

Oral Infections Causing Systemic Diseases

K. M. K. MASTHAN, N. ANITHA, J. JENITA JACOBINA* and N. ARAVINDHA BABU*

Department of Oral Pathology, Sree Balaji Dental College and Hospital,
Bharath University, Pallikaranai, Chennai – 600100, India.

<http://dx.doi.org/10.13005/bpj/1019>

(Received: July 01, 2016; Accepted: August 20, 2016)

ABSTRACT

Oral cavity is a site for many infectious and inflammatory diseases that are associated with systemic diseases like diabetes mellitus, cardiovascular disease and pre- term births. Oral cavity is said to be the window to the body because oral manifestations often accompany many systemic diseases. This article focuses on the systemic manifestations of oral diseases and stresses on the importance of good oral health to maintain good general health.

Keywords: Oral infections, inflammatory diseases, systemic manifestations.

INTRODUCTION

Oral cavity can act as the site of origin for pathogenic microorganisms to disseminate to other distant sites of the body, especially in immunocompromised patients such as those with malignancies, rheumatoid arthritis, diabetes and those on corticosteroid therapy. Dr. William Hunter in 1910, put forward the concept of 'focal infection', whereby disease at a distant site such as the oral cavity can contribute to anemias, gastritis, colitis etc. The fact that periodontal disease by itself can cause cardiovascular disorders, low birth- weight babies was discussed in March 1997 at the Conference held at the University of North Carolina in Chapel Hill. Periodontal therapy can stabilize systemic blood sugar levels¹.

Bacteremia

The only non-shedding surfaces of our body are the teeth and bacterial levels can reach to about 10^{11} microorganisms/mg of dental plaque. Periodontal and endodontic infections are frequently associated with complex microflora, of

which many are anaerobic gram negative rods^{2,3}. Bacteremia following dental procedures like tooth extraction, endodontic therapy, periodontal therapy and dental scaling are well documented^{4,5,6,7,8,9}. Phenotypic and genetic methods were used by Debelian et al in 1998 to trace microorganisms that are released into the bloodstream during and following endodontic therapy back to their presumed source, the root canal¹⁰. There are various barriers in the oral cavity that prevent bacterial penetration into the tissue from dental plaque. These include, the oral epithelium, acting as a physical barrier; defensins, host- derived antibiotics; immunological barrier of antibody- forming cells and the reticuloendothelial system^{11,12}. Under normal conditions, these barrier mechanisms act together to prevent and eliminate invading bacteria. When this state of equilibrium is disturbed by a breach (eg. Trauma, neutropenia, AIDS, immunosuppressant therapy), microorganisms can propagate and cause infections at distant sites of the body¹³. When oral hygiene is poor, the prevalence and magnitude of bacteremia can increase several fold.

The 3 pathways that link oral infection to systemic diseases

3 mechanisms have been suggested as pathways that link oral infection to systemic effects¹⁴.

Metastatic infection

Oral infections and dental procedures can cause transient bacteremia. Microorganisms that enter the bloodstream and circulate throughout the body. They are normally eliminated within minutes by the reticuloendothelial system. They usually cause a slight increase in body temperature¹⁵. However, they may settle at a particular site, finding favorable conditions and after a time lag begin to multiply.

Metastatic injury

Certain gram- positive and negative bacteria have the ability to produce diffusible proteins or exotoxins. They include cytotoxic enzymes and dimeric toxins having A and B subunits. Exotoxins are considered to be lethal¹⁶. Endotoxins which are lipopolysaccharides are part of the outer cell membranes are released after death of the cell and cause various pathologic manifestations. They are shed continuously from periodontal gram – negative rods during their growth *in vivo*¹⁷.

Metastatic inflammation

A macromolecular complex may form when a soluble antigen enters the bloodstream and reacts with a circulating specific antibody. These immune complexes may cause various acute and chronic inflammatory reactions at their site of deposition.

The possible pathways of oral infections that link to secondary systemic diseases:

1. Metastatic infection from oral cavity via transient bacteremia à Sub-acute infective endocarditis, acute bacterial myocarditis, brain abscess, cavernous sinus thrombosis, sinusitis, lung infection/ abscess, Ludwig's angina, orbital cellulitis, skin ulcer, osteomyelitis, prosthetic joint infection.
2. Metastatic injury through circulation of oral microbial toxins à Cerebral infarction, acute

myocardial infarction, abnormal pregnancy outcome, persistent pyrexia, idiopathic trigeminal neuralgia, toxic shock syndrome, systemic granulocytic cell defects, chronic meningitis.

3. Metastatic inflammation through immunological injury caused by oral organisms à Behcet's syndrome, chronic urticarial, uveitis, inflammatory bowel disease, Crohn's disease^{18,19}.

Periodontal infections causing cardiovascular diseases

3 biologic mechanisms have been proposed to explain the association between periodontal diseases and cardiovascular diseases²⁰:

1. Bacteria causing periodontal infection enter the bloodstream and invade the heart causing their toxic effects.
2. The inflammatory mediators that are produced in response to periodontal infection travel through the bloodstream and reach the heart and blood vessels.
3. Lipopolysaccharides that are bacterial products travel through the bloodstream to reach the heart.

Porphyromonas gingivalis is reported to colonize cells in the coronary artery and cause structural and immunological changes associated with early stages of heart disease²¹. Bacteria that normally colonize the tooth can get displaced to reach the bloodstream during dental procedures, flossing or even chewing food. Though these microbes are relatively harmless, they have an affinity for damaged endothelial cells and blood clots in the heart, where they multiply and trigger endocarditis. C- reactive protein is reported to be elevated in patients with periodontal diseases and hence testing for this protein is considered a valuable tool to predict the occurrence of heart disease²². C- reactive protein (CRP) has gained significance as a risk factor for atherosclerosis²³. Slade et al has demonstrated that CRP remains increased in patients with periodontal diseases even after controlling the risk factors that increase CRP.

Periodontal disease causing preterm birth

Low birth weight is defined as a birth weight of less than 2500g. Periodontal pathogens may target the placental membranes. It is proposed that preterm labor is induced by infection or inflammation at a distant site from the uterus which results in release of prostaglandins that result in uterine contractions at an inappropriate time^{24,25}.

Cecilia Gonzales et al tested gastric aspirates of 57 newborn babies and found that of the 46 different species of microorganisms, 2 were reported to originate from the mouth²⁶.

Oral infections causing other systemic diseases

Bacterial pathogens have been aspirated from elderly patients with pneumonia²⁷. Patients with blood dyscrasias and white blood cell disorders benefit from periodontal maintenance through the reduction of oral bacterial load²⁸. Inflammatory cytokines, lipopolysaccharides and bacteria are released into circulation from the inflamed periodontium. They promote atherosclerosis and affect coagulation of blood contributing to stroke. Bacteria in the blood stream may lodge on the abnormal heart valves or damaged heart tissue and cause infective endocarditis²⁹. Periodontal diseases often co-exist with diabetes mellitus. Diabetes is

considered a risk factor for periodontal diseases. The converse can also occur.

CONCLUSION

Oral infections, specifically periodontal infections are a contributing factor to various systemic infections. There is still however no sufficient evidence to claim a causal association between oral infection and systemic diseases. Slots has defined the criteria for causal link between periodontal and systemic diseases: The incidence and prevalence of the systemic disease of concern should be significantly higher in periodontitis patients than in periodontally healthy individuals; the onset of systemic diseases must follow the onset of periodontitis; removal of causative factors should decrease the incidence of systemic diseases; the microorganisms of the systemic diseases should be of the same species, biotype, serotype as genotype as the oral microorganisms; experimental animals with periodontitis should develop more systemic diseases than periodontally healthy animals³⁰. These criteria indicate the directions that future researches should take. As a causal link between oral diseases and systemic diseases is reported, good oral health is crucial not only to prevent oral diseases but also to maintain good general health.

REFERENCES

1. Overview of the links between oral and systemic health with emphasis on periodontal and cardiovascular disease. North America: ILSI; Jan1 Beck JD, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. *J Periodontol*; **67**(Suppl 10):1123-37 (1996).
2. Moore, W. E. C., and L. V. H. Moore. 1994. The bacteria of periodontal disease. *Periodontol*. **5**:66–77 (2000).
3. Tronstad, L. Recent development in endodontic research. *Scan. J. Dent. Res.* **100**: 52–59 (1992).
4. Baltch, A. L., H. L. Pressman, C. Schaffer, R. P. Smith, M. C. Hammer, M. Shayegani, and P. Michelsen. 1988. Bacteremia in patients undergoing prophylaxis as recommended by the American Heart Association, *Arch. Intern. Med.* **148**:1084–1088 (1977).
5. Carroll, G. C., and R. J. Sebor. Dental flossing and its relationship to transient bacteremia. *J. Periodontol.* **51**: 691–692 (1980).
6. Debelian, G. J., I. Olsen, and L. Tronstad. Anaerobic bacteremia and fungemia in patients undergoing endodontic therapy: an overview. *Ann. Periodontol.* **3**: 281–287 (1998).
7. Drinnan, A. J., and C. Gogan. Bacteremia and dental treatment. *J. Am. Dent. Assoc.* **120**: 378 (1990).
8. Heimdahl, A., G. Hall, M. Hedberg, H. Sandberg, P. O. Soder, K. Tuner, and C. E. Nord. Detection and quantitation by lysis-

- filtration of bacteremia after different oral surgical procedures. *J. Clin. Microbiol.* **28**: 2205–2209 (1990).
9. Lofthus, J. E., M. Y. Waki, D. L. Jolkovsky, J. Otomo-Corgel, M. G. Newman, T. Flemmig, and S. Nachnani. Bacteremia following subgingival irrigation and scaling and root planing. *J. Periodontol.* **62**: 602–607 (1991).
 10. Debelian, G. J., I. Olsen, and L. Tronstad. Anaerobic bacteremia and fungemia in patients undergoing endodontic therapy: an overview. *Ann. Periodontol.* **3**: 281–287 (1998).
 11. Loesche, W. J., and D. E. Lopatin. 1998. Interactions between periodontal disease, medical diseases and immunity in the older individual. *Periodontol.* **16**: 80–105 (2000).
 12. Weinberg, A., S. Krisanaprakornkit, and B. A. Dale. Epithelial antimicrobial peptides: review and significance for oral applications. *Crit. Rev. Oral Biol. Med.* **9**: 399–414 (1998).
 13. Loesche, W. J. Periodontal disease as a risk factor for heart disease. *Compendium* **15**: 976, 978–982, 985–986 (1994)
 14. Thoden van Velzen, S. K., L. Abraham-Inpijn, and W. R. Moorer. Plaque and systemic disease: a reappraisal of the focal infection concept. *J. Clin. Periodontol.* **11**: 209–220 (1984).
 15. Kilian, M. Systemic disease: manifestations of oral bacteria, p. 832–838. *In* J. R. McGhee, S. M. Michalek, and G. H. Cassell (ed.), *Dental microbiology*. Harpers & Row, Philadelphia, Pa (1982).
 16. Hammond, B. F. Major bacterial diseases, p. 165–190. *In* J. Slots and M. A. Taubman (ed.), *Contemporary oral microbiology and immunology*. Mosby, St. Louis, Mo (1992).
 17. McGhee, J. R. Microbial pathogenic mechanisms, p. 374–387. *In* J. R. McGhee, S. M. Michalek, and G. H. Cassell (ed.), *Dental microbiology*. Harper & Row, Philadelphia, Pa (1982).
 18. Okuda, K., and Y. Ebihara. Relationships between chronic oral infectious diseases and systemic diseases. *Bull. Tokyo Dent. Coll.* **39**: 165–174 (1998).
 19. Rams, T. E., and J. Slots. 1992. Systemic manifestations of oral infections, p. 500–523. *In* J. Slots and M. A. Taubman (ed.), *Contemporary oral microbiology and immunology*. Mosby, St. Louis, Mo.
 20. Rodrigues and Progulska Fox Sept 30, First gene profile of oral pathogen as it invades coronary artery. U.S.: NIDCR; 2005.
 21. Hahn, Schenkein, Tew. Aug 12, Important clue in how certain oral bacteria might contribute to heart condition. U.S.: NIDCR. 2005.
 22. Slade GD, Offenbacher S, Bexk JD, Heiss G, Pankow JS. Acute phase inflammatory response to periodontal disease in the U. S population. *J Dent Res*; **79**: 49-57 (2000).
 23. Kiran M, Arpak N, Unsal E, Erdogan MF. The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. *J Clin Periodontol*, **32**: 266-72 (2005).
 24. Heasman PA, Lauffart BL, Preshaw PM. Crevicular fluid prostaglandin EZ levels in periodontitis- resistant and periodontitis susceptible adults. *J Clin Periodontol*; **25**: 1003-7 (1998).
 25. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura, *et al.* Inflammatory markers and the risk of coronary heart disease in men and women. *N Engl J Med*; **351**: 2599-610 (2004).
 26. Gonzales-Marin C; Collegues, Queen Mary University. Body and Soul. India: Times of India; 18 Apr 2009.
 27. Heasman PA, Lauffart BL, Preshaw PM. Crevicular fluid prostaglandin EZ levels in periodontitis- resistant and periodontitis susceptible adults. *J Clin Periodontol*; **25**: 1003-7 (1998).
 28. Loe H, Silness J. Periodontal disease in pregnancy: Prevalence and severity. *Acta Odontol Scand*; **21**: 532-51 (1963).
 29. Boon, N. A., and K. A. A. Fox. 1995. Disease of the cardiovascular system, p. 191–312. *In* C. R. W. Edwards, I. A. D. Bouchier, C. Haslett, and E. R. Chilvers (ed.), *Davidson's principles and practice of medicine*, 17th ed. Churchill Livingstone, New York, N.Y.
 30. Slots, J. Casual or causal relationship between periodontal infection and non-oral disease. *J. Dent. Res.* **77**: 1764–1765 (1998).