

ETIOPATHOGENESIS OF CHRONIC INFLAMMATORY PERIODONTITIS

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ABSTRACT

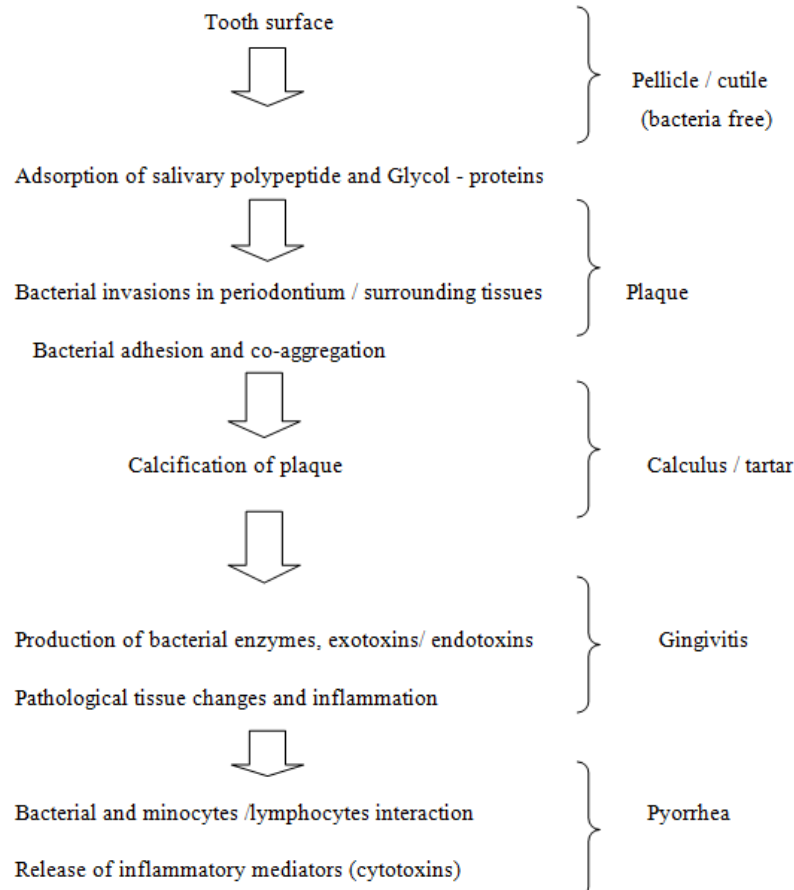
Periodontal diseases have been considered as "infections" in which microorganisms initiate and maintain the destructive inflammatory response. However, the nature of the periodontal disease resulting from dental plaque appears to depend to a large extent on the interaction among the bacterial agent, the environment, and the response of the host's defence mechanisms to the bacterial assault. A thorough understanding of the etiopathogenesis of periodontal disease has provided the clinicians and researchers with a number of diagnostic tools and technique that has widened the treatment options. Periodontitis, a disease involving supportive structures of the teeth prevails in all groups, ethnicities, races and both genders and dental plaque is considered as primary etiologic agent. A complete knowledge of the microbial factors, their pathogenicity as well as host factors are of the essential importance for pathogenesis of periodontal disease. In this way, it could be possible to treat the periodontal patients adequately.

Keywords: Periodontal tissues, Microorganisms, Periodontitis, Pathogenicity.

INTRODUCTION

The periodontium, defined as those tissues supporting and investing the tooth, comprises root cementum, periodontal ligament, bone lining the tooth socket (alveolar bone), and that part of the gingiva facing the tooth (dentogingival junction). It is a multifactorial infection with complex and interconnected mechanisms of pathogenesis¹. (Figure 1) The interplay between bacteria within the sulcus and periodontal pocket and the response they elicit in the

host defense mechanisms, which in turn can be modified by genetic and acquired risk factors, produces the prospects of a large number of possible permutations of how the disease might present clinically and how it might progress². Bacteria have long been established as the etiologic agents³. More than 700 species of aerobic and anaerobic bacteria have been identified in the oral cavity⁴. Only a few, however, have been associated with the connective tissue dissolution, apical migration of the epithelial attachment, and alveolar bone loss that characterize the disease process⁵.



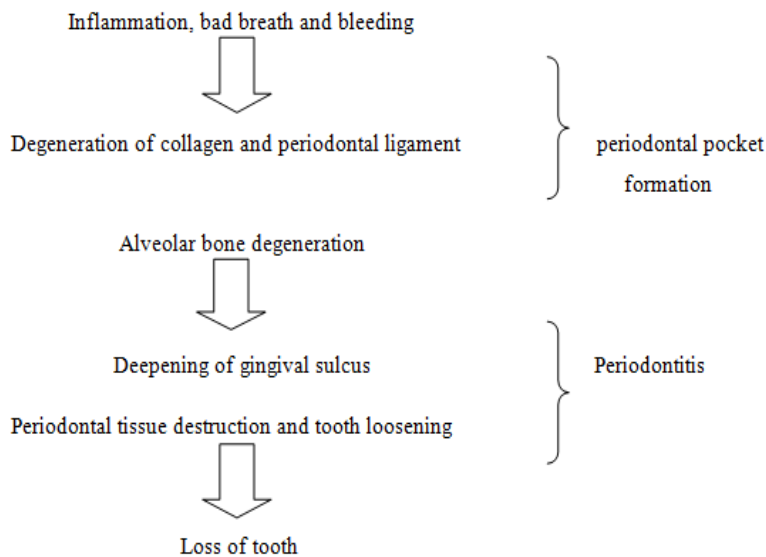


Fig. 1: Flow chart showing pathogenesis of periodontitis

Chronic periodontitis is a common disease characterized by a painless, slow progression (Table 1). It may occur in most age groups, (Table 2) but is most prevalent among adults and seniors worldwide, with approximately 35% of adults (30–90 years) in the US being affected by at least one site with CAL > 3 mm and probing depth (PD) >4 mm ⁶. The first challenge in treating periodontitis is a timely and proper diagnosis. Disease diagnosis and treatment in its earliest stages will prevent future breakdown. Because the disease is painless, patients rarely seek care. Thus, it is not uncommon for the disease to go undiagnosed until progression has reached moderate to advanced degrees of severity, characterized by obvious radiographic bone loss and/or tooth mobility. The second challenge is diagnosing and properly controlling all the factors contributing to this disease. The primary etiology for periodontal diseases is bacteria, which can cause direct and indirect destruction of the host

supporting tissues. In fact, most cases of chronic periodontitis are successfully managed by mechanical removal/reduction of bacterial mass and calculus in the sub gingival environment by scaling and root planning ⁷⁻¹⁰. However, any factor that influences either the local environment or the host response may contribute to disease progression. Generally putative periodontal pathogens are a constant presence not only in patients with periodontitis but are also present consistently in those who are healthy and resistant to periodontal disease (Figure 2). Disease sets in when these organisms are present in sufficiently large numbers to promote the release of inflammatory cytokines that would result in periodontal breakdown. It seems therefore significant that the modulation of the dental plaque to ensure that it is colonized by bacteria that are associated with health, could accrue more benefits to individuals at risk to periodontal disease.

Table 1: Clinical features of periodontal disease

S. NO	Symptoms	Signs
1	Bad breathe	Inflamed gingiva
2	Swelling & painful gums	Bleeding on probing
3	Bleeding gums	Increased pocket depth
4	Pain during chewing	Clinical attachment loss
5	Loose teeth	Tooth mobility

Table 2: Comparison of clinical characteristics of Periodontitis ³⁵

Condition	Chronic periodontitis	Localized aggressive periodontitis	Generalized aggressive periodontitis
Prevalence -	Most prevalent in adults but can occur in adults.	Usually occur in adolescents (circumpubertal onset).	Usually affects people under 30 years of age.
Progress -	Slow to moderate rate of progression.	Rapid rate of progression.	Rapid rate of progression (Pronounced episodic periods of progression).
Effects of microbial pattern	Amount of microbial deposits consistent with severity of destruction.	Amount of microbial deposits not consistent with severity of destruction.	Amount of microbial deposits sometimes consistent with severity of destruction.
Distribution Pattern	Variable distribution of periodontal destruction; No dissemble pattern - No marked familial aggregation. - Frequent presence of subgingival calculus.	Periodontal destruction localized to permanent first molars and incisors - marked familial aggregation. - Subgingival calculus usually absent.	Periodontal destruction affects many teeth in addition to permanent first molars and incisors. - marked familial aggregation. - Subgingival calculus may or may not be present.

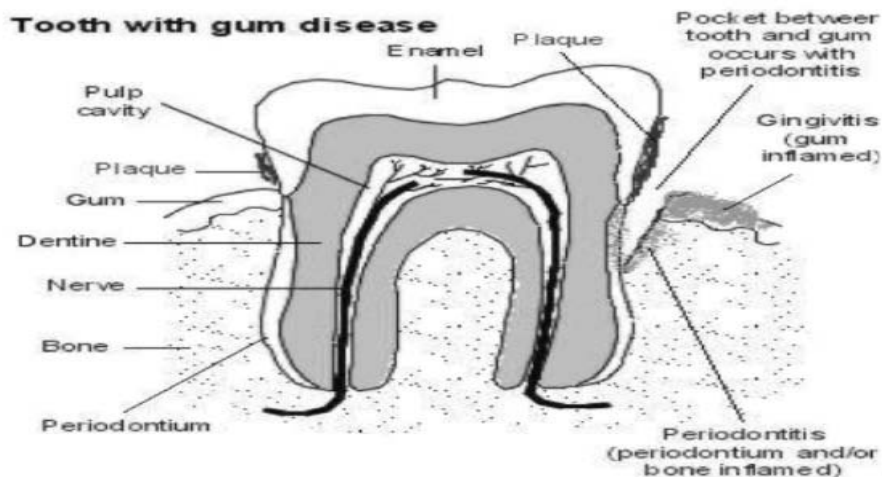


Fig. 2: Tooth with Gum Disease

Healthy periodontal tissues

It is important to understand that each of the periodontal components has its very specialized structure and that these structural characteristics directly define function. Indeed, proper functioning of the periodontium is only achieved through structural integrity and interaction between its components. Periodontal tissues include four defined structures: gingiva, cementum, alveolar bone, and the periodontal ligament.

The dentogingival junction¹¹

The dentogingival junction (gingiva facing the tooth) is an adaptation of the oral mucosa that comprises epithelial and connective tissue components. The epithelium is divided into three functional compartments—gingival, sulcular and junctional epithelium – and the connective tissue into superficial and deep compartments. The junctional epithelium plays a crucial role since it essentially seals off periodontal tissues from the oral environment. Its integrity is thus essential for maintaining a healthy periodontium.

The junctional epithelium¹²

The junctional epithelium arises from the reduced enamel epithelium as the tooth erupts into the oral cavity. It forms a collar around the cervical portion of the tooth that follows the cemento-enamel junction. The free surface of this collar constitutes the floor of the gingival sulcus. Basically, the junctional epithelium is a nondifferentiated, stratified squamous epithelium with a very high rate of cell turn over. It is thickest near the bottom of the gingival sulcus and tapers to a thickness of a few cells as it descends apically along the tooth surface. This epithelium is made up of flattened cells oriented parallel to the tooth that derive from a layer of cuboidal basal cells situated away from the tooth surface that rest on a basement membrane.

Connective tissue compartment¹³

The connective tissue supporting the junctional epithelium is structurally different from that supporting the oral gingival epithelium. The gingival connective tissue adjacent to the junctional epithelium contains an extensive vascular plexus. Inflammatory cells such as polymorphonuclear leukocytes and T-lymphocytes continually extravasate from this dense capillary and post capillary venule network, and migrate across the junctional epithelium into the gingival sulcus and eventually the oral fluid. The special nature of the junctional epithelium is believed to reflect the fact that the connective tissue supporting it is functionally different than that of the sulcular epithelium, a difference with important implications for understanding the progression of periodontal disease and the regeneration of the dentogingival junction after periodontal surgery. The sub epithelial connective tissue (lamina propria) is believed to

provide instructive signals for the normal progression of stratified squamous epithelia^{14,15}.

Cementum¹⁶

The cementum covers the dentin of the root surface of the tooth. It is histologically similar in structure to bone. It is thicker apically than coronally and is capable of both necrosis and some regeneration by cementoblasts. Both the periodontal ligament and gingiva anchor fibres into the cementum. There are basically two varieties of cementum distinguished on the basis of the presence or absence of cells within it and the origin of the collagen fibers of the matrix. As a bulk, it contains about 50% mineral and 50% organic matrix. Type I collagen is the predominant organic component, constituting up to 90% of the organic matrix. Other collagens associated with cementum include type III, a less cross linked collagen found in high concentrations during development and repair/regeneration of mineralized tissues, and type XII, a fibril associated collagen with interrupted triple helices (FACIT) that binds to type I collagen and also to noncollagenous matrix proteins. Trace amounts of other collagens, including type V, VI, and type XIV, are also found in extracts of mature cementum, however, these may be contaminants from the periodontal ligament region associated with fibres inserted into cementum. Almost all noncollagenous matrix proteins identified in cementum are also found in bone¹⁷.

Periodontal ligament¹⁸ (Figure 3)

The periodontal ligament is comprised of tough collagen fibre. It is very vascular and contains nerves, which include proprioceptive fibres as well as pain fibres (unlike the pulp). The bulk of the periodontal ligament is that soft, specialized connective tissue situated between the cementum covering the root of the tooth and the bone forming the socket wall (alveolodental ligament). It ranges in width from 0.15 to 0.38 mm, with its thinnest portion around the middle third of the root, showing a progressive decrease in thickness with age. It is a connective tissue particularly well adapted to its principal function, supporting the teeth in their sockets and at the same time permitting them to withstand the considerable forces of mastication. In addition, the periodontal ligament has the capacity to act as a sensory receptor necessary for the proper positioning of the jaws during mastication and, very importantly, it is a cell reservoir for tissue homeostasis and repair / regeneration. Similar to all other connective tissues, the periodontal ligament consists of cells and an extracellular compartment comprising collagenous and noncollagenous matrix constituents. The cells include osteoblasts and osteoclasts, fibroblasts, epithelial cell rests of Malassez, monocytes and macrophages, undifferentiated mesenchymal cells, and cementoblasts and odontoclasts. The extracellular compartment consists mainly of well defined collagen fibre bundles embedded in an amorphous background material, the ground substances.

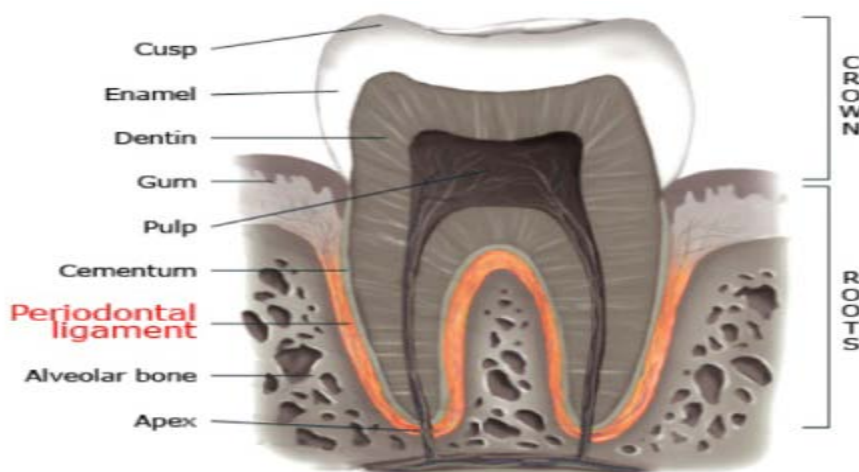


Fig. 3: Periodontal ligament

Fibroblasts: The principal cells of the periodontal ligament are fibroblasts. Although all fibroblasts look alike microscopically, heterogeneous cell populations exist between different connective tissues and also within the same connective tissue. The fibroblasts of the periodontal ligament are characterized by their rapid turnover of the extracellular compartment, in particular, collagen. Periodontal ligament fibroblasts are large cells with an extensive cytoplasm containing an abundance of organelles associated with protein synthesis and secretion¹⁸.

Epithelial cells: The epithelial cells in the periodontal ligament are remnants of HERS and known as the epithelial cell rests of Malassez. They occur close to the cementum as a cluster of cells that form an epithelial network, and seem to be more evident or abundant in furcating areas. The function of these rests is unclear but they could be involved in periodontal repair/regeneration reflecting the functional demands placed on the cells.

Undifferentiated mesenchymal cells: An important cellular constituent of the periodontal ligament is the undifferentiated mesenchymal cell, or progenitor cell. The fact that new cells are being produced for the periodontal ligament whereas cells of the ligament are in a steady state means that selective deletion of cells by apoptosis must balance the production of new cells. In periodontal wound healing, the periodontal ligament contributes cells not only for its own repair but also to restore lost bone and cementum¹⁹. Recently, cells with stem cell characteristics have been isolated from the human periodontal ligament²⁰.

Fibers: The predominant collagens of the periodontal ligament are type I, III, and XII, with individual fibrils having a relatively smaller average diameter than tendon collagen fibrils, a difference believed to reflect the relatively short half-life of ligament collagen, and hence less time for fibrillar assembly. The vast majority of collagen fibrils in the periodontal ligament are

arranged in definite and distinct fibre bundles, and these are termed principal fibers.

Noncollagenous matrix proteins: Several noncollagenous matrix proteins produced locally by resident cells or brought in by the circulation are found in the periodontal ligament, these include alkaline phosphatase²¹, proteoglycans²², and glycoprotein such as undulin, tenascin, and fibronectin²³.

Alveolar bone

The alveolar process is that bone of the jaws containing the sockets (alveoli) for the teeth. It consists of outer cortical plates (buccal, lingual, and palatal) of compact bone, a central spongiosa, and bone lining the alveolus (alveolar bone). The cortical plate and bone lining the alveolus meet at the alveolar crest. The bone lining the socket is specifically referred to as bundle bone because it provides attachment for the periodontal ligament fiber bundles.

Classification

The 1999 classification system for periodontal diseases and conditions listed seven major categories of periodontal diseases,²⁴ of which the last six are termed *destructive* periodontal disease because they are essentially irreversible. The seven categories are as follows:

1. Gingivitis
2. Chronic periodontitis
3. Aggressive periodontitis
4. Periodontitis as a manifestation of systemic disease
5. Necrotizing ulcerative gingivitis/periodontitis
6. Abscesses of the periodontium
7. Combined periodontic-endodontic lesions

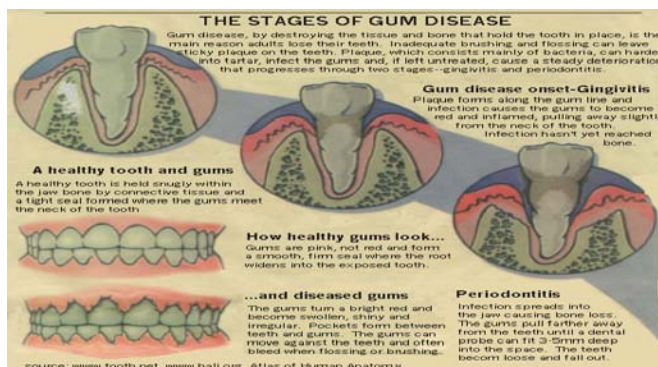


Fig. 4: The Stages of Gum Disease

Extent of periodontal disease (Figure 4)

The extent of disease refers to the proportion of the dentition affected by the disease in terms of percentage of sites. Sites are defined as the positions at which probing measurements are taken around each tooth and, generally, six probing sites around each tooth are recorded, as follows:

1. mesiobuccal
2. mid-buccal
3. distobuccal
4. mesiolingual
5. mid-lingual
6. distolingual

If up to 30% of sites in the mouth are affected, the manifestation is classification as *localized*; for more than 30%, the term *generalized* is used.

Severity

The *severity* of disease refers to the amount of periodontal ligament fibres that have been lost, termed clinical attachment loss. According to the American Academy of Periodontology, the classification of severity is as follows ²⁵.

- Mild: 1–2 mm of attachment loss
- Moderate: 3–4 mm of attachment loss
- Severe: \geq 5 mm of attachment loss

Risk Factors

- **Smoking.** Need another reason to quit smoking? Smoking is one of the most significant risk factors associated with the development of periodontitis. Additionally, smoking can lower the chances of success of some treatments
- **Hormonal changes in girls/women.** These changes can make gums more sensitive and make it easier for gingivitis to develop
- **Diabetes.** People with diabetes are at higher risk for developing infections, including periodontal disease
- **Stress.** Research shows that stress can make it more difficult for our bodies to fight infection, including periodontal disease
- **Medications.** Some drugs, such as antidepressants and some heart medicines, can affect oral health because they lessen the flow of saliva. (Saliva has a protective effect on teeth and gums.)
- **Illnesses.** Diseases like cancer or AIDS and their treatments can also affect the health of gums
- **Genetic susceptibility.** Some people are more prone to severe periodontal disease than others ²⁶.

Periodontal pathogen

The microorganisms could produce disease directly, by invasion on the tissues, or indirectly by bacterial enzymes and toxins.

In order to be a periodontal pathogen, a microorganism must have the following:

- The organism must occur at higher numbers in disease active sites than at disease inactive sites
- Elimination of the organism should arrest disease progression
- The organism should possess virulence factors relevant to the disease process

- The organism should elicit a humoral or cellular immune response
- Animal pathogenicity testing should infer disease potential ²⁷.

Aggregatibacter actinomycetemcomitans

Aggregatibacter actinomycetemcomitans (Aa) is an oral commensal found also in severe infections in the oral cavity, mainly the periodontium. *A. actinomycetemcomitans*, previously *Actinobacillus actinomycetemcomitans*, is a gram negative facultative non-motile rod. It is also associated with non-oral infections. It is one of the bacteria which might be implicated in destructive periodontal disease. Although it has been found more frequently in localized aggressive periodontitis, prevalence in any population is rather high. It has also been isolated from actinomycotic lesions (mixed infection with certain *Actinomyces* species, in particular *Actinomyces israelii*). It possesses certain virulence factors that enable it to invade tissues, such as leukotoxin ²⁸.

Porphyromonas gingivalis

*Porphyromonas gingivalis*²⁹ belongs to the phylum Bacteroidetes and is a non-motile, gram-negative, rod shaped, anaerobic pathogenic bacterium. It forms black colonies on blood agar. It is found in the oral cavity, where it is implicated in certain forms of periodontal disease, as well as the upper gastrointestinal tract, respiratory tract, and in the colon. Collagen degradation that is observed in chronic periodontal disease results in part from the collagenase enzymes of this species. In patients harbouring *Porphyromonas gingivalis* one finds high levels of specific antibody in the serum. Additionally *Porphyromonas gingivalis* has been linked to rheumatoid arthritis.

Fusobacterium nucleatum

Fusobacterium nucleatum ³⁰ is an oral bacterium, indigenous to the human oral cavity that plays a role in periodontal disease. This organism is commonly recovered from different monomicrobial and mixed infections in humans and animals. It is a key component of periodontal plaque due to its abundance and its ability to coaggregate with other species in the oral cavity. Research has emerged implicating periodontal disease caused by *F. nucleatum* with preterm births in humans.

Bacteroides forsythus

Bacteroides forsythus has been shown to be prevalent among patients with periodontitis. *Bacteroides forsythus* is one of the many species found prevalent in patients with refractory or recurrent periodontitis, and it has been particularly associated with destructive adult periodontitis.

Prevotella intermedia

Prevotella intermedia (formerly *Bacteroides intermedius*) is a gram negative obligate anaerobic pathogen involved in periodontal infections, including gingivitis and periodontitis, and often found in Acute necrotizing ulcerative gingivitis. It is commonly isolated from Dentoalveolar abscesses, where obligate anaerobes predominate. *Prevotella intermedia* use steroids as growth factors. For that reason *P. intermedia*'s number is higher in pregnant women ³¹.

Diagnostic Criteria

Diagnostic criteria include

- Clinical signs of inflammation (e.g., redness, tissue oedema)
- Gingival bleeding upon probing
- Probing depth
- Furcation involvement (based upon radiographic evidence)
- Tooth mobility
- Clinical attachment loss
- Medical and dental histories

- Periodontal risk factors (e.g., age, gender, medications, smoking, systemic disease, oral hygiene)
- Other clinical signs and symptoms (e.g., pain, ulceration, plaque, and calculus)³².

Prevention

Daily oral hygiene measures to prevent periodontal disease include:

- Brushing properly on a regular basis (at least twice daily), with the patient attempting to direct the toothbrush bristles underneath the gum-line, to help disrupt the bacterial-mycotic growth and formation of subgingival plaque.
- Flossing daily and using interdental brushes (if there is a sufficiently large space between teeth), as well as cleaning behind the last tooth, the third molar, in each quarter.
- Using an antiseptic mouthwash. Chlorhexidine gluconate based mouthwash in combination with careful oral hygiene may cure gingivitis, although they cannot reverse any attachment loss due to periodontitis.
- Using a 'soft' tooth brush to prevent damage to tooth enamel and sensitive gums.
- Using periodontal trays to maintain dentist-prescribed medications at the source of the disease. The use of trays allows the medication to stay in place long enough to penetrate the biofilms where the microorganism are found.
- Regular dental check-ups and professional teeth cleaning as required. Dental check-ups serve to monitor the person's oral hygiene methods and levels of attachment around teeth, identify any early signs of periodontitis, and monitor response to treatment.

The periodontal pocket provides an ideal environment for the growth and proliferation of anaerobic pathogenic bacteria³³. Without daily oral hygiene, periodontal disease will not be overcome, especially if the patient has a history of extensive periodontal disease. Periodontal disease and tooth loss are associated with an increased risk of cancer³⁴.

CONCLUSION

Indeed, knowledge of how tissue structure develops and how it relates to function is fundamental for understanding the disease process, and for devising effective therapeutic strategies, particularly in the case where tissue destruction, and hence a concomitant loss of function, ensues. The present chapter has been assembled with this in mind, and with the hope of providing investigators with solid bases for regenerative therapies. Periodontal disease sets in when the structure of the junctional epithelium starts to fail, an excellent example of how structure determines function. Although bacteria are essential for periodontitis to develop, the fact that it develops to variable degrees in different individuals suggests a multifactorial etiology.

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