Kaposi's sarcoma of the palate. J Max-Fac Surg 1982; 10: 187-189.

13. Hanto DW. et al. Epstein-Barr virus-induced B cell lymphoma after renal transplantation. N Engl J Med 1980; 306: 913-918.

14. Kellett M. Oral white plaques in uraemic patients. Br Dent J 1983; 154: 366-368.

15. Daley TD, Wysocki GP, Day C. Clinical and pharmacological correlations in cyclosporin-induced gingival hyperplasia. Oral Surg 1986; 62: 417-421.

16. Reznik V. et al. Changes in facial appearance during cyclosporin treatment. Lancet 1987; i: 1405-1407.

17. Seto, BG. Oral mucositis in patients undergoing bone marrow transplantation.

    Oral Surg 1985; 60: 493-497.

18. Barret AP. Oral complications of bone marrow transplantation. Aust NZ J Med 1986; 16: 239-240.

19. Heimdahl A, Johnson G, Danielson KH. Oral condition of patients with leukaemia and severe aplastic anaemia. Oral Surg 1985; 60: 498-504.

20. Berkowitz RJ, Starandford S, Jones P et al. Stomatologic complications of bone marrow transplantation in a pediatric population. Pediat Dent 1987; 9: 105-110.

21. Dreizen S. Stomatotoxic manifestations of cancer chemotherapy. J Prosthet Dent 1978: 40: 650-655.

22. Scully C, Elkom M. Lichen planus: review and update on pathogenesis. J. Oral Pathol 1985; 14: 431-458.

23. Scully C, Pott S J, Hanburger R J, et al. Lichen planus and liver disease: how strong is the association? J Oral Pathol 1984; 14: 224-226.

24. Mobaken H, Nilsson L. Olsson R et al. Incidence of liver disease in chronic lichen planus of the mouth. Acta Derm. Venereol. (Stockh) 1984; 64: 70-73.

25. El-Kabir MA, Scully C, Porter S et al. Liver disease and oral lichen planus in English patients. Clin Exp Dermatol 1993; 18: 12-16.

26. Potts AJC, Hamburger J, Scully C. The medication of patients with oral lichen palnus and the association of non-steroidal anti-inflammatory drugs with erosive lesions. Oral Surg 1987; 64: 541-543.

27. Lind PO, Hurlen, B. Lyberg, T et al. Amalgam related oral lichenoid reaction. Scand J Dent Res 1986; 94: 448-451.

28. Banoczy J, Roed-Petersen B, Pindborg JJ et al. Clinical and histologic studies on electrogalvanic induced oral white lesions. Oral Surg 1979; 48: 219-223.

29. Lundstrom IMC. Allergy and corrosion of dental materials in patients with oral lichen planus. Int J Oral Surg 1984; 13: 16-24.

30. Eversole LR, Ringer M. The role of dental restorative metals in the pathogenesis of oral lichen planus. Oral Surg 1984; 57: 383-387.

31. Mobacken H, Hersle K, Sloberg K et al. Oral lichen planus: hypersensivity to dental restorative materials. Contact Dermatitis 1984; 10: 11-15.

32. Finne K, Goransson K, Winckler L. Oral lichen planus and contact allergy to mercury. Int J Oral Surg 1982; 11: 236-239.

33. James J, Ferguson MM, Forsyth A et al. Oral lichenoid reactions related to mercury sensivity. Brit J Oral Max-Fac Surg 1987; 25: 474-480.

34. Hietanen J, Pihlman K, Forstrom L et al. No evidence of hypersensivity to dental restorative metals in oral lichen planus. Scand J Dent Res 1987; 95: 320-327.

35. Lind PO. Oral lichenoid reactions related to composite restoratives. Acta Odontol Scand 1988; 46: 63-65.

36. Gorsky M, Raviv M. Efficacy of etretinate (Tigason) in symptomatic oral lichen planus. Oral Surg 1992; 73: 52-55.

37. Duxbury AJ. Systemic pharmacotherapy. In Jones, J.H., Mason, D.K. (Eds). Oral manifestations of systemic disease. 2nd Ed. Balliere Tindall London; 1990; pp 411-479.

38. Hay KD, Reade PC. Spectrum of oral disease induced by drugs and other bioactive agents. Drugs 1983; 26: 268-277.

39. Scully C, Eveson JW. Oral granulomatosis (Leading Article). Lancet 1991; 38: 20-21.

40. Scully C, Cochran KM, Russel RI. et al. Crohn's disease of the mouth: an indication of intestinal involvement. Gut 1982; 23: 198-201.

41. Wiesenfeld DW, Ferguson MM, Mitchell D et al. Orofacial granulomatosis: a clinical and pathological analysis. Quart J Med 1985; 54: 101-113.

42. James J, Patton DW, Lewis CJ et al. Orofacial granulamatosis and clinical atopy. J Oral Med 1986; 41: 29-30.

43. Patton DW, Ferguson MM, Forsyth, A et al. Orofacial granulomatosis: a possible allergic basis. Brit J Oral Maxillofac Surg 1985; 23: 235-242.

44. Sweatman MC, Tasker R, Warner JO et al. Orofacial granulomatosis. Response to elemental diet and provocation by food additives. Clinical Allergy 1986; 16: 331-338.

45. William PM, Greenberg MS. Management of cheilitis granulomatosa. Oral Surg 1991; 72: 436-439.

46. Timms MS, Sloan P. Association of supraglottic and gingival idiopathic plasmacytosis. Oral Surg 1991; 71: 451-453.

47. Beacham BE, Kurgansky D, Gould WM. Circumoral dermatitis and cheilitis caused by tartar control dentifrices. J Am Acad Dermatol 1990; 22: 1029-1032.

48. Lamey PJ, Lewis MAO, Rees TD, Fowler, C, bInnie WH. Sensitivity reaction to the cinnamonaldehyde component of toothpaste. Brit Dent J 1990; 168: 115-118.

49. Williams DM. et al. Benign mucous membrane (cicatricial) pemphigoid revisited: a clinical and immunological re-appraisal. Brit Dent J 1984; 157: 313-316.

50. Manton S, Scully C. Mucous membrane pemphigoid - an elusive diagnosis. Oral Surg 1988; 66: 37-40.

51. Laskaris GC. et al. Bullous pemphigoid, cicatricial pemphigoid and pemphigus vulgaris: a comparative clinical survey of 278 cases. Oral Surg 1982; 54: 656-662.

52. Wiesenfeld D. Martin A, Scully C et al. Oral manifestations in linear IgA disease. Brit Dent J 1982; 153: 389-399.

53. Stephenson P, Lamey P-J, Scully C et al. Angina bullosa haemorrhagica - clinical and laboratory features in 30 patients. Oral Surg 1987; 63: 560-565.

54. Stephenson P. Scully C, Prime SS et al. Angina bullosa haemorrhagica: lesional immunostaining and haematological findings. Brit J Oral Maxillofac Surg 1987; 25: 488-491.

55. Lozada-Nur F, Huang MZ, Zhou G. Open preliminary clinical trial of clobetasol propionate ointment in adhesive paste for treatment of chronic oral vesiculoerosive diseases. Oral Surg 1991; 71: 283-287.

56. Eveson JW. Superficial mucoceles. Pitfall in clinical and pathological diagnosis. Oral Surg 1988; 66: 318-322.

57. Connolly GN, Winn DM, Hecht SS et al. The re-emergence of smokeless tobacco. N Engl J Med 1986; 314; 1020.

58. Editorial. Oral snuff: a preventable carcinogenic hazard. Lancet 1986; ii; 198-200.

59. Consensus conference. Health implications of smokeless tobacco use. JAMA 1986; 255; 1045-1048.

60. Council on Scientific Affairs. Health effects of smokeless tobacco. JAMA 1986; 255; 1038-1044.

61. Heuch I, Kvale, G, Jacobsen, BK et al. Use of alcohol, tobacco, and coffee and the risk of pancreatic cancer. Br J Cancer 1983; 48: 637.

62. Greer RO, Poulson TC. Oral tissue alterations associated with the use of smokeless tobacco by teenagers-clinical findings. Oral Surg 1983; 56; 275-284.

63. Christen AG, Armstrong WR, McDaniel RK. Intraoral leukoplakia, abrasion, periondontal breakdown, and tooth loss in a snuff dipper. JADA 1979; 98; 584-586.

64. Offenbacher S, Weathers DR. Effects of smokeless tobacco on the periodontal mucosal and caries status of adolescent males. J Oral Pathol 1985; 14; 169-181.

65. Modeer T, Lavstedt S, Ahlund C. Relation between tobacco consumption and oral health in Swedish school children, Acta Odont Scand 1980; 38; 223-227.

66. Wolfe MD, Carlos JP. Oral health effects of smokeless tobacco use in Navajo Indian adolescents. Community Dent Oral Epidemiol 1987; 15; 230-235.

67. Winn DM. Smokeless tobacco and oral/pharynx cancer; the role of cofactors. Banbury Report No. 23. 361-375. Cold Spring Harbor, 1986.

68. Advisory Committee to the Surgeon General. The health consequences of using smokeless tobacco, Bethesda. Maryland. US Dept. Of Health and Human Services. Public Health Sevice. NIH Publ. No 86-2874, 1986.

69. Van der Waal 1. The Burning Mouth Syndrome. Munksgaard, Copenhagen, 1990.

70. Maragou P, Ivanyi L. Serum zinc levels in patients with burning mouth syndrome . Oral Surg 1991; 71: 447-450.

71. Lamey PJ, Hammon A, Allan BF. et al. Vitamin status of patients with burning mouth syndrome and the response to replacement therapy. Br Dent J 1986; 160: 81-84.

72. Hugoson A, Thorstensson B. Vitamin B status and response to replacement therapy in patients with burning mouth syndrome. Acta Odontol Scand 1991; 49: 367-375.

73. Ferguson MM, MacFadyen EE, Haworth RPJ at al. Stomatitis as a consequence of intolerance to bovine products. NZ Dent J 1987; 83: 101-103.

74. Whitley BD, Holmes AR, Shepherd MG. Peanut sensivity as a cause of burning mouth. Oral Surg 1991; 72: 671-674.