The endo-perio lesion: a critical appraisal of the disease condition

ILAN ROTSTEIN & JAMES H. SIMON

Endodontic-periodontal lesions present challenges to the clinician as far as diagnosis and prognosis of the involved teeth are concerned. Etiologic factors such as bacteria, fungi, and viruses as well as various contributing factors such as trauma, root resorptions, perforations, and dental malformations play an important role in the development and progression of such lesions. Treatment and prognosis of endodontic-periodontal diseases vary and depend on the cause and the correct diagnosis of each specific condition. This article will appraise the interrelationship between endodontic and periodontal diseases and provide biological and clinical evidence of significance for diagnosis, prognosis, and decision-making in the treatment of these conditions.

Introduction

The dental pulp and periodontal tissues are closely related. The pulp originates from the dental papilla and the periodontal ligament from the dental follicle and is separated by Hertwig's epithelial root sheet. As the tooth matures and the root is formed, three main avenues for exchange of infectious elements and other irritants between the two compartments are created by (1) dentinal tubules, (2) lateral and accessory canals, and (3) the apical foramen. This article aims to provide a biological and clinical background to diagnosis, prognosis, and decision-making in the clinical management of these conditions.

Pathways of communications

Dentinal tubules

Exposed dentinal tubules in areas devoid of cementum may serve as communication pathways between the pulp and the periodontal ligament. Exposure of dentinal tubules may occur due to developmental defects, disease processes, or periodontal or surgical procedures. Radicular dentin tubules extend from the pulp to the cemento-dentinal junction (CDJ) (1). They run a relatively straight course. The diameter ranges

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from 1 μ m in the periphery to 3 μ m near the pulp (2). The tubular lumen decreases with age or as a response to chronic low-grade stimuli causing apposition of highly mineralized peritubular dentin. The density of dentin tubules varies from approximately 15 000 per square millimeter at the CDJ in the cervical portion of the root to 8000 near the apex, whereas at the pulpal ends the number increases to 57000 per square millimeter (2). When the cementum and enamel do not meet at the cemento-enamel junction (CEJ), these tubules remain exposed, thus creating pathways of communication between the pulp and the periodontal ligament. Cervical dentin hypersensitivity may be an effect of such a phenomenon (see further the article by Gillam & Orchardson in this volume of Endodontic Topics page 13).

Scanning electron microscopic studies have demonstrated that dentin exposure at the CEJ occurred in about 18% of teeth in general and in 25% of anterior teeth in particular (3). In addition, the same tooth may have different CEJ characteristics presenting dentin exposure on one side while the other sides are covered with cementum (4). This area becomes important in assessing the progression of endodontic pathogens, as well as the effect of root scaling and planing on cementum integrity, trauma, and bleaching-induced pathosis (5–7). Other areas of dentinal communication



Fig. 1. Non-surgical endodontic treatment of a maxillary central incisor with a lateral radiolucency. (A) Preoperative radiograph showing previously treated canal with mesial lateral lesion. (B) Tooth was retreated and the root canal filled with thermoplasticized gutta-percha. Note, lateral canal extending toward the lesion. (C) Oneyear recall shows resolution of lesion in progress.

may be through developmental grooves including both palato-gingival and apical (8).

Lateral and accessory canals

Lateral and accessory canals can be present anywhere along the root (Fig. 1). Their incidence and location have been well documented in both animal and human teeth (9–15). It is estimated that 30–40% of all teeth have lateral or accessory canals and the majority of them are found in the apical third of the root (1). DeDeus (12) found that 17% of teeth presented lateral canals in the apical third of the root, about 9% in the middle third, and less than 2% in the coronal third. However, it seems that the incidence of periodontal disease associated with lateral canals caused by irritants in the dental pulp is low. Kirkham (13), studying 1000 human teeth with extensive periodontal disease, found only 2% of lateral canals associated with the involved periodontal pocket.

Accessory canals in the furcation of molars may also be a direct pathway of communication between the pulp and the periodontium (10, 14). The incidence of accessory canals may vary from 23% to 76% (11, 12, 16). These accessory canals contain connective tissue and blood vessels that connect the circulatory system of the pulp with that of the periodontium. However, not all these canals extend the full length from the pulp chamber to the floor of the furcation (16). Seltzer et al. (17) reported that pulpal inflammation may cause inflammatory reaction in the interradicular periodontal tissues. The presence of patent accessory canals is a potential pathway for the spread of microorganisms



Fig. 2. Micrograph stained with Masson Trichrome of a maxillary lateral incisor with a necrotic pulp associated with a lateral inflammatory process in the periodontal ligament. Main canal, accessory canal, and the resultant inflammatory response in the periodontal ligament are evident. The area shows chronic inflammation with proliferating epithelium.

and their toxic byproducts from the pulp to the periodontal ligament and vice versa, resulting in an inflammatory process in the involved tissues (Fig. 2).

Apical foramen

The apical foramen is the principal route of communication between the pulp and the periodontium. Bacterial byproducts and inflammatory mediators in a diseased pulp may exit readily through the apical foramen to cause periapical pathosis. The apex is also a portal of entry of inflammatory elements from deep periodontal pockets to the pulp. Pulp inflammation or pulp necrosis extends into the periapical tissues, causing a local inflammatory response often associated with bone and root resorption.

Endodontic disease and the periodontium

When the pulp becomes inflamed/infected, it elicits an inflammatory response of the periodontal ligament at

the apical foramen and/or adjacent to openings of accessory canals (18). Noxious elements of pulpal origin including inflammatory mediators and bacterial byproducts may leach out through the apex, lateral and accessory canals, and dentinal tubules to trigger an inflammatory response in the periodontium including an early expression of antigen presentation (19). Products released are from living bacterial strains including spirochetes as well as of non-living pathogens (20–24). Fungi and viruses are also implicated (25–28). In certain cases, epithelial growth will be stimulated that will affect the integrity of the periradicular tissues (29–34).

Periodontal disease and the pulp

The effect of periodontal inflammation on the pulp is controversial and conflicting studies abound (17, 35-42). It has been suggested that periodontal disease has no effect on the pulp before it involves the apex (37). On the other hand, several studies suggested that the effect of periodontal disease on the pulp is degenerative in nature including an increase in calcifications, fibrosis, and collagen resorption, in addition to the direct inflammatory sequelae (43, 44). It appears that the pulp is usually not severly affected by periodontal disease until the periodontal tissue breakdown has opened an accessory canal to the oral environment (9). At this stage, pathogens leaking from the oral cavity through the accessory canal into the pulp may cause a chronic inflammatory reaction, followed by pulp necrosis. However, if the mircovasculature of the apical foramen remains intact, the pulp may maintain its vitality (43). The effect of periodontal treatment on the pulp is similar and scaling, curettage as well as periodontal surgery may not induce severe inflammatory changes of the pulp (45).

Blomlöf et al. (46) created defects on root surfaces of intentionally extracted monkey teeth with either open or mature apices. The canals were either infected or filled with calcium hydroxide and replanted back in their sockets. After 20 weeks, marginal epithelial downgrowth was found on the denuded dentin surface of the infected teeth. Jansson et al. (47) assessed the effect of endodontic pathogens on marginal periodontal wound healing of denuded dentinal surfaces surrounded by healthy periodontal ligament. Their results showed that in infected teeth, the defects were covered by 20% more epithelium while the noninfected teeth showed only 10% more connective tissue coverage. They concluded that pathogens in necrotic root canals may stimulate epithelial downgrowth along denuded dentin surfaces with marginal communication and thus augment periodontal disease. The same investigators (48), in a retrospective radiographic 3 years study, evaluated 175 endodontically treated single-rooted teeth of 133 patients. Patients who were more prone to periodontitis and exhibited evidence of endodontic treatment failures showed an approximately three-fold increase in marginal bone loss as compared with patients without endodontic infection. In addition, the effects of endodontic infection on periodontal probing depth and the presence of furcation involvement in mandibular molars were also investigated (49). It was found that endodontic infection in mandibular molars was associated with more attachment loss in the furca. These authors suggested that endodontic infection in molars associated with periodontal disease might enhance periodontitis progression by spreading pathogens through accessory canals and dentinal tubules. In contrast to these findings, Miyashita et al. (50) failed to observe a correlation between a reduced marginal bone support and endodontic status.

Live pathogens and infectious biofilms

Among the live pathogens encountered in a diseased pulp that can cause lesions in the periodontal tissues are bacteria, fungi, and viruses. These pathogens and their byproducts may affect the periodontium in a variety of ways and need to be eliminated during root canal treatment.

Bacteria

Bacteria play a critical role in endodontic and periodontal disease (26, 51–58). The periapical tissues become involved when bacteria invade the pulp, causing either partial or total necrosis. Kakehashi et al. (51) demonstrated the relationship between the presence of bacteria and the pulp and periapical diseases in a classic work. In this study, pulps of normal rats were exposed and left open to the oral environment. Consequently, pulp necrosis ensued, followed by periapical inflammation and periapical lesion formation. However, when the same procedure was performed in germ-free rats, not only did the pulps remain vital and relatively non-inflamed, but the exposure sites were repaired by dentin. The study demonstrated that without bacteria and their products, periapical lesions of endodontic origin do not occur. Möller et al. (53) confirmed these findings in monkeys. They found that non-infected necrotic pulp tissue did not induce periapical lesions or inflammatory reactions. However, once the pulp became infected, periapical lesions and inflammation in the apical tissues occurred. Others (52) reported similar results and suggested that pulpal infections are usually mixed by nature.

Proteolytic bacteria predominate the root canal flora, which changes over time to a more anaerobic microbiota (59, 60). Rupf et al. (61) studied the profiles of periodontal pathogens in pulpal and periodontal diseases associated with the same tooth. Specific PCR methods were used to detect Actinobacillus actinomycetemcomitans, Bacteroides forsythus, Eikenella corro-Fusobacterium nucleatum, Porphyromonas dens. gingivalis, Prevotella intermedia, and Treponema denticola. These pathogens were found in all endodontic samples and the same pathogens were found in teeth with chronic apical periodontitis and chronic adult periodontitis. It therefore appears that periodontal pathogens accompany endodontic infections and that endodontic-periodontal interrelationships are a critical pathway for both diseases.

Spirochetes are another type of microorganism associated with both endodontic and periodontal diseases. Spirochetes are usually found more frequently in the subgingival plaque than in root canals. Several studies showed a large diversity of oral treponemes present in subgingival biofilms of periodontal pockets (62–64). It has been previously proposed that the presence or absence of oral spirochetes can be used to differentiate between endodontic and periodontal abscesses (21). Currently, the presence of spirochetes in the root canal system is well documented and has been demonstrated by different identification techniques such as dark-field, electron microscopy, and biochemical identification (23, 24, 65, 66).

The differences in the incidence of spirochetes associated with endodontic disease reported by the various authors may be attributed to the different detection methods used. It has been demonstrated that the spirochete species most frequently found in root

canals are T. denticola (67, 68) and T. maltophilium (69). The main virulence factor of T. denticola includes surface-expressed proteins with cytotoxic activities such as the major surface protein and the chymotrypsin-like protease complex, extracellular or membrane-associated proteolytic and hydrolytic enzymes, and metabolites (70). This microorganism possesses an array of virulence factors associated with periodontal disease and may also participate in the pathogenesis of periradicular disease (68). T. maltophilum is a small, motile treponeme with two periplasmic flagella. Although the virulence factors of this microorganism have not yet been fully elucidated, it was proposed that the motility of T. maltophilum, caused by the rotation of its periplasmic flagella, might contribute to its pathogenicity (71). T. maltophilum was also frequently isolated from patients with rapidly progressive periodontitis (72).

L-form bacteria may also have a role in periapical disease (73). Some bacterial strains can undergo morphological transition to their L-form after exposure to certain agents, particularly penicillin (74). The L-form and the bacterium may appear individually or together and may transform from one variant to another with numerous intermediate L-form transitional stages. This may occur either spontaneously or by induction in a cyclic manner. Under certain conditions, depending on host resistance factors and bacterial virulence, the L-forms revert to their original pathogenic bacterial form and may then be responsible for acute exacerbation of chronic apical lesions (73).

Fungi (yeasts)

The presence and prevalence of fungi associated with endodontic infections are well documented (27, 75). Yeast colonization associated with periradicular pathosis has been demonstrated in untreated root caries (76, 77), dentinal tubules, (78–80), failing root canal treatments (81–84), apices of teeth with asymptomatic apical periodontitis (85), and in periapical tissues (86). Many studies reported that the prevalence of fungi in cultured samples taken from infected root canal systems varied from 0.5% to 26% in untreated root canals (76, 87–91) and 3.7% to 33% in cases of previously treated canals (76, 82, 83, 86, 92). Some, however, have demonstrated a higher prevalence of up to 55% (80, 93). The majority of the recovered fungi were *Candida albicans* (92). *C. albicans* has been detected in 21% of infected root canals using 18S rRNA-directed speciesspecific primers (90). Fungi also colonize canal walls and invade dentinal tubules (94). Other species such as *C. glabrata*, *C. guillermondii* and *C. incospicia* (92), and *Rodotorula mucilaginosa* (25) were also detected.

Factors affecting the colonization of the root canal by fungi are not fully understood. It appears, however, that among the predisposing factors of this process are immunocompromising diseases such as cancer (79), certain intracanal medicaments (76), local and systemic antibiotics (77, 95), and previous unsuccessful endodontic therapy (83, 96). It has been suggested that the reduction of specific strains of bacteria in the root canal during endodontic treatment may allow fungi overgrowth in the remaining low-nutrient environment (83, 96). Another possibility is that fungi may gain access to the root canal from the oral cavity as a result of poor asepsis during endodontic treatment or postpreparation procedures. It has been found that approximately 20% of adult periodontitis patients also harbor subgingival yeasts (97, 98). As in endodontic infections, C. albicans was also the most common species isolated (99). In addition, it has been demonstrated that the presence of fungi in root canals is directly associated with their presence in saliva (25). These findings further stress the importance of using aseptic endodontic and periodontal techniques, maintaining the integrity of dental hard tissues, and covering the tooth crown as soon as practical with a well-sealed permanent restoration in order to prevent re-infection.

Viruses

There is increasing evidence suggesting that viruses play an important role in the pathogenesis of both endodontic and periodontal disease. In patients with periodontal disease, the herpes simplex virus was frequently detected in gingival crevicular fluid and in gingival biopsies of periodontal lesions (100, 101). Human cytomegalovirus was observed in about 65% of periodontal pocket samples and in about 85% of gingival tissue samples (100). Epstein–Barr virus type I was observed in more than 40% of pocket samples and in about 80% of the gingival tissue samples (100). Gingival herpesviruses were found to be associated with increased occurrence of subgingival *P. gingivalis, B. forsythus, P. intermedia, P. nigrescens, T. denticola,* and *Actinobacillus actinomycetemcomitans,* thus suggesting their role in overgrowth of periodontal pathogenic bacteria (102).

The presence of viruses in the dental pulp was first reported in a patient with AIDS (103). DNA of HIV virus was also detected in periradicular lesions (104). However, it has not been established that HIV virus can directly cause pulpal disease. The herpes simplex virus was also studied in relation to endodontic disease. It seems, however, unlike its role in periodontal disease, that the herpes simplex virus is not associated with inflammatory pulpal lesions (105, 106).

On the other hand, recent data suggest that other common types of human viruses may be involved in pulpal disease and associated periapical pathoses. Sabeti et al. (107, 108) suggested that human cytomegalovirus and the Epstein-Barr virus play a role in the pathogenesis of symptomatic periapical lesions. It appears that active virus infection may give rise to production of an array of cytokines and chemokines with the potential to induce immunosuppression and tissue destruction (109). Herpesvirus activation in periapical inflammatory cells may impair the host defense mechanisms and give rise to overgrowth of bacteria, as seen in periodontal lesions. Herpesvirusmediated immune suppression may also be detrimental in periapical infections due to already compromised host-resistent factors and affected connective tissues in situ (110). Alterations between prolonged periods of herpesvirus latency interrupted by periods of activation may explain some burst-like symptomatic episodes of periapical disease. Frequent reactivation of periapical herpesvirus may support rapid periapical breakdown. The absence of herpesvirus infection or viral reactivation may be the reason why some periapical lesions remain clinically stable for extended periods of time (107). More research is needed to demonstrate a causal relationship of viral infections with both pulpal and periodontal disease processes.

Infectious biofilms

The majority of bacteria in virtually all natural ecosystems grow in biofilms and their growth in affected tissues is characterized by matrix-enclosed communities (111, 112). Biofilm micro-colonies are composed of approximately 15% cells (by volume) embedded in 85% matrix material (113). They are bisected by ramifying water channels that carry bulk fluid into the community by convective flow (114). The

structural composition of biofilms indicates that these communities are regulated by signals analogous to the hormones and pheromeones that regulate many cellular eukaryotic communities (113).

Biofilm formation has a developmental sequence that results in the formation of mature community of towershaped and mushroom-shaped micro-colonies, with some variation between species. The sequence of events usually involved is microbial surface attachement, cell proliferation, matrix production, and detachment (115). Biofilm formation and detachment are under the control of chemical signals that regulate and guide the formation of slime-enclosed micro-colonies and water channels (113). It has been stated that microbial biofilms constitute the most 'defensive' life strategy that can be adopted by prokaryotic cells (116). In very hostile environments such as extreme heat, acidicy, or dryness, this stationary mode of growth is inherently defensive, because bacterial cells are not swept into areas where they can be killed (113).

Infectious biofilms are difficult to detect in routine diagnostic methods and are inherently tolerant to host defenses and antibiotic therapies (115). In addition, biofilms facilitate the spread of antibiotic resistence by promoting horizontal gene transfer. They are also actively adapted to environmental stresses, such as alteration in nutritional quality, cell density, temperature, pH, and osmolarity (117). Prolonged starvation induces loss of cultivability under standard conditions, while the microorganism remains metabolically active and structurally intact (118). This is considered the main reason for the low detection rate of biofilm infections by routine culture methods. The exact role of biofilms in endodontic infections has not been well established as yet and merits further investigation (119).

Non-living pathogens

Non-living pathogens can be either extrinsic such as foreign bodies or intrinsic including a variety of tissue components.

Foreign bodies

Foreign bodies are often found to be associated with the inflammatory process of the periradicular tissues. Although endodontic and periodontal diseases are primarily associated with the presence of microorganisms, the presence of certain foreign substances in situ may explain the emergence or persistence of some apical pathoses, substances such as dentin and cementum chips (120–122), amalgam (122, 123), root canal filling materials (120, 122-124), cellulose fibers from absorbent paper points (123, 125, 126), gingival retraction cords (127), leguminous foods (128), and calculus-like deposits (129). A foreign body response may occur in any of these substances and the clinical reaction may be either acute or chronic. Therefore, clinically, such conditions may be either symptomatic or asymptomatic. Microscopically, these lesions demonstrate the presence of multinucleated giant cells surrounding the foreign material in a chronic inflammatory infiltrate. Mechanical or surgical removal of the foreign bodies is usually the treatment of choice.

Epithelial rests of Malassez

Epithelial rests of Malassez are normal constituents of both the lateral and apical periodontal ligament. The term rests is misleading in that it evokes a vision of discrete islands of epithelial cells. It has been shown that these rests are actually a fishnet-like, three-dimensional, interconnected network of epithelial cells. In many periapical lesions, the epithelium is not present and therefore presumed to have been destroyed (130). If the rests remain, they may respond to the stimuli and proliferate in an attempt to wall off the irritants coming through the apical foramen. The epithelium can be surrounded by chronic inflammation. This lesion is termed epitheliated granuloma and if not treated, the epithelium will continue to proliferate in an attempt to wall off the source of irritation communicating from the apical foramen.

The term 'bay' cyst was introduced to depict a chronic inflammatory periapical lesion that has an epithelium lining surrounding the cyst lumen, and has a direct communication with the root canal system (34) (Fig. 3). The term 'true' cyst was given to a three-dimensional, epithelium-lined cavity with no communication between the lumen and the canal system (Fig. 4). When periapical lesions are studied in relation to the root canal, a clear distinction between these two entities should be made (33, 34).

There has been some confusion regarding the diagnosis when lesions are studied only on curetted biopsy material. As the tooth is not attached to the



Fig. 3. Photomicrograph showing a bay cyst associated with a root canal that opens directly into the lumen of the lesion.

lesion, orientation to the apex is lost. Therefore, the criterion used for the diagnosis of a cyst is a strip of epithelium that appears to be lining a cavity. It is therefore apparent that curetting both a 'bay' cyst and a 'true' cyst could lead to the same microscopic diagnosis. A 'bay' cyst could be sectioned in such a way that it could resemble or give the appearance of a 'true' cyst. This distinction between a 'bay' and a 'true' cyst is important from the standpoint of healing. It may be that 'true' cysts must be surgically removed, but 'bay' cysts that communicated with the root canal may heal with nonsurgical root canal therapy. As root canal therapy can directly affect the lumen of the 'bay' cyst, the environmental change may bring about resolution of the lesion. The 'true' cyst is independent of the root canal system and therefore conventional root canal therapy may not have an effect on the 'true' cyst (34, 131). However, the incidence of 'true' cysts is probably less than 10% (34). This may explain the relatively high success rate of non-surgical root canal treatment in teeth associated with periapical lession.



Fig. 4. Photomicrograph of a true inflammatory cyst stained with Masson's Trichrome showing a three dimensional epithelial-lined lesion with no connection to the root canal system and apical foramen.

Cholesterol crystals

The presence of cholesterol crystals in apical periodontitis has been reported in histopathological findings (132–136). During processing, the cholesterol crystals are dissolved and washed away, leaving behind spaces as clefts. The reported occurrence of cholesterol clefts in periapical disease varies from 18% to 44% (132, 134, 135). It has been suggested that the crystals could be formed from cholesterol released by either disintegrating erythrocytes of stagnant blood vessels within the periapical lesion (134), lymphocytes, plasma cells, and macrophages that die in great numbers and disintegrate in chronic periapical lesions (135), or by the circulating plasma lipids (132). It is possible, however, that all of these factors may contribute to the accumulation, concentration, and crystallization of cholesterol in a periapical lesion.



Fig. 5. (A) Photomicrograph of a periapical lesion showing presence of Russell bodies. (B) Transmission electron micrograph demonstrates the round amorphous shape of these structures.

It has been suggested that accumulation of cholesterol crystals in inflamed periapical tissues in some cases might cause failure of endodontic therapy (30, 136). It seems that the macrophages and the multinucleated giant cells that congregate around cholesterol crystals are not efficient enough to destroy the crystals completely. In addition, the accumulation of macrophages and giant cells around the cholesterol clefts in the absence of other inflammatory cells, such as neutrophils, lymphocytes, and plasma cells, suggests that the cholesterol crystals induce a typical foreignbody reaction (30).

Russell bodies

Russell bodies can be found in most inflamed tissues throughout the body including the periradicular tissues (Fig. 5). These are small, spherical accumulations of an eosinophilic substance found within or near plasma cells and other lymphoid cells. The presence and occurrence of Russell bodies in oral tissues and periapical lesions is well documented (137, 138).

Studies have indicated the presence of Russell bodies in about 80% of periradicular lesions. Recently, large intracellular and extracellular Russell bodies were also found in inflammatory pulpal tissue of carious primary teeth (31). It is hypothesized that Russell bodies are caused by synthesis of excessive amounts of normal secretory protein in certain plasma cells engaged in active synthesis of immunoglobulines. The endoplasmic reticulum becomes greatly distended, thus producing large homogeneous eosinophilic inclusions (139). However, the incidence of Russell bodies, their production mechanism as well as their exact role in pulpal inflammation have not yet been fully elucidated.

Rushton hyaline bodies

The presence of Rushton hyaline bodies is a feature unique to some odontogenic cysts. Their frequency varies from 2.6% to 9.5% (140). Rushton hyaline bodies usually appear either within the epithelial lining or the cyst lumen (Fig. 6). They have a variety of morphological forms, including linear (straight or curved), irregular, rounded, and polycyclic structures, or they may appear granular (29, 140).

The exact nature of Rushton hyaline bodies is not fully understood. It has been suggested that they are keratinous in nature (132), of hematogenous origin (141), a specialized secretory product of odontogenic epithelium (142), or degenerated red blood cells (29). Some authors suggested that Rushton hyaline bodies were material left behind at the time of a previous surgical operation (143). It is not yet clear why the Rushton hyaline bodies form mostly within the epithelium.

Charcot-Leyden crystals

Charcot–Leyden crystals are naturally occurring hexagonal bipyramidal crystals derived from the intracellular granules of eosinophils and basophils (144–146). Their presence is most often associated with increased numbers of peripheral blood or tissue eosinophils in parasitic, allergic, neoplastic, and inflammatory diseases (144, 145, 147). Activated macrophages were reported to have an important role in the formation of Charcot–



Fig. 6. (A) Photomicrograph showing Rushton bodies in the epithelial lining of a periapical cyst. (B) Higher magnification demonstrating pleumorphism of these bodies.

Leyden crystals in several disease processes (148). Charcot–Leyden crystals' and damaged eosinophils, along with their granules, have been observed within macrophages (147–149). It has been proposed that after the degranulation of eosinophils, Charcot–Leyden crystals' protein could be phagocytized into acidified membrane-bound lysosomes (147). At some point, Charcot–Leyden crystals protein would begin to crystallize, forming discrete particles that increase in volume and density over time. Ultimately, these crystals would be released via phagosomal exocytosis or by piercing through the membrane of the phagosome and macrophage cytoplasm becoming free in the stromal tissue.

Recent findings support the theory that activated macrophages have a role in the formation of Charcot– Leyden crystals (32). In addition, the presence of Charcot–Leyden crystals can be detected within a periapical lesion that failed to resolve after conventional



Fig. 7. Charcot-Leyden crystals in a periapical lesion. (A) Maxillary lateral incisor with necrotic pulp and periapical lesion. (B) Nine-month after endodontic treatment the tooth is still symptomatic and the lesion is larger. Polarized light (C) and May-Grunwald-Giemsa stain (D) demonstrates the Charcot-Leyden crystals.

endodontic treatment (Fig. 7). Although the biological and pathological role of Charcot–Leyden crystals in endodontic and periodontal disease is still unknown, they may be attributed to some cases of treatment failures.

Contributing factors to endodontic lesions in the periodontium

Inadequate endodontic treatment

Proper endodontic procedures and techniques are key factors for treatment success. When assessing the retention rate of endodontically treated teeth, it has been found that nonsurgical endodontic treatment is a predictable procedure with excellent long-term prognosis (150–152). It is imperative to completely clean, shape, and obturate the canal system well in order to enhance successful outcomes. Poor endodontic treatment allows canal re-infection, which may often lead to treatment failure (153).

Endodontic failures can be treated either by orthograde or retrograde retreatment with good success rates. It seems that the success rate is similar to that of initial conventional endodontic treatment if the cause of failure was properly diagnosed and corrected (154). In recent years, retreatment techniques have improved dramatically due to use of the operating microscope and development of new armamentarium.

Coronal leakage

Coronal leakage is the term used to designate leakage of bacterial elements from the oral environment along restoration margins to the endodontic filling. Studies have indicated that this factor may be an important cause of endodontic treatment failure (155–158). Root canals may become re-contaminated by microorganisms due to delay in placement of a coronal restoration and fracture of the coronal restoration and/or the tooth (155). Madison & Wilcox (156) found that exposure of root canals to the oral environment allowed coronal leakage to occur, and in some cases along the entire length of the root canal. Ray & Trope (157) reported that defective restorations and adequate root canal fillings had a higher incidence of failures than teeth with inadequate root canal fillings and adequate restorations. Teeth in which both the root canal fillings and restorations were adequate had only 9% failure, while teeth in which both root canal fillings and restorations were defective had about 82% failure (157). Saunders & Saunders (158) showed that coronal leakage was a significant clinical problem in root-filled molars. In an *in-vitro* study, they found that packing excess gutta-percha and sealer over the floor of the pulp

chamber, after completion of root canal filling, did not provide a better seal of the root canals. It was therefore recommended that excess of gutta-percha filling should be removed to the level of the canal orifices and that the floor of the pulp chamber be protected with a wellsealed restorative material (158).

Coronal restoration is the primary barrier against coronal leakage and bacterial contamination of the root canal treatment. It has been shown that lack of coronal coverage following endodontic treatment can significantly compromise tooth prognosis (151). Therefore, it is essential that the root canal system be protected by good endodontic obturation and a well-sealed coronal restoration. Nevertheless, even popular permanent restorative materials may not always prevent coronal leakage (159). Cemented full crowns (160, 161), as well as dentin-bonded crowns (162) also leaked.

A review of the literature examined the factors associated with long-term prognosis of endodontically treated teeth (163). It was concluded that: (1) post space preparation and cementation should be performed with rubber-dam isolation, (2) the post space should be prepared with a heated plugger, (3) a minimum of 3 mm of root canal filling should remain in the preparation, (4) the post space should be irrigated and dressed as during root canal treatment, (5) leak-proof restorations should be placed as soon as possible after endodontic treatment, and (6) endodontic retreatment should be considered for teeth with a coronal seal compromised for longer than 3 months (163).

Trauma

Trauma to teeth and alveolar bone may involve the pulp and the periodontal ligament. Both tissues can be affected either directly or indirectly. Dental injuries may take on many shapes but generally can be classified as enamel fractures, crown fractures without pulp involvement, crown fractures with pulp involvement, crown-root fracture, root fracture, luxation, and avulsion (164). Treatment of traumatic dental injuries varies depending on the type of injury and it will determine pulpal and periodontal ligament healing prognosis (165–170).

Resorptions

Root resorption is a condition associated with either a physiologic or a pathologic process resulting in a loss of

dentin, cementum, and/or bone (171). Despite the extensive literature, this complex process presents some confusion, mainly because of the many classifications used. The following classification is therefore suggested: non-infective root resorption and infective root resorption.

Non-infective root resorption

This process occurs as a result of a tissular response to non-microbial stimuli in the affected tissues. It includes transient root resorption, pressure-induced root resorption, chemical-induced root resorption, and replacement resorption.

Transient root resorption

Transient root resorption, or remodeling resorption, is a reparative process that occurs in response to minor trama to the normal functioning teeth. Microscopically, small areas of cemental and dentinal resorption repaired by the cementum are seen. This phenomenon does not present a clinical problem and can only be appreciated microscopically.

Pressure-induced root resorption

Succedaneous teeth or tooth impactions can create pressure on roots causing resorption. Once the source of pressure is removed, the resorptive process stops. Similarly, expanding lesions that excert pressure, e.g. tumors or cysts, may cause root resorption. Removal of the lesion will arrest the resorptive process. This type of resorption is usually asymptomatic unless secondary infection occurs.

Iatrogenic pressure, such as excessive orthodontic movements, can also result in root resorption. Depending on their nature, these forces can cause blunting and areas of resorption along the root surfaces. The resorption will stop once the stimulus is removed.

Chemical-induced root resorption

Certain chemicals used in dentistry have the potential to cause root resorption. Clinical reports (6, 172–177) have shown that intracoronal bleaching with highly concentrated oxiding agents, such as 30–35% hydrogen peroxide, can induce root resorption. The irritating chemical may diffuse through the dentinal tubules and

when combined with heat, they are likely to cause necrosis of the cementum, inflammation of the periodontal ligament, and subsequently root resorption (7, 176, 178). The process is liable to be enhanced in the presence of bacteria (173, 179). Previous traumatic injury and young age may act as predisposing factors (172).

Replacement root resorption

Replacement root resorption, or ankylosis, occurs following extensive necrosis of the periodontal ligament with formation of bone onto a denuded area of the root surface (180). This condition is most often seen as a complication of luxation injuries, especially in avulsed teeth that have been out of their sockets under dry conditions for several hours.

Certain periodontal procedures were reported to induce replacement root resorption (181). Potential for replacement resorption was also associated with periodontal wound healing (182). Granulation tissue derived from bone or gingival connective tissue may induce root resorption and ankylosis. It seems that the inability to form connective tissue attachment on a denuded root surface is the culprit. The only cells within the periodontium that appear to have the capacity for doing so are the periodontal ligament cells (183). In general, if less than 20% of the root surface is involved, reversal of the ankylosis can occur (184). If not, ankylosed teeth are incorporated into the alveolar bone and become part of the normal remodeling process of bone. This is a gradual process and the speed by which the teeth are replaced by bone varies depending mainly on the metabolic rate of the patient. In most cases, it may take years before the root is completely resorbed.

Clinically, replacement root resorption is diagnosed when lack of mobility of the ankylosed teeth is determined (184). The teeth will also have a specific metallic sound upon percussion, and after a period of time will be in infraocclusion. Radiographically, the absence of a periodontal ligament space is evident and the ingrowth of bone into the root will present a characteristic 'moth-eaten' appearance (180).

Extracanal invasive root resorption

Extracanal invasive root resorption is a relatively uncommon form of root resorption (185–187). It is

characterized by its cervical location, and invasive nature. Invasion of the cervical region of the root is predominated by fibrovascular tissue derived from the periodontal ligament. The process progressively resorbs cementum, enamel, and dentin and later may involve the pulp space. There may be no signs or symptoms unless the resorption is associated with pulpal or periodontal infection. Secondary bacterial invasion into the pulp or periodontal ligament space will cause an inflammation of the tissues accompanied by pain. Frequently, however, the resorptive defect is

will cause an inflammation of the tissues accompanied by pain. Frequently, however, the resorptive defect is only detected by routine radiographic examination. Where the lesion is visible, the clinical features vary from a small defect at the gingival margin to a pink coronal discoloration of the tooth crown (185). Radiographically, the lesion varies from a well-delineated to irregularly boarded radiolucencies. A characteristic radiopaque line generally separates the image of the lesion from that of the root canal, because the pulp remains protected by a thin layer of predentin until late in the process (185).

The etiology of invasive cervical resorption is not fully understood. It seems, however, that potential predisposing factors are traumatic injuries, orthodontic treatment, and intracoronal bleaching with highly concentrated oxidizing agents (6, 186). Treatment of the condition presents clinical problems because the resorptive tissue is highly vascular and the resulting hemorrhage may impede visualization and compromise placement of a restoration (187). Successful treatment relies upon the complete removal or inactivation of the resorptive tissue. This is difficult to obtain in more advanced lesions characterized by a series of small channels often interconnecting with the periodontal ligament apical to the main lesion. In most cases, surgery is necessary to gain access to the resorptive defect and often may cause loss of bone and periodontal attachment. Topical application of a 90% aqueous solution of trichloracetic acid, curettage, and sealing of the defect proved successful in many cases (187). It appears that 90% trichloracetic acid has a softening effect on dental hard tissues (188). Large defects associated with advanced stages of this condition have a poor prognosis.

Replacement root resorption and extracanal invasive root resorption have been usually classified separately in the literature. However, on a closer look, they appear to be very similar. Histologically, the cementum and dentin are invaded and resorbed by non-inflammed tissue. Later, a hard bone-like tissue is deposited on the resorbed dentin surface leading to ankylosis.

Infective root resorption

This process occurs due to a vascular response to microorganisms invading the affected tissues. It may occur in both the pulp space and the periodontium and may be located either within the root canal space (internal resorption) or on the external root surface of the root (external resorption). In the pulp, this process is associated with an inflammatory response that progresses until the pulp becomes necrotic. Usually, this is also accompanied by periradicular inflammation. Practically, almost all teeth with apical periodontitis will exhibit a certain degree of root resorption (189). It can be located either on the apical or lateral aspects of the root but more frequently at the apex. During the initial stages, the resorption cannot be detected radiographically; however, it is evident in histological sections. If allowed to progress, the resorptive process can destroy the entire root. If detected and treated early, the prognosis is good. Removal of the inflammed pulpal tissue and obturation of the root canal system is the treatment of choice (190, 191).

In some cases, an internal root resorption process occurs as a result of multinucleated giant cells' activity in an inflammed pulp. The origin of this condition is not fully understood but appears to be related to chronic pulpal inflammation associated with infected coronal pulp space (192). This resorption will only take place in the presence of granulation tissue and if the odontoblastic layer and predentin are affected or lost (180, 193).

The etiology of this type of root resorption is usually trauma (192). Extreme heat was suggested as a possible cause for this type of resorption (194). Therefore, the clinician must use sufficient irrigating solutions when performing root scaling with ultrasonic devices as well as when using cauterization during surgical procedures.

Internal root resorption is usually asymptomatic and diagnosed during a routine radiographic examination. Early diagnosis is critical for the prognosis. The radiographic appearance of the resorptive defect discloses a distorted outline of the root canal. A round or an oval-shaped enlargement of the root canal space is usually found. In most cases, resorption of the adjacent bone does not occur unless large parts of the pulp become infected. Histologically, pulpal granulation tissue associated with multinucleated giant cells and coronal pulp necrosis is commonly found. When diagnosed at an early stage, endodontic treatment of such lesions is usually uneventful and the prognosis is excellent.

Perforations

Root perforations are undesirable clinical complications that may lead to periodontal lesions. When root perforation occurs, communications between the root canal system and either peri-radicular tissues or the oral cavity may often reduce the prognosis of treatment. Root perforations may result from extensive carious lesions, resorption, or from operator error occurring during root canal instrumentation or post preparation (195, 196).

Treatment prognosis of root perforations depends on the size, location, time of diagnosis and treatment, degree of periodontal damage as well as the sealing ability and biocompatibility of the repair material (197). It has been recognized that treatment success depends mainly on immediate sealing of the perforation and appropriate infection control. Several materials have been recommended to seal root perforations that included, among others, MTA, Super EBA, Cavit, IRM, glass ionomer cements, composites, and amalgam (198–202). Today, MTA is most widely used (see further the article by Tsesis & Fuss in this volume of *Endodontic Topics* page 95).

An excellent and conservative treatment modality for perforations, root resorptions, and certain root fractures is controlled root extrusion (203). The procedure has good prognosis and a low risk of relapse and its versatility has been demonstrated in multiple clinical situations (204–206). It can be performed either immediately or over a few weeks' period depending on each individual case. The goal of controlled root extrusion is to modify the soft tissues and bone and is therefore used to correct gingival discrepancies and osseous defects of periodontally involved teeth (204). It is also used in the management of nonrestorable teeth.

The objective of forced eruption in prosthetically compromised endodontically treated teeth is to allow the restoration of subcrestal defect by elevating the defect to a point where access is no longer a problem (207). In all cases, the epithelial attachment remains at the CEJ level. Forced eruption also presents a good alternative to crown lengthening as it prevents esthetic alterations and unnecessary reduction of bony support of adjacent teeth.

Developmental malformations

Teeth with developmental malformations tend to fail to respond to treatment when they are directly associated with an invagination or a vertical developmental radicular groove. Such conditions can lead to an untreatable periodontal condition. These grooves usually begin in the central fossa of maxillary central and lateral incisors crossing over the cingulum, and continuing apically down the root for varying distances. Such a groove is probably the result of an attempt of the tooth germ to form another root. As long as the epithelial attachment remains intact, the periodontium remains healthy. However, once this attachment is breached and the groove becomes contaminated, a self-sustaining infrabony pocket can be formed along its entire lengh. This fissure-like channel provides a nidus for accumulation of bacterial biofilm and an avenue for the progression of periodontal disease that may also affect the pulp. Radiographically, the area of bone destruction follows the course of the groove.

From the diagnosis standpoint, the patient may present symptoms of a periodontal abscess or a variety of asymptomatic endodontic conditions. If the condition is purely periodontal, it can be diagnosed by visually following the groove to the gingival margin and by probing the depth of the pocket, which is usually tubular in form and localized to this one area, as opposed to a more generalized periodontal problem. The tooth will respond to pulp-testing procedures. Bone destruction that vertically follows the groove may be apparent radiographically. If this condition is also associated with an endodontic disease, the patient may present clinically with any of the spectrum of endodontic symptoms.

The prognosis of root canal treatment in such cases is guarded, depending upon the apical extent of the groove. The clinician must look for the groove as it may have been altered by a previous access opening or restoration placed in the access cavity. The appearance of a teardrop-shaped area on the radiograph should immediately arouse suspicion. The developmental groove may actually be visible on the radiograph. If so, it will appear as a dark vertical line. This condition must be differentiated from a vertical fracture, which may give a similar radiographic appearance.

Treatment consists of burring out the groove, placing bone substitutes, and surgical management of the soft tissues and underlying bone. Clinical case using Emdogain as a treatment adjunct was recently described (208). Radicular grooves are self-sustaining infrabony pockets and therefore scaling and root planing will not suffice. Although the acute nature of the problem may be alleviated initially, the source of the chronic or acute inflammation must be eradicated by a surgical approach. Occasionally, the tooth needs to be extracted due to poor prognosis.

Differential diagnosis considerations

For differential diagnostic purposes, the so-called 'endo-perio lesions' are best classified as endodontic, periodontal, or a combined diseases (209). They can also be classified by treatment depending on whether endodontic, periodontal, or combined treatment modalities are necessary. They include: (1) primary endodontic diseases, (2) primary periodontal diseases, and (3) combined diseases. The combined diseases include: (1) primary endodontic disease with secondary periodontal involvement, (2) primary periodontal disease with secondary endodontic involvement, and (3) true combined diseases.

This classification is based on the theoretic pathways explaining how these radiographic lesions are formed. By understanding the pathogenesis, the clinician can then suggest an appropriate course of treatment and assess the prognosis. Once the lesions progress to their final involvement, they give a similar radiographic picture and the differential diagnosis becomes more challenging.

Primary endodontic diseases

An acute exacerbation of a chronic apical lesion in a tooth with a necrotic pulp may drain coronally through the periodontal ligament into the gingival sulcus. This condition may mimic clinically the presence of a periodontal abscess. In reality, it is a sinus tract from pulpal origin that opens through the periodontal ligament area. For diagnosis purposes, it is essential for the clinician to insert a gutta-percha cone, or another tracking instrument, into the sinus tract and to take one or more radiographs to determine the origin of the lesion. When the pocket is probed, it is narrow and lacks width. A similar situation occurs where drainage from the apex of a molar tooth extends coronally into the furcation area. This may also occur in the presence of lateral canals extending from a necrotic pulp into the furcation area.

Primary endodontic diseases usually heal following root canal treatment. The sinus tract extending into the gingival sulcus or furcation area disappears at an early stage once the affected pulp has been removed and the root canals well cleaned, shaped, and obturated (Fig. 8).

Primary periodontal diseases

These lesions are caused primarily by periodontal pathogens. In this process, chronic marginal periodontitis progresses apically along the root surface. In most cases, pulp-tests indicate a clinically normal pulpal reaction (Fig. 9). There is frequently an accumulation of plaque and calculus and the pockets are wider.

The prognosis depends upon the stage of periodontal disease and the efficacy of periodontal treatment (see the article by Wennström & Tomasi in this volume of



Fig. 8. Primary endodontic disease in a mandibular first molar with a necrotic pulp. (A) Preoperative radiograph showing periradicular radiolucency associated with the distal root. (B) Clinically, a deep narrow buccal periodontal defect can be probed. (C) One-year after root canal therapy, resolution of the periradicular bone lesion is evident. (D) Clinically, the buccal defect healed and pocket probing depth is normal.



Fig. 9. Primary periodontal lesion simulating an endodontic lesion. (A) Radiograph of mandibular first molar showing periradicular radiolucency and periapical resorption. (B) Lingual view of the affected tooth. Note, gingival swelling and evidence of periodontal disease. In addition, an occulsal filling is present close to the pulp chamber. Inspite of the clinical and radiographic picture, the pulp responded normal to vitality testing procedures indicating the radiolucency, resorption and gingival swelling are of periodontal origin.



Fig. 10. Primary periodontal disease in a maxillary second premolar (A) Radiograph showing alveolar bone loss and a periapical radiolucency. Clinically, a deep narrow pocket was found at the mesial aspect of the root. There was no evidence of caries and the tooth responded normally to pulp sensitivity tests. (B) Radiograph showing pocket tracking with gutta-percha cone to the apical area. It was decide to extract the tooth. (C) Clinical view of the extracted tooth with the attached lesion. Note a deep mesial radicular development groove. (D) Photomicrograph of the apex of the tooth with the attached lesion. (G) Histologic section of the pulp chamber shows uninflammed pulp tissue.

Endodontic Topics page 3). The clinician must also be aware of the radiographic appearance of periodontal disease associated with developmental radicular malformations (Fig. 10).

Combined diseases

Primary endodontic disease with secondary periodontal involvement

If after a period of time a suppurating primary endodontic disease remains untreated, it may then become secondarily involved with marginal periodontal breakdown. Plaque forms at the gingival margin of the sinus tract and leads to marginal periodontitis. When plaque or calculus is present, the treatment and prognosis of the tooth are different from those of teeth involved with only primary endodontic disease. The tooth now requires both endodontic and periodontal treatments. If the endodontic treatment is adequate, the prognosis depends on the severity of the marginal periodontal damage and the efficacy of periodontal treatment. With endodontic treatment alone, only part of the lesion will heal to the level of the secondary periodontal lesion. In general, healing of the tissues damaged by suppuration from the pulp can be anticipated.

Primary endodontic lesions with secondary periodontal involvement may also occur as a result of root perforation during root canal treatment, or where pins or posts have been misplaced during coronal restoration. Symptoms may be acute, with periodontal abscess formation associated with pain, swelling, pus exudate, pocket formation, and tooth mobility. A more chronic response may sometimes occur without pain, and involves the sudden appearance of a pocket with bleeding on probing or exudation of pus.

When the root perforation is situated close to the alveolar crest, it may be possible to raise a flap and repair the defect with an appropriate filling material. In deeper perforations, or in the roof of the furcation, immediate repair of the perforation has a better prognosis than management of an infected one. It has been shown that the use of mineral trioxide aggregate in such cases may enhance cemental healing following immediate perforation repair (210).

Root fractures may also present as primary endodontic lesions with secondary periodontal involvement. These typically occur on root-treated teeth often with post and crowns. The signs may range from a local deepening of a periodontal pocket, to more acute periodontal abscess formation. Root fractures have also become an increasing problem with molar teeth that have been treated by root resection (211, 212).

Primary periodontal disease with secondary endodontic involvement

The apical progression of a periodontal pocket may continue until the apical tissues are involved. In this case, the pulp may become necrotic as a result of infection entering via lateral canals or the apical foramen. In singlerooted teeth, the prognosis is usually poor. In molar teeth, the prognosis may be better. As not all the roots may undergo the same loss of supporting tissues, root resection can be considered as a treatment alternative.

The effect of progressive periodontitis on the vitality of the pulp is controversial (40, 41, 43). As long as the neuro-vascular supply of the pulp remains intact, prospects for survival are good. If lost to periodontal disease, pulpal necrosis is about to occur (43). In these cases, bacteria originating from the periodontal pocket are the source of root canal infection. A strong correlation between the presence of microorganisms in root canals and their presence in periodontal pockets of advanced periodontitis has been demonstrated, indicating that similar pathogens may be involved in both diseases (213, 214).

The treatment of periodontal disease can also lead to secondary endodontic involvement. Lateral canals and dentinal tubules may be opened to the oral environment by curettage, scaling, or surgical flap procedures. It is possible for a blood vessel within a lateral canal to be severed by a curette and for microorganisms to be pushed into the area during treatment, thus resulting in pulp inflammation and necrosis (Fig. 11).

True combined diseases

True combined endodontic-periodontal disease occurs with less frequency. It is formed when an endodontic



Fig. 11. Primary periodontal disease with secondary endodontic involvement in a maxillary premolar. (A) Radiograph showing bone loss in one third of the root and separate periapical radiolucency. The crown was intact but pulp sensitivity tests were negative and the pulp was necrotic on entry. (B) Radiograph taken immediately after root canal therapy showing sealer in lateral canal that was exposed due to the bone loss.



Fig. 12. True combined endodontic-periodontal disease in a mandibular first molar. Radiograph showing separate progression of endodontic disease and periodontal disease. The tooth remained untreated and consequently the two lesions joined together.



Fig. 13. True combined endodontic-periodontal disease. (A) Radiograph showing bone loss in two thirds of the root with calculus present and separate periapical radiolucency. (B) Clinical examination revealed coronal color change of the tooth involved and pus exuding from the gingival crevis. Pulp sensitivity tests were negative.

disease progressing coronally joins with an infected periodontal pocket progressing apically (17, 215). The degree of attachment loss in this type of lesion is invariably large and the prognosis is guarded (Fig. 12). This is particularly true in single-rooted teeth (Fig. 13). In molar teeth, root resection can be considered as a treatment alternative if not all roots are severely involved. Sometimes, supplementary surgical procedures are necessary. In most cases, periapical healing may be anticipated following successful endodontic treatment. The periodontal tissues, however, may not respond well to treatment and will depend on the severity of the combined disease.

The radiographic appearance of combined endodontic-periodontal disease may be similar to that of a vertically fractured tooth. A fracture that has invaded the pulp space, with resultant necrosis, may also be labeled a true combined lesion and yet not be amenable to successful treatment. If a sinus tract is present, it may be necessary to raise a flap to determine the etiology of the lesion (see also the article by Tamse in this volume of *Endodontic Topics* page 84).

Treatment appraisal and prognosis

Treatment appraisal and prognosis depend primarily on the diagnosis of the specific endodontic and/or periodontal disease. The main factors to consider for treatment decision-making are pulp vitality and type and extent of the periodontal defect. Diagnosis of primary endodontic disease and primary periodontal disease usually presents no clinical difficulty. In primary endodontic disease, the pulp is infected and non-vital. On the other hand, in a tooth with primary periodontal disease, the pulp is vital and responsive to testing. However, primary endodontic disease with secondary periodontal involvement, primary periodontal disease with secondary endodontic involvement, or true combine diseases are clinically and radiographically very similar. If a lesion is diagnosed and treated as a primarily endodontic disease due to lack of evidence of marginal periodontitis, and there is soft-tissue healing on clinical probing and bone healing on a recall radiogragh, a valid retrospective diagnosis can then be made. The degree of healing that has taken place following root canal treatment will determine the retrospective classification. In the absence of adequate healing, further periodontal treatment may be indicated.

The prognosis and treatment of each endodonticperiodontal disease type varies. Primary endodontic disease should only be treated by endodontic therapy. Good prognosis is to be expected if treatment is carried out properly with a focus on infection control. Primary periodontal disease should only be treated by periodontal therapy. In this case, the prognosis depends on the severity of the periodontal disease and the patient response. Primary endodontic disease with secondary periodontal involvement should first be treated with endodontic therapy. Treatment results should be evaluated in 2-3 months and only then periodontal treatment should be considered. This sequence of treatment allows sufficient time for initial tissue healing and better assessment of the periodontal condition (15, 216). It also reduces the potential risk of introducing bacteria and their byproducts during the initial phase of healing. In this regard, it was suggested that aggressive removal of the periodontal ligament and underlying cementum during interim endodontic therapy may

adversely affect periodontal healing (217). Areas of the roots that were not aggressively treated showed unremarkable healing (217). Consequently, the prognosis for treatment of primary endodontic disease with secondary periodontal involvement depends primarily on the severity of periodontal involvement, periodontal treatment, and patient response.

Primary periodontal disease with secondary endodontic involvement and true combined endodonticperiodontal diseases require both endodontic and periodontal therapies. It has been suggested that intrapulpal infection tends to promote marginal epithelial downgrowth along a denuded dentin surface (46). Additionally, experimentally induced periodontal defects in infected teeth were associated with 20% more epithelium than non-infected teeth (22). Non-infected teeth showed 10% more connective tissue coverage than infected teeth (22). The prognosis of primary periodontal disease with secondary endodontic involvement and true combined diseases depends primarily upon severity of the periodontal disease and periodontal tissues response to treatment.

True combined diseases usually have a more guarded prognosis. In general, assuming the endodontic therapy is adequate, what is of endodontic origin will heal. Thus, the prognosis of combined diseases rests with the efficacy of periodontal therapy.

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