

Macronutrients, Micronutrients, and Oral Health

Kamudi Joshipura, Assistant Professor

**Department of Oral Health Policy and Epidemiology, Harvard School of Dental Medicine,
Department of Epidemiology, Harvard School of Public Health**

Introduction

There are several conditions affecting the oral cavity, ranging from very common conditions such as dental caries (cavities) and periodontal (gum) disease, to rare conditions such as oral cancer. Oral diseases include very innocuous as well as debilitating or fatal diseases. This report will be limited to the diseases selected either because of their high frequency of occurrence, severity, or relation to nutrition, as a comprehensive review would be too extensive. The diseases are described in chronological order starting from birth defects in the newborn to diseases affecting the elderly. Since the main function of the mouth is eating, this report also discusses how oral health may impact food selection and systemic disease.

Conditions at Birth

Teeth formation of the infant begins in utero, hence, nutrition counseling for good oral health should begin with the pregnant mother. Inadequate amounts of calcium, phosphorus, or vitamins A, C and D during pregnancy could lead to enamel hypoplasia¹, which in turn could lead to increased susceptibility for caries. Several studies have suggested that adequate intake of folic acid could help prevent cleft lip and palate in the infant^{2,4}, however the evidence is yet inconclusive.

Dental Caries

Macronutrients are important in the development of caries. The quantity and type of sugar and other carbohydrate intake are major risk factors for dental caries. A classic experiment showed that ingestion of sugars caused an immediate sharp drop in plaque pH, followed by a gradual return to normal pH from salivary buffer action⁵. Although early studies suggested that frequency of carbohydrate intake was an important factor in dental caries, two later well conducted studies did not confirm this. In Britain, a two-year follow-up study was conducted among 405 children from a low fluoride area, who were 11.5 years of age on average⁶. In this study, caries increment was significantly but weakly correlated with total intake of sugars. A second study based in a low fluoride area of Michigan, followed 499 children, aged 11 to 15, for 3 years⁷. This study found that caries experience was weakly related to total intake of sugars only among the 'high caries' group. Both studies showed no relationship between caries and frequency of sugar

consumption. Contrary to popular belief, there is no epidemiologic evidence that consumption of sticky foods is more strongly associated with caries than are sugared drinks⁸.

Although, cheese has been found to be protective against caries, probably due to the calcium and phosphorous content⁹, the primary protective factor for caries is fluoride^{10,11}. The majority of fluoride intake is from water either naturally or artificially fluoridated. Fluoride is also available from toothpaste, mouth rinse, drops and tablets. In some countries mainly in Latin America, fluoride is added to salt. Caries on the root surface of the teeth occur when the root surface is exposed, due to gingival recession. Root caries share many of the same dietary¹² and other risk factors as coronal caries.

Periodontal Disease

Deficiencies in vitamin C or folate are related to increased risk of gingivitis (inflammation of the gums)¹³. Periodontal disease is a disease that affects the tissues surrounding the tooth, leading to loss of attachment, and alveolar bone. The few studies that have evaluated the association between nutrients and periodontal disease have been mostly cross-sectional, with some methodological limitations such as small samples and/or lack of adjustment for confounders. However, recent studies have been relatively well designed. These studies suggest that high intake of vitamins A, C¹⁴, D, E, calcium^{15,16} and phosphorus are protective against periodontal disease. A recent study suggests that increased levels of total serum cholesterol (but not HDL) are associated with periodontal disease¹⁷. Malnutrition could also be a risk factor for periodontal disease^{18,19}. Further studies are needed to evaluate dietary risk factors for periodontal disease.

Oral Cancer

Oral and pharyngeal cancers (OC) include tumors affecting the oral cavity and pharynx, the majority of which are squamous cell carcinoma. About 30,000 people in the US develop oral cancer each year²⁰. The overall five-year survival rate is about 52%; early detection is the key to improving the survival rate²⁰. Oral cancer is generally preceded by pre-cancerous lesions, which include oral epithelial dysplasia, erythroplakia, leukoplakia, lichen planus, and submucous fibrosis (rare in western countries). The major risk factors for OC are tobacco, and

alcohol. In Asian countries chewing tobacco, beetle nut and beetle quid are major risk factors. The practice of chewing tobacco is increasing in the US.

Food and macronutrients

A protective effect of fiber was observed for both oral submucous fibrosis and leukoplakia²¹ and for oral cancer^{22,23}. There is a suggestion that meat^{24,25,27}, desserts, maize, and saturated fats and/or butter may be risk factors^{25,27} and that olive oil may be protective²⁶. Nitrate, nitrite, and nitrate reductase activity in saliva²⁸ and high intake of nitrite containing meats²², have been linked with increased risk. Iron may be protective against OC²⁹ and leukoplakia³⁰.

Fruits and vegetables

A consistent finding across numerous studies is that a diet high in fruits and vegetables is protective against oral precancer^{21,31} and cancer^{22,32}. Fruits are associated with a 20-80% reduced risk of OC even when smoking and alcohol intake and other factors including total caloric intake are taken into account^{30,33,34}. While vegetables are generally believed to protect against OC^{35,32}, some studies did not show a protective effect³⁶. The inconsistencies may be explained by variation in specific vegetables consumed and a suggestion that raw vegetables may be more protective than cooked vegetables.

A study evaluating specific fruits and vegetables suggested that green vegetables, salad, and apples were most protective. Tomato shows a strong and consistent protective effect for oral cancer in 12 of 15 studies³⁷, and in one study on leukoplakia²¹. Raw tomatoes were more protective than cooked tomatoes³⁷. A protective effect was also found for raw vegetables among the Japanese³⁸. Glutathione, an anti-oxidant, was protective only if it was derived from fruits and raw vegetables³⁹.

Anti-oxidants

Several anti-oxidants found in vegetables and fruits show a protective effect. There are varying degrees of evidence regarding the protective effect of specific anti-oxidants which include vitamin A, vitamin B12, vitamin C, tocopherol (vitamin E), retinoids, carotenoids, lycopene, beta-carotene, folate, glutathione, thiamine, vitamin B6, folic acid, niacin, α -tocopherol, and lutein have been shown to be protective

against oral cancer^{23,30,40-44} and pre-cancer^{21,29,45-47} in other studies. Studies that have evaluated subgroups have generally found a more profound effect of fruits and vegetables and their constituent micronutrients, particularly among smokers and drinkers⁴⁸.

Evidence from clinical trials on anti-oxidants

Retinoids and beta-carotene in controlled therapeutic doses show protective effects, with fewer new primary tumors in persons with previous oral cancers and reversals or reduction in size of premalignant lesions⁴⁹⁻⁵¹. High doses of 13-cis-retinoic acid (50-100 mg/sq-m body surface area/day) for a year have been effective in the treatment of oral leukoplakia⁴⁴. 67% showed major decreases in lesion size vs. 10% among placebo group and in prevention of second primary tumors⁵²; 2% had secondary tumors after a median follow up of 32 months vs. 12% in placebo group. Trials using beta-carotene supplements (60 mg/day for 6 months) have shown reduced risk of oral cancers and remission of precancers with an improvement of at least one grade dysplasia in 39% and no change in 61%⁵³.

Other Soft Tissue Lesions

Soft tissue conditions such as oral mucositis^{54,55} have been related to vitamin deficiencies, especially the B vitamins. Tenderness of the tongue and palate are associated with deficiencies in vitamin B complex⁵⁶, or iron. Vitamin E deficiency is related to atrophy of the tongue papilla⁵⁷. Recurrent aphthous ulcers⁵⁸ have been

associated with nutritional deficiencies including iron, folic acid, B vitamins. Angular cheilitis is associated with iron deficiency⁵⁹. Malnutrition is associated with some diseases that are relatively uncommon in the developed world such as acute necrotizing ulcerative gingivitis, and oro-facial gangrene⁶⁰.

Impact of Oral Health on Nutrition and Systemic Disease

In recent years there has been growing interest in research related to oral conditions and systemic disease. This research suggests that periodontal disease and tooth loss are risk factors for systemic disease such as cardiovascular disease, respiratory disease and diabetes⁶¹. The results to date are inconsistent and inconclusive, and more rigorous studies are needed, but a causal relationship mediated through inflammatory mediators, dietary factors, or other factors is plausible⁶¹.

Studies have shown reduced masticatory capacity in people with extensive tooth loss, in spite of prosthetic replacement⁶². Tooth loss could thus lead to detrimental changes in diet, which in turn may lead to increased risk of CVD (cardiovascular disease), cancer or early all-cause mortality. Recent studies suggest that tooth loss leads to reduced consumption of certain hard to chew foods such as some fruits and vegetables. Reduced intake of dietary fiber and specific carotenoids has been associated with increased risk of CVD and cancer⁶³, even with denture use⁶⁴. Several dietary factors have been linked with systemic disease and all-cause mortality in follow-up studies. Hence, tooth loss may be related to systemic disease through diet.

In summary, both macronutrients and micronutrients play a role in several oral diseases including dental caries and oral cancer. Dental diseases also may lead to change in diet and nutritional status.

The Whitehall-Robins Report is a Whitehall-Robins publication that focuses on current issues on the role of vitamins and minerals in health promotion and disease prevention. Complimentary copies are distributed to Canadian health care professionals active or with a special interest in nutrition. Each issue is written and/or reviewed by independent health care professionals with expertise in the chosen topic.

Editor: Whitehall-Robins Inc.

If you have any comments about the Whitehall-Robins Report or would like to be added to the mailing list, please write to:

The Editor: The Whitehall-Robins Report,
5975 Whittle Road, Mississauga, ON L4Z 3M6



© 2002-May. May be reproduced without permission provided source is recognized.

- References** 1. Depaola DP, Palmer CA. Nutrition in relation to dental medicines. In: Shils ME, Shike M, Ross CA, eds. *Modern nutrition in health and disease*. Baltimore: Williams and Wilkins, 1999:1099-124. 2. Conway H. Effects of supplemental vitamin therapy on the limitation of incidence of cleft lip and cleft lip palate in humans. *Plast Reconstr Surg* 1958; 22:450-3. 3. Tolarova M, Harris J. Reduced recurrence of orofacial clefts after periconceptional supplementation with high-dose folic acid and multivitamins. *Teratology* 1995; 51:71-8. 4. Werler MM, Hayes C, Louik C, Shapiro S, Mitchell AA. Multivitamin supplementation and risk of birth defects. *Am J Epidemiol* 1999; 150:675-82. 5. Stephan RM. Changes in hydrogen-ion concentration on tooth surfaces and in carious lesions. *J Am Dent Assoc* 1940; 27:718-23. 6. Rugg-Gunn AJ, Hackett AF, Appleton DR, Jenkins GN, Eastoe JE. Relationship between dietary habits and caries increment assessed over two years in 405 English adolescent school children. *Arch Oral Biol* 1984; 29:983-92. 7. Burt BA, Eklund SA, Morgan KJ, et al. The effects of sugars intake and frequency of ingestion on dental caries increment in a three-year longitudinal study. *J Dent Res* 1988; 67:1422-9. 8. Ismail AI, Burt BA, Eklund SA. The cariogenicity of soft drinks in the United States. *J Am Dent Assoc* 1984; 109:241-5. 9. Jensen ME. Diet and dental caries. *Dent Clin North Am* 1999; 43:615-33. 10. Dean HT, AFI, Jay P, Knutson JW. Studies on mass control of dental caries through fluoridation of the public water supply. *Public Health Rep* 1950; 65:403-8. 11. Heller KE, Eklund SA, Burt BA. Dental caries and dental fluorosis at varying water fluoride concentrations. *J Public Health Dent* 1997; 57:136-43. 12. Papas AS, Joshi A, Palmer CA, Giunta JL, Dwyer JT. Relationship of diet to root caries. *Am J Clin Nutr* 1995; 61:423S-429S. 13. Leggett PJ, Robertson PB, Jacob RA, Zambon JJ, Walsh M, Armitage GC. Effects of ascorbic acid depletion and supplementation on periodontal health and subgingival microflora in humans. *J Dent Res* 1991; 70:1531-6. 14. Nishida M, Grossi SG, Dunford RG, Ho AW, Trevisan M, Genco RJ. Dietary vitamin C and the risk for periodontal disease. *J Periodontol* 2000; 71:1215-23. 15. Spiller WF, Jr. A clinical evaluation of calcium therapy for periodontal disease. *Dent Dig* 1971; 77:522-6. 16. Krall EA, Wehler C, Garcia RI, Harris SS, Dawson-Hughes B. Calcium and vitamin D supplements reduce tooth loss in the elderly. *Am J Med* 2001; 111:452-6. 17. Wu T, Trevisan M, Genco RJ, Falkner KL, Dorn JP, Sempos CT. Examination of the relation between periodontal health status and cardiovascular risk factors: serum total and high density lipoprotein cholesterol, C-reactive protein, and plasma fibrinogen. *Am J Epidemiol* 2000; 151:273-82. 18. Russell AL, LE, Consolazio CF, Van Reen R. Periodontal disease and nutrition in South Vietnam. *J Dent Res* 1965; 44:775-82. 19. Carlos JP, Wolfe MD. Methodological and nutritional issues in assessing the oral health of aged subjects. *Am J Clin Nutr* 1989; 50:1210-8; discussion 1231-5. 20. Oral health in America: a report of the Surgeon General. *J Calif Dent Assoc* 2000; 28:685-95. 21. Gupta PC, Hebert JR, Bhonsle RB, Sinor PN, Mehta H, Mehta FS. Dietary factors in oral leukoplakia and submucous fibrosis in a population-based case-control study in Gujarat, India. *Oral Dis* 1998; 4:200-6. 22. Gridley G, McLaughlin JK, Block G, et al. Diet and oral and pharyngeal cancer among blacks. *Nutr Cancer* 1990; 14:219-25. 23. Zheng W, Blot WJ, Diamond LE, et al. Serum micronutrients and the subsequent risk of oral and pharyngeal cancer. *Cancer Res* 1993; 53:795-8. 24. Hebert JR, Landon J, Miller DR. Consumption of meat and fruit in relation to oral and esophageal cancer: a cross-national study. *Nutr Cancer* 1993; 19:169-79. 25. Garrote LF, Herrero R, Reyes RM, et al. Risk factors for cancer of the oral cavity and oro-pharynx in Cuba. *Br J Cancer* 2001; 85:46-54. 26. Franceschi S, Favero A, Conti E, et al. Food groups, oils and butter, and cancer of the oral cavity and pharynx. *Br J Cancer* 1999; 80:614-20. 27. Fioretti F, Bosetti C, Tavani A, Franceschi S, La Vecchia C. Risk factors for oral and pharyngeal cancer in never smokers. *Oral Oncol* 1999; 35:375-8. 28. Badawi AF, Hosny G, el-Hadary M, Mostafa MH. Salivary nitrate, nitrite and nitrate reductase activity in relation to risk of oral cancer in Egypt. *Dis Markers* 1998; 14:91-7. 29. Negri E, Franceschi S, Bosetti C, et al. Selected micronutrients and oral and pharyngeal cancer. *Int J Cancer* 2000; 86:122-7. 30. Gupta PC, Hebert JR, Bhonsle RB, Murli PR, Mehta H, Mehta FS. Influence of dietary factors on oral precancerous lesions in a population-based case-control study in Kerala, India. *Cancer* 1999; 85:1885-93. 31. Morse DE, Pendry DG, Katz RV, et al. Food group intake and the risk of oral epithelial dysplasia in a United States population. *Cancer Causes Control* 2000; 11:713-20. 32. Levi F, Pasche C, La Vecchia C, Lucchini F, Franceschi S, Monnier P. Food groups and risk of oral and pharyngeal cancer. *Int J Cancer* 1998; 77:705-9. 33. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer prevention: a review. *J Am Diet Assoc* 1996; 96:1027-39. 34. Winn DM. Diet and nutrition in the etiology of oral cancer. *Am J Clin Nutr* 1995; 61:437S-445S. 35. Day GL, Shore RE, Blot WJ, et al. Dietary factors and second primary cancers: a follow-up of oral and pharyngeal cancer patients. *Nutr Cancer* 1994; 21:223-32. 36. McLaughlin JK, Gridley G, Block G, et al. Dietary factors in oral and pharyngeal cancer. *J Natl Cancer Inst* 1988; 80:1237-43. 37. De Stefani E, Oreggia F, Boffetta P, Deneo-Pellegrini H, Ronco A, Mendilaharsu M. Tomatoes, tomato-rich foods, lycopene and cancer of the upper aerodigestive tract: a case-control in Uruguay. *Oral Oncol* 2000; 36:47-53. 38. Takezaki T, Hirose K, Inoue M, et al. Tobacco, alcohol and dietary factors associated with the risk of oral cancer among Japanese. *Jpn J Cancer Res* 1996; 87:555-62. 39. Flagg EW, Coates RJ, Jones DP, et al. Dietary glutathione intake and the risk of oral and pharyngeal cancer. *Am J Epidemiol* 1994; 139:453-65. 40. Barone J, Taioli E, Hebert JR, Wynder EL. Vitamin supplement use and risk for oral and esophageal cancer. *Nutr Cancer* 1992; 18:31-41. 41. Benner SE, Winn RJ, Lippman SM, et al. Regression of oral leukoplakia with alpha-tocopherol: a community clinical oncology program chemoprevention study. *J Natl Cancer Inst* 1993; 85:44-7. 42. Blot WJ, Li JY, Taylor PR, et al. Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst* 1993; 85:1483-92. 43. Garewal HS. Beta-carotene and vitamin E in oral cancer prevention. *J Cell Biochem Suppl* 1993;262-9. 44. Hong WK, Endicott J, Itri LM, et al. 13-cis-retinoic acid in the treatment of oral leukoplakia. *N Engl J Med* 1986; 315:1501-5. 45. Nagao T, Ikeda N, Warnakulasuriya S, et al. Serum antioxidant micronutrients and the risk of oral leukoplakia among Japanese. *Oral Oncol* 2000; 36:466-70. 46. Ramaswamy G, Rao VR, Kumaraswamy SV, Anantha N. Serum vitamins' status in oral leukoplakias—a preliminary study. *Eur J Cancer B Oral Oncol* 1996; 32B:120-2. 47. Zain R B RZ, Fukano H, Nagao T, Abang Z, Razak I A, et al. Oral habits, serum micronutrients and oral mucosal lesions among the Indigenous people of Sarawak. *Oral Oncol* 1999; 6, Macmillan, India:185-8. 48. Tavani A, Gallus S, La Vecchia C, et al. Diet and risk of oral and pharyngeal cancer. An Italian case-control study. *Eur J Cancer Prev* 2001; 10:191-5. 49. Khuri FR, Lippman SM, Spitz MR, Lotan R, Hong WK. Molecular epidemiology and retinoid chemoprevention of head and neck cancer. *J Natl Cancer Inst* 1997; 89:199-211. 50. Papadimitrakopoulou VA, Hong WK. Retinoids in head and neck chemoprevention. *Proc Soc Exp Biol Med* 1997; 216:283-90. 51. Zain RB. Cultural and dietary risk factors of oral cancer and precancer—a brief overview. *Oral Oncol* 2001; 37:205-10. 52. Hong WK, Lippman SM, Itri LM, et al. Prevention of second primary tumors with isotretinoin in squamous-cell carcinoma of the head and neck. *N Engl J Med* 1990; 323:795-801. 53. Garewal HS, Katz RV, Meyskens F, et al. Beta-carotene produces sustained remissions in patients with oral leukoplakia: results of a multicenter prospective trial. *Arch Otolaryngol Head Neck Surg* 1999; 125:1305-10. 54. Osaki T, Ueta E, Yoneda K, Hirota J, Yamamoto T. Prophylaxis of oral mucositis associated with chemoradiotherapy for oral carcinoma by Azelastine hydrochloride (Azelastine) with other antioxidants. *Head Neck* 1994; 16:331-9. 55. Wadleigh RG, Redman RS, Graham ML, Krasnow SH, Anderson A, Cohen MH. Vitamin E in the treatment of chemotherapy-induced mucositis. *Am J Med* 1992; 92:481-4. 56. Field EA, Speechley JA, Rugman FR, Varga E, Tyldesley WR. Oral signs and symptoms in patients with undiagnosed vitamin B12 deficiency. *J Oral Pathol Med* 1995; 24:468-70. 57. Drinka PJ, Langer EH, Voeks SK, Scott L, Morrow FD. Nutritional correlates of atrophic glossitis: possible role of vitamin E in papillary atrophy. *J Am Coll Nutr* 1993; 12:14-20. 58. Nolan A, McIntosh WB, Allam BF, Lamey PJ. Recurrent aphthous ulceration: vitamin B1, B2 and B6 status and response to replacement therapy. *J Oral Pathol Med* 1991; 20:389-91. 59. Murphy NC, Bissada NF. Iron deficiency: an overlooked predisposing factor in angular cheilitis. *J Am Dent Assoc* 1979; 99:640-1. 60. Enwonwu CO, Falkler WA, Jr., Idigbe EO, et al. Pathogenesis of cancrum oris (noma): confounding interactions of malnutrition with infection. *Am J Trop Med Hyg* 1999; 60:223-32. 61. Josphipura KJ, Ritchie CS, Douglass CW. Strength of Evidence Linking Oral and Systemic Disease. *Compendium* 2000; 21:12-23. 62. Waylor AH, Chauncey HH. Impact of complete dentures and impaired natural dentition on masticatory performance and food choice in healthy aging men. *J Prosthet Dent* 1983; 49:427-33. 63. Josphipura KJ, Willett WC, Douglass CW. The impact of edentulousness on food and nutrient intake. *J Am Dent Assoc* 1996; 127:459-67. 64. Posner BM, Jette A, Smigelski C, Miller D, Mitchell P. Nutritional risk in New England elders. *J Gerontol* 1994; 49:M123-32.