ABSTRACT
Multitude of etiologies can cause diseases in various systems. One important etiology is focal sepsis in the oral cavity which has been hypothesized till now to cause various diseases. This hypothesis has now been proved beyond doubt. This article aims to throw light at the effects of oral focal sepsis on the systems, their management and the role of the dentist in prevention of these manifestations.

Keywords: Oral focal sepsis, Antibiotic prophylaxis, Systemic manifestation.

How to cite this article: Krishnan V. Systemic Affliction of Oral Focal Sepsis. J Indian Aca Oral Med Radiol 2012;24(2):137-141.

INTRODUCTION
Diseases in the various parts of the body can be caused by multitude of etiologies. Mouth reflects the signs of systemic diseases clearly and early too. Vice versa, systemic diseases in different organs are caused by sepsis in the mouth.1 This theory of systemic diseases being caused by sepsis in the mouth dates back to as early as1891, when Miller published a report entitled ‘The human mouth as a focus of infection’ followed by Ayrapaa in 1902 and William Hunter in 1910.

By definition, sepsis—is the presence in the blood (or) other tissues, of pathogenic microorganisms (or) their toxins. The circulatory blood not only transports oxygen and nutrition to various parts of the body, but also eliminates the metabolic waste products from the tissues. In any part of the body, if septic materials are present, these materials are also carried by blood, thus bacteremia, pyemia, septicemia and toxemia will occur in the body. In cases of improper oral hygiene and various disease processes, the microorganisms and their toxins starts to accumulate in localized areas of different parts of the tooth, such as root canal, carious cavity, and also different parts of the oral mucosa, such as periodontal pocket and pericoronal flap. On stimulation of this site, these oral pathogens and their toxins enter the circulation and reach the remote parts of the body, where they initiate the disease process by immunological injury and subsequent metastatic inflammation.2

This localized area of chronic infection causes inflammation, suppuration, liberation of toxins resulting in toxemia, septicemia with fatal outcome. This infectious and inflammatory process in the oral cavity is called ‘focal sepsis’.

DEFINITION
Foci of infection: Persistent infection with microorganisms and septic material constantly localized anywhere in the body, which on stimulation disseminates to other parts of the body causing diseases in remote parts.

Oral foci of infection: Localized area of persistent infection containing microorganisms and septic materials in any part of the oral cavity, which on stimulation disseminates to other parts of the body causing diseases in remote parts.

Pathogenesis: These localized areas of chronic infection, i.e. focal sepsis, require minor surgical procedures to prevent and cure the diseases. When these procedures are carried out, the areas of focal sepsis get manipulated, causing the microorganisms in localized areas to disseminate to other parts of the body through hematogenous and lymphogenous spread giving rise to bacteremia3 and diseases in remote parts of the body. Generally, the microorganisms are eliminated by the system within a few minutes. But bacteremia is a potential hazard to patients with abnormal heart valves or other cardiac abnormalities predisposing them to infective endocarditis.4

MECHANISM OF SPREAD OF FOCI OF INFECTION
Transmission through the Lymphatics
The usual route for the bacteria that gain entrance to the body is along the lymph channels where they are usually arrested and stay in hibernation. In acute phases, this causes lymphadenitis and palpable lymph nodes. The lymph nodes act as a reservoir. In severe sepsis, necrotizing lymphadenitis may cause bacteremia, bacilemia, toxemia and fatal outcome. On trauma/surgical manipulation they spread systemically.

Transmission through the Blood Stream
Bacteria usually live as commensals and also due to disease processes in focal sepsis region. Strong evidences suggest that trauma/surgical manipulations to the infected area especially in immune-compromised states may cause bacteremia. Various studies have proved the recovery of the most common disease causing bacteria, such as Streptococcus viridans, nonhemolytic groups, occasional Streptococcus pneumoniae, Staphylococcus albus and dipheroids from blood, after management/manipulation of
dental diseases. The postulated route in addition to general circulation, maybe via the kinin system through which the vascular barricade is penetrated.\textsuperscript{5}

**Immunological Response**

Immunological injury and subsequent metastatic inflammation are caused from oral pathogens and their toxins.\textsuperscript{2} In cases of systemic allergies with the presence of oral foci especially periapical periodontitis, there was a marked elevation of the IgE levels indicating an over-reactive immunologic host response.\textsuperscript{6,7}

**Aspirations**

It has been demonstrated in recent years that bacteria inhabiting the oral cavity can cause bacterial pneumonia by aspiration. Pneumonia is one of the most common causes of death in the hospitalized and institutionalized elderly medically compromised patients.\textsuperscript{8-11} Dental plaque is colonized by nonoral respiratory pathogens also which then acts as a reservoir of bacteria.\textsuperscript{12}

**ORAL FOCI CAUSING VARIOUS SYSTEMIC DISEASES**

About the 300 and above species of bacteria forming populations of several hundred billion in the human oral cavity, reaches a thousand billion when the mouth is not sufficiently cleaned. These bacteria create ecological niches on tooth surfaces, gingival crevices, saliva dorsum linguae and buccal and pharyngeal mucosa, threatening oral and systemic health. The implications of oral focal sepsis extend into almost every system. It is known that primary lesions of these chronic bacterial infections secondarily cause nephritis,\textsuperscript{13} rheumatoid arthritis and dermatitis.\textsuperscript{14} A brief insight into the effects systemwise is documented as follows.

**Cardiovascular System**

Dental foci of infection cause acute bacterial myocarditis, infective endocarditis and coronary heart diseases. Any infection or inflammation seems to increase susceptibility to myocardial infarction.\textsuperscript{10,15,16} Recent study showed that the chronic infection including the periodontal disease associated bacteria, through bacteremia aids progression of atherosclerosis, increasing the risk of coronary vascular diseases (CVD) and stroke by stimulation of systemic inflammation and autoimmunity.

To concur with this, among subjects with chronic infections, atherosclerosis risk was highest in those with prominent inflammatory responses. Indicators of systemic inflammation, like soluble adhesion molecules, circulating bacterial toxins, soluble human heat shock protein 60 and antibodies to mycobacterial heat shock protein 65 were increased in patients with chronic infections. These were prognostic of greater risk of atherosclerosis as proved by a large population study.\textsuperscript{17} A recent case of descending necrotizing mediastinitis was reported following dental extraction.\textsuperscript{5}

Odontogenic infection causing Lemierre syndrome, due to disseminated septic thrombophlebitis with the characteristic features of thrombosis of jugular vein, distant septic emboli, and superadded infection with \textit{Fusobacterium necrophorum} was also documented.\textsuperscript{18,19} Its effects extend into the central nervous system and respiratory system.

**Central Nervous System**

Existing proof\textsuperscript{13,20} links oral focal sepsis to trigeminal, atypical neuralgias, unilateral paralysis of the face and brain infarctions. Infections and inflammations in the body alter the values of leukocytes, fibrinogen and coagulation factors, causing myocardial and brain infarctions.\textsuperscript{21-26}

Any focal sepsis, including oral focal sepsis contains bacteria\textsuperscript{10} which can increase manifold and circulate into the blood stream causing life-threatening conditions, such as brain abscesses. The postulated entry of oral microorganisms into the cranium maybe by, along the facial planes, hematogenous route—through general circulation, veins which lack valves, through cavernous sinus, lymphogenous route, and indirectly by extraoral odontogenic infections.

Bacterial lipopolysaccharide endotoxins and host-produced inflammatory cytokines may also aid in the development of atheroma’s and thus infarctions.\textsuperscript{25,27}

**Eye**

Uveitis or iritis\textsuperscript{6,7,10} is the most common manifestations of metastatic inflammation due to an immunologically exuberant host response in conjunction with oral foci.

**Respiratory System**

When bacteria in the oral cavity are aspirated, particularly in cases of periodontal disease have caused pneumonia in the elderly hospitalized patients and in immunocompromised patients.\textsuperscript{8-11} Pathogens which are not present in the oral cavity are also able to inhabit the dental plaque, which then acts as a ‘pool’ for these bacteria, later implanting them into the lungs.\textsuperscript{12}

**Excretory System**

Evidence has it that glomerulonephritis, is aggravated in the presence of oral infections. Removal of these infections resulted in reduction in severity of the disease.\textsuperscript{22}
Oral focal sepsis is related to such differing diseases\textsuperscript{20,15} as neutrophil disorders, abscesses of liver and also adverse pregnancy effects.

In a case of brain and liver abscesses, contrast-enhanced computed tomography and magnetic resonance imaging respectively confirmed the diagnosis. An oral foci of infection was also found. Interestingly, \textit{Streptococcus intermedius} was isolated from the oral smear, liver, ventricular drainage and blood sample. Once the antibiotic therapy was started, abscesses were drained, and eradication of oral foci, thorough recovery, was noted.\textsuperscript{28}

**Skeletal System and GIT**

Removal of dental focal sepsis has shown remarkable alleviation in the state of infectious arthritis.\textsuperscript{29}

Systemic allergy\textsuperscript{30,31} with increased levels of IgE\textsuperscript{6,7} was an important finding in patients with periapical periodontitis. Oral infections have been seen to aggravate arthritis and Crohn’s disease, while an improvement of symptoms follows the abolition of oral foci.\textsuperscript{32,33}

**Skin**

Rosacea is a long-term skin disorder which involves the facial convexities, characterized by recurrent flushing, persistent erythema and telangiectasia. Also associated with papules, pustules and swelling during periods of inflammation. Removal of infectious foci specifically dental foci caused a major improvement and led to recovery.\textsuperscript{34}

In a case of neurodermatitis, when the foci was eliminated, it has been reported to have retreated from its severe form.\textsuperscript{35}

An interesting report of three cases of chronic urticaria had abscessed tooth and severe periodontitis. On treatment of oral disease, resolution of urticaria was present.\textsuperscript{14}

Tropical skin ulcers of high probability of oral etiology have been documented.\textsuperscript{36,37}

**Hormonal**

**Diabetes**

A representative sample study of National Health and Nutrition Examination Survey-NHANES-I\textsuperscript{38} by researchers of University of Edinburgh\textsuperscript{39} has suggested periodontal disease as prognosticator of incident diabetes.

**TREATMENT MODALITIES**

The frequency of bacteremia after health care procedures vary. Generally, it was the highest for dental and oral procedures as per the data from multiple studies reviewed by Durack et al.\textsuperscript{40} The representative rates of bacteremia after tooth extraction were 18 to 85\% and periodontal surgery was 60 to 90\%. Hence, prophylaxis should be targeted to patients at higher risk including, elderly\textsuperscript{41} and medically compromised patients,\textsuperscript{42} i.e. dental procedures which are known to induce gingival or mucosal bleeding. But the choice of an appropriate cutoff point below which the risk is too low to require prophylaxis remains arbitrary.

A thorough review of all available data to determine the need for antibiotic prophylaxis stratified dental treatments with higher incidence of bacteremia. Data indicates IV or oral penicillin decreased the bacteremia rates significantly including the retrieval of \textit{Streptococci}.

Lawrence Dall et al\textsuperscript{43} in his study with rabbits, of experimental aortic valve endocarditis caused by high glycocalyx producing Viridans \textit{Streptococci}, associated it with hindered antimicrobial sterilization. The effect of clindamycin (30 mg/kg, subcutaneous three times daily) is augmented by the enzymatic assimilation of this glycocalyx with dextranase. It was hypothesized that clindamycin inhibits glycocalyx production \textit{in vivo} allowing better antimicrobial penetration in the infected cardiac vegetation.

In spite of these facts, the dentists, prescription many a times did not match the recommended dose,\textsuperscript{44,45} route of administration, or time period of the AHA guidelines as proven by Erno Gutschik and Soren Lippert\textsuperscript{46} in their questionnaire analysis. Though more than half of the dentists knew about the patients with prosthetic heart valves, only about 14\% carried out oral prophylaxis with antibiotics. To ensure this dentists, doctors and patients should be exposed to proper information on the recent updates of antibiotic schedules, in order to save the patients risk.

**SUMMARY**

AHA\textsuperscript{47} has recommended preoperative medication for patients with:

- Congenital, rheumatic or other acquired valvular heart disease
- Idiopathic hypertrophic, subaortic stenosis
- Mitral valve prolapse syndrome
- Before dental procedures that are likely to cause gingival bleeding.

The advisory statements of AAOS (American Association of Orthopedic Surgeons) after complete review of dental patients who have undergone total joint arthroplasties,\textsuperscript{47-55} and ADA (American Dental Association) recommended antibiotic coverage for:

- Patients with total joint replacement and compromised immune systems
- Type 1 diabetes mellitus
- Recent (within 2 years) joint replacement
4. Previous prosthetic joint infections
5. Malnourishment or hemophilia
6. In cardiac patients with newly placed shunts, the initial 2 weeks after placement is the time of highest risk of infections.
7. Patients with renal diseases who are undergoing hemodialysis and transplant.
8. Patients with VA shunts.

Dental procedures considered for antibiotic prophylaxis in susceptible patients include:
1. Dental extractions
2. Periodontal procedures including surgery, scaling, root planning and probing
3. Dental implant placement
4. Endodontic instrumentation or surgery beyond the tooth apex
5. Prophylactic cleaning of teeth or implants with anticipated bleeding
6. Intraligamentary LA injections.

In the recommendation of NICE guidance (Apr 5th 2008) for prophylaxis against infective endocarditis, regular everyday activities have been evidenced to cause higher risk of infective endocarditis than dental procedures.

**CONCLUSION**

Taking into account, all data and recommendations evidence that oral sepsis doubles the risk of bacteremia has been proved beyond doubt. To reduce oral infections and systemic complications, the importance of sustaining good oral health cannot be overemphasized. This considerably minimizes everyday bacteremia, thus, in turn the prospect of infective endocarditis and other bacteremic infections in patients at risk.

This is as important as that of carrying out dental treatments under antibiotic cover for patients at risk. In addition, dentists must be made aware of current protocols, benefits of the judicial usage of antibiotics with proper dosage, route of administration, frequency in patients at risk.

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