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Impact of Periodontal Infection on Systemic Health

Periodontal disease is an inflammatory disease **initiated by** bacterial pathogens. Environmental, physical, social, and host stresses may affect and modify disease expression through a multitude of pathways. Certain systemic conditions can affect the initiation and progression of gingivitis and periodontitis. Systemic disorders that affect neutrophil, monocyte, macrophage, and lymphocyte function result in the altered production or activity of host inflammatory mediators.

These alterations may manifest clinically as the early onset of periodontal destruction or as a more rapid rate of destruction than would occur in the absence of such disorders. There are many systemic conditions that can modify the host's susceptibility to periodontitis. For example, patients with immune suppression may not be able to mount an effective host response to subgingival microorganisms, thereby resulting in more rapid and severe periodontal destruction. Conversely, individuals with a significant increase in the production of proinflammatory mediators may respond to periodontal pathogens with an exuberant inflammatory response that results in the destruction of periodontal tissues.

Conditions in which the influences of periodontal infection are documented include coronary heart disease (CHD) and CHD-related events such as angina, infarction, atherosclerosis, and other vascular conditions; stroke; diabetes mellitus; preterm labor, low-birth-weight delivery, and respiratory conditions such as chronic obstructive pulmonary disease.

Subgingival environment as a reservoir for bacteria

The subgingival microbiota in patients with periodontitis provides a significant and persistent gram-negative bacterial challenge to the host that is met by a potent immunoinflammatory response. These organisms and their products, such as lipopolysaccharide (LPSs), have ready access to the periodontal tissues and to the circulation via the sulcular epithelium, which is frequently ulcerated and discontinuous. Even with treatment, the complete eradication of these organisms is difficult.

The mechanisms by which periodontal infections may influence systemic health have been described as follows:

1.Oral-hematogenous spread of periodontal pathogens and direct effects to target organs.

2.Transtracheal spread of periodontal pathogens and direct effects to target organs.

3.Oral-hematogenous spread of cytokines and antibodies with effects at distant organs

Periodontal Disease and Coronary Heart Disease/Atherosclerosis/stroke

To further explore the association between periodontal disease and CHD/atherosclerosis, investigators have studied specific systemic disorders and medical outcomes to determine their relationship to periodontal status. CHD-related events are a major cause of death.

Myocardial infarction (MI) has been associated with acute systemic bacterial and viral infections. Traditional risk factors such as smoking, dyslipidemia, hypertension, and diabetes mellitus do not explain the presence of coronary atherosclerosis in a large number of patients. Localized infection that results in a chronic inflammatory reaction has been suggested as mechanism underlying CHD in these individuals. The association between poor dental health and MI was independent of known risk factors for heart disease, such as age, cholesterol levels, hypertension, diabetes, and smoking. Because atherosclerosis is a major determinant of CHD-related events, dental health has also been related to coronary atheromatosis.

Damage to the vascular endothelium, with a subsequent inflammatory reaction, plays a major role in atherosclerosis and ischemic organ damage. **Increased viscosity of blood** may promote major ischemic heart disease and cerebrovascular accident (stroke) by **increasing the risk of thrombus formation** because of **increased fibrinogen levels** which **increase blood viscosity**. Fibrinogen levels and white blood cell counts are often **increased** in patients with periodontal disease, so individuals with poor oral health may also have significant elevations in coagulation factor VIII. Thus, periodontal infection may also promote increased blood viscosity and thrombogenesis, which leads to an increased risk for central and peripheral vascular disease.

C reactive protein (CRP) induces monocytes and macrophages to produce tissue factor, which stimulates the coagulation pathway and increases blood coagulability. Periodontal infections may contribute to atherosclerosis and thromboembolic events by repeatedly challenging the vascular endothelium and arterial wall with bacterial LPSs and proinflammatory cytokines. Thus, periodontal

diseases may have both direct effects on the major blood vessels (e.g., atheroma formation) and indirect effects that stimulate changes in the cardiovascular system (e.g., elevation of systemic inflammatory responses). Oral organisms may be involved in coronary thrombogenesis. Platelets **selectively bind** some strains of **Streptococcus sanguinis**, which is a common component of supragingival plaque, and **Porphyromonas gingivalis**, which is a pathogen closely associated with periodontitis.

It has been found that **gram negative bacteria & associated lipopolysaccharides (LPSs)** plays an important role in atherogenesis because it has the ability to trigger the release of interleukin 1, tumor necrosis factor- alfa (TNF-α) & thromboxane that initiate platelet aggregation, promote the deposition of cholesterol & enhance atheroma formation.

The role of (LPSs) as a systemic trigger for the **development of atheroma** has led the investigators to search for an infection site which would provide a source for (LPSs). In individuals with periodontitis, the periodontium can serve as a reservoir for (LPSs)& inflammatory cytokines.

Many studies have demonstrated a significant association between periodontal disease severity & stroke, myocardial infarction & coronary atherosclerosis. These investigations seem to suggest that because of chronicity of periodontal diseases & sustained release of bacteria & endotoxins into blood stream, periodontitis can contribute to systemic effects as atheroma development.

Ischemic cerebral infarction, or stroke, is often preceded by systemic bacterial or viral infection. Stroke is **classified as** either hemorrhagic or nonhemorrhagic.

Non-hemorrhagic stroke, or ischemic stroke, is usually caused by thromboembolic events and cerebrovascular atherosclerosis, whereas **hemorrhagic stroke** often results from a vascular bleed such as an aneurysm. **Periodontal disease has been associated primarily with an increased risk of nonhemorrhagic stroke**.

Numerous studies have shown that periodontal disease is associated with an increased risk of stroke. Dental diseases may be indicators of general health practices. For example, periodontal disease and CHD are both related to lifestyle and share numerous risk factors, including smoking, diabetes, and low socioeconomic status. Bacterial infections have significant effects on endothelial cells, blood coagulation, lipid metabolism, and monocytes and macrophages.

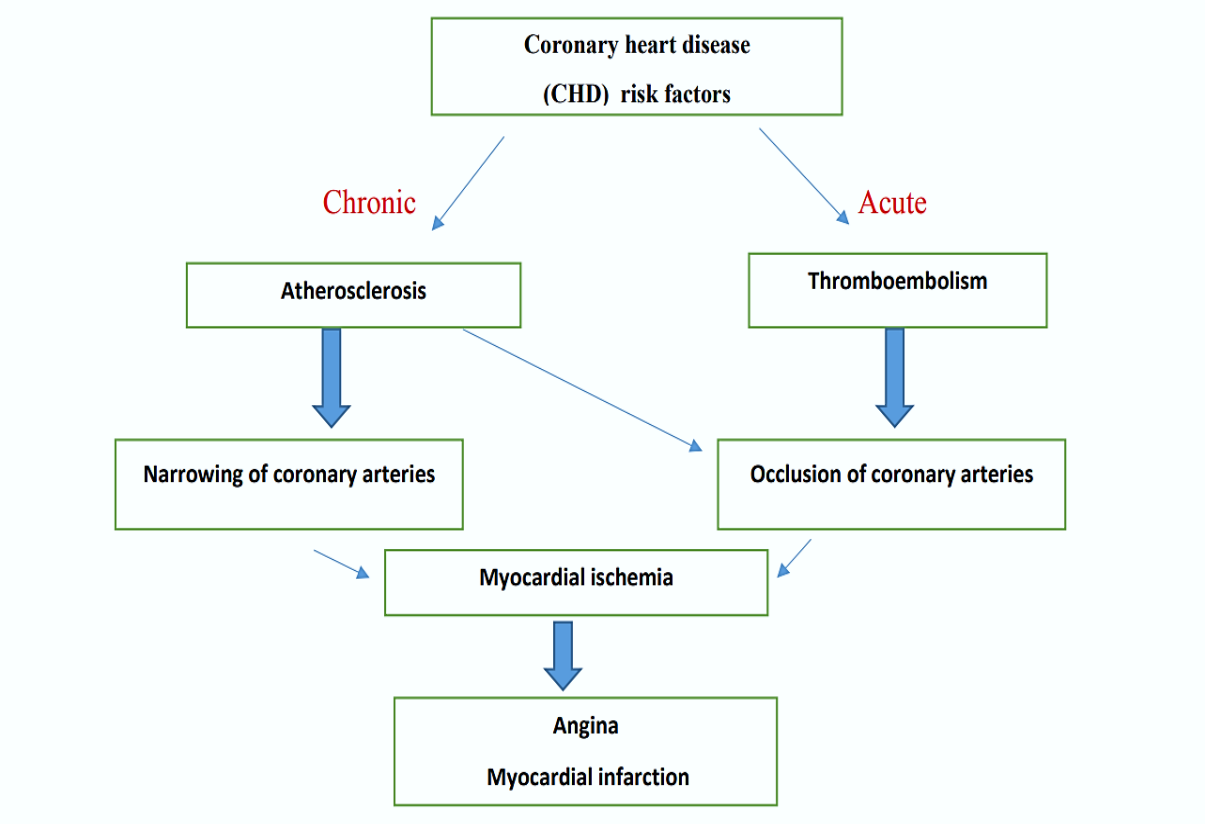

Fig. :- Acute and chronic pathways to ischemic heart disease. Coronary heart disease–related events, such as angina and myocardial infarction, may be precipitated by either pathway or both pathway.

Factors that affect blood viscosity in health:-

- Plasma fibrinogen
- Plasma lipoproteins **(Low-density lipoprotein LDL, very-low-density lipoprotein VLDL)**
- White blood cell count

Systemic Infections

Systemic infections are known to induce a **hypercoagulable state** and increase blood viscosity. Fibrinogen levels and white blood cell counts are often **increased** in patients with periodontal disease. Individuals with poor oral health may also have significant elevations in **coagulation factor VIII/von Willebrand factor antigen**, thereby **increasing the risk of thrombus formation**. Thus, periodontal infection may also **promote increased blood viscosity** and **thrombogenesis**, which **leads to an increased** risk for central and peripheral vascular disease.

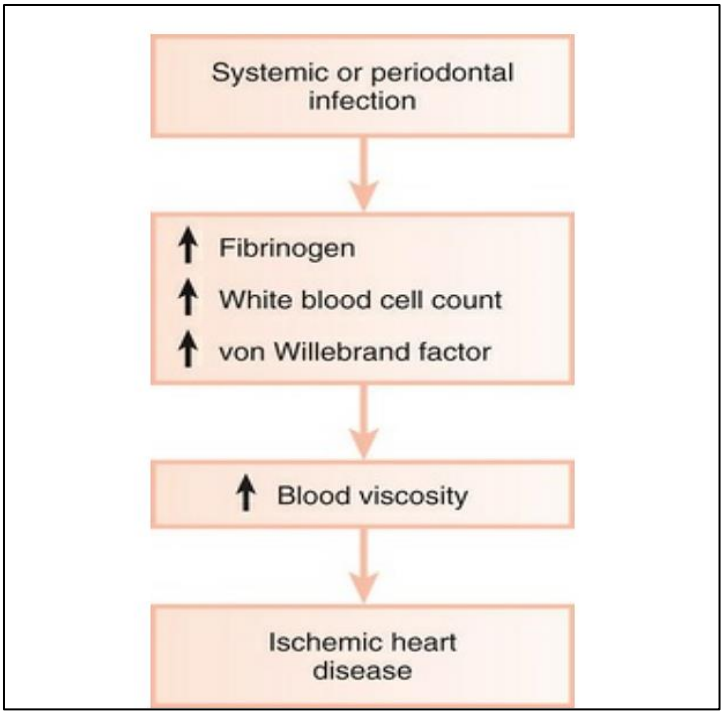

Fig.:- The effect of infection on blood viscosity. Increased plasma fibrinogen and von Willebrand factor cause hypercoagulability. When they are combined with an increased white blood cell count, the blood viscosity increases, thereby increasing the risk of coronary ischemia.

Atherosclerosis

Atherosclerosis is a **focal thickening of the arterial intima**, the innermost layer lining the vessel lumen, and the media, the thick layer under the intima that consists of smooth muscle, collagen, and elastic fibers. The formation of atherosclerotic plaques is precipitated by damage to vascular endothelium that results in an inflammatory response in which circulating monocytes adhere to the vascular endothelium. Damage to vascular endothelium can occur because of the presence of intravascular microorganisms and their products; chemical damage, often resulting from elements of tobacco and other exogenous toxins; and increased shear force along the vascular lining, such as that occurring in hypertension.

The adherence of monocytes to the damaged vascular endothelium is mediated by several adhesion molecules on the endothelial cell surface, including intercellular adhesion molecule-1 (ICAM-1), endothelial leukocyte adhesion molecule-1 (ELAM-1), and vascular cell adhesion molecule-1 (VCAM-1). These adhesion molecules are up-regulated by a number of factors, including bacterial LPSs, prostaglandins, and proinflammatory cytokines. After binding to the endothelial cell lining, monocytes penetrate the endothelium and migrate under the arterial intima. The monocytes ingest circulating low-density lipoprotein in its oxidized

state and become engorged, thereby forming the foam cells that are characteristic of atheromatous plaque. After entering the arterial media, monocytes may also transform to macrophages.

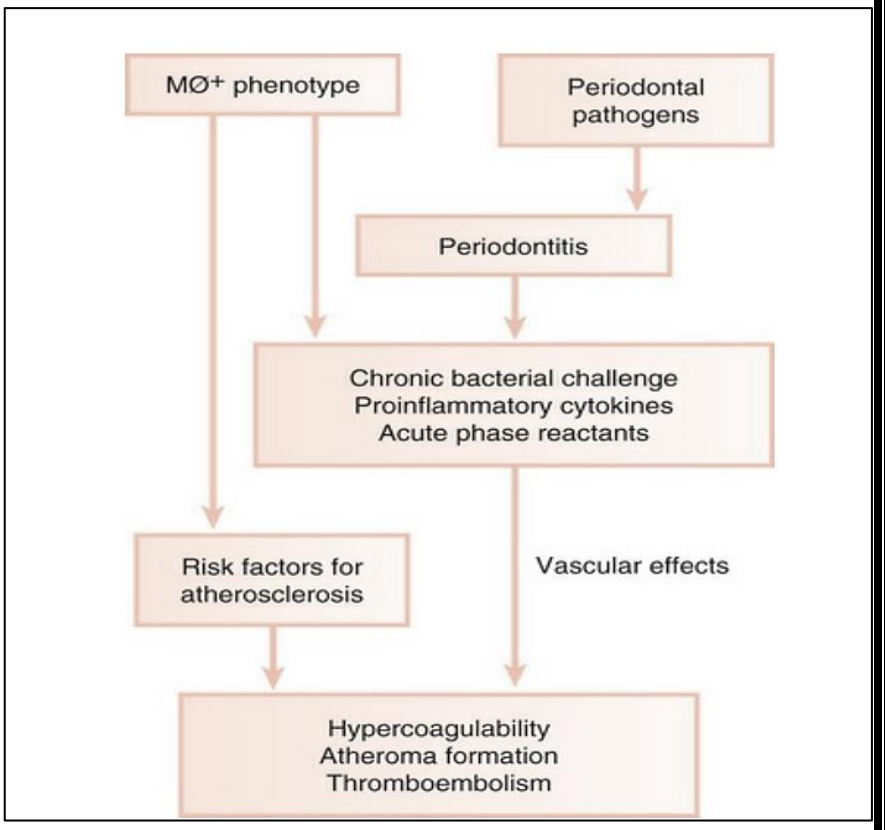

Fig. The cardiovascular and periodontal consequences of the hyperresponsive monocyte /macrophage phenotype (MØ+). In combination with other risk factors, the MØ+ phenotype predisposes individuals to both atherosclerosis and periodontitis. Bacterial products and inflammatory mediators associated with periodontitis affect vascular endothelium, monocytes and macrophages, platelets, and smooth muscle and may increase blood coagulability. This may further increase atherosclerosis and may result in thromboembolism and ischemic events.

Periodontal disease and diabetes mellitus

The role of diabetes in periodontal disease is **bi-directional**, that is diabetes is a known risk factor for periodontitis and periodontitis in turn affects the glycemic control in individuals with diabetes. Periodontal infections result in an elevation of serum pro-inflammatory markers, these may adversely affect metabolic control, may result in insulin resistance which in turn over time can lead to hyperglycemia and type II diabetes. Chronic gram negative periodontal infections in individual with diabetes may also worsen glycemic control.

Complications of Diabetes Mellitus

1. Retinopathy **2. Nephropathy** **3. Neuropathy**
4. Macrovascular disease **5. Altered wound healing** **6. Periodontal disease.**

Patients that harbor periodontal pathogens have significantly **higher markers** of systemic inflammation like C-reactive protein (CRP), IL-6 and fibrinogen than patients without these pathogens. This mechanism would explain the worsening of glycemic control associated with severe periodontitis. Because type II diabetes is strongly associated with insulin resistance, periodontal therapy that reduces systemic inflammation may improve insulin sensitivity and result in improved glycemic control. Conversely, type I diabetes is not strongly associated with insulin resistance, so reduced inflammation after periodontal therapy may not have a major effect on insulin sensitivity in patients with type I diabetes, which would minimize the impact of periodontal treatment in these patients.

Periodontal disease and pregnancy outcome

Infants born before the completion of **37 weeks** of gestation are referred to as preterm infants. Preterm infants weigh usually **lower at birth (< 2500 gm)** and prematurity is associated with increased perinatal mortality. The most significant factor for preterm delivery is maternal infections attributing to about half of the preterm births. Bacteria from the maternal genital tract infections elicit a proinflammatory response in the mother, which ultimately results in release of prostaglandins and matrix metalloproteinases. This in turn causes smooth muscle contraction and membrane weakening respectively and triggers premature cervical ripening. This bacterial- host inflammatory response is considered to be the association between maternal periodontal disease and adverse pregnancy outcomes. In addition to the above pathway, bacteremia associated with periodontal disease may reach the uterus thus exposing the maternal-fetal unit to the bacteria and their products. This may elicit the above mentioned inflammatory response leading to preterm delivery.

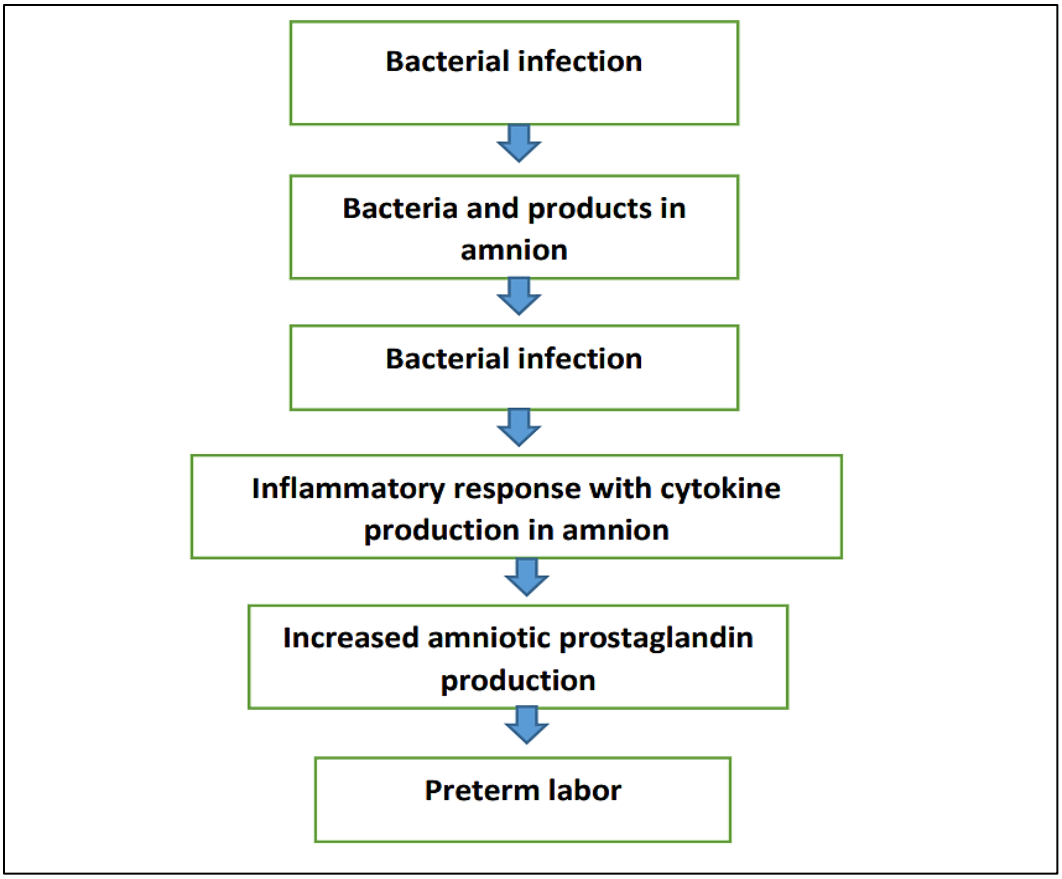

Fig.:- Mechanisms by which infection may induce preterm labor.

Periodontal infection and respiratory disorders

The oral cavity plays an important role in infections acquired in hospitals and nursing homes, especially infections of the respiratory tract. Several studies have demonstrated that the teeth of patients in the intensive care unit (ICU) became colonized by **respiratory pathogens** such as Pseudomonas aeruginosa, Enteric species and Staphylococcus aureus. Similar studies have shown that the teeth of nursing home residents can also serve as reservoirs for respiratory infection.

An association between oral conditions such as periodontal infections and respiratory conditions such as pneumonias and chronic obstructive pulmonary disease has beenfound. Evidence has suggested the oropharyngeal region as a likely source of bacteria implicated in respiratory infection.

Oral periodontopathic bacteria can be aspirated into the lung to cause aspiration pneumonia. Respiratory pathogens have been shown to colonize the dental plaque of hospitalized intensive care and nursing home patients. Once established in the mouth, these pathogens can be aspirated into the lung to cause infection. Cytokines

originating from periodontal tissues may change respiratory epithelium to promote infection by respiratory pathogens. A systematic review of the epidemiologic and clinical evidence found that poor periodontal health increases the risk of developing chronic obstructive pulmonary disease (COPD).

Chronic Obstructive Pulmonary Disease (COPD):

Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction that results from chronic bronchitis or emphysema. Bronchial mucous glands enlarge, and an inflammatory process occurs during which neutrophils and mononuclear inflammatory cells accumulate within the lung tissue.

Periodontal Disease and Acute Respiratory Infections:- COPD shares similar pathogenic mechanisms with periodontal disease. With both diseases, a host inflammatory response is mounted in response to chronic challenge by bacteria in periodontal disease and by factors such as cigarette smoking in COPD. The resulting neutrophil influx leads to the release of oxidative and hydrolytic enzymes that cause tissue destruction directly. The recruitment of monocytes and macrophages leads to further release of proinflammatory mediators.

Periodontal Disease and Acute Respiratory Infections

The upper respiratory passages are often contaminated with organisms derived from the oral, nasal, and pharyngeal regions. Pneumonia is an infection of the lungs that is caused by bacteria, viruses, fungi, or mycoplasma and is broadly categorized as either community-acquired or hospital-acquired. A wide variety of bacteria can cause pneumonia, and the spectrum of offending organisms differs greatly between community-acquired and hospital-acquired infections. Community acquired bacterial pneumonia is caused primarily by the inhalation of infectious aerosols or the aspiration of oropharyngeal organisms. **Streptococcus pneumoniae and Haemophilus influenzae** are the most common, although numerous other species may be found, including anaerobic bacteria. Antibiotic therapy is highly successful for the resolution of most cases of community-acquired bacterial pneumonia. To date, no associations have been found between oral hygiene or periodontal disease and the risk for acute respiratory conditions such as pneumonia in communitydwelling individuals. The same cannot be said for individuals in the hospital setting. Hospital-acquired (nosocomial) bacterial pneumonia has a very high morbidity and mortality rate. The incidence of nosocomial pneumonia is highest among severely ill patients, such as those in intensive care units or on ventilatory support. Although nosocomial pneumonia is most often caused by

gram-negative aerobic organisms, many cases are the result of infection by anaerobic bacteria, including those that are typically found in the subgingival environment. Hospital-acquired pneumonia is usually caused by the aspiration of oropharyngeal contents.

Periodontal disease and asthma

Asthma is a chronic disease of the airways characterized by inflammation and bronchoconstriction that occurs in people of all ages. Children with chronic medical disorders, like asthma, who require long-term medication have an increased susceptibility to dental diseases in three ways: frequent use of sugar containing syrups, use of sedatives causing a decreased saliva secretion, and use of corticosteroids.

The possible interactions between medications used for asthma and the induction of periodontal changes have also been positively correlated in the literature data from some studies suggest that inhalers can lead to changes in pH and a decrease in saliva production and therefore increase biofilm accumulation and calculus. In addition, the immunosuppressive effect of corticosteroids may have some influence on the response of the periodontal tissues. These agents act by inhibiting the host response, thus hampering the clinical expression of gingivitis. The association between periodontal disease and respiratory/lung diseases has been shown previously.

Once installed, gingival diseases (Gingivitis / periodontitis) may contribute indirectly through recurrence or worsening of respiratory attacks. Some mechanisms for the interrelationship between diseases have been proposed, such as aspiration of biofilm and hematogenous dissemination or inflammatory chemical mediators from the periodontal pockets. Thus, treatment and maintenance of gingival health can improve pulmonary function and decrease the frequency of respiratory attacks.

Conclusion: There is sufficient evidence to suggest that periodontal disease and systemic health have a two- way relationship, in that, the periodontal disease can cause adverse systemic conditions and that certain systemic diseases cause periodontal disease. It is vital that the physicians and other health care providers educate the patients about this association and to recommend dental care facilitate restoration of oral health in these individuals. The evidence suggests that treatment of one disease could lead to better outcomes for the other. This knowledge should be used to attain better patient outcomes in future.