REVIEW

Aetiology of root canal treatment failure: why well-treated teeth can fail

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Abstract

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Literature review Root canal treatment usually fails when the treatment is carried out inadequately. However, there are some cases in which the treatment has followed the highest standards yet still results in failure. In most of the cases, the endodontic failure results from persistent or secondary intraradicular infec-

tion. Extraradicular infections may also be implicated in the failure of some cases. In addition, it has been claimed that a few cases can fail because of intrinsic or extrinsic nonmicrobial factors. The purpose of this paper is to discuss the aetiology of the failure of root canal treatment, particularly in cases of well-treated root canals. Indications for the treatment of endodontic failures are also discussed.

Keywords: aetiology, endodontic failure, treatment.

Introduction

Root canal treatment usually fails when treatment falls short of acceptable standards (Seltzer *et al.* 1963, Engström *et al.* 1964, Sjögren 1996, Sundqvist *et al.* 1998). The reason many teeth do not respond to root canal treatment is because of procedural errors that prevent the control and prevention of intracanal endodontic infection (Lopes & Siqueira 1999). Undoubtedly, the major factors associated with endodontic failure are the persistence of microbial infection in the root canal system and/or the periradicular area (Nair *et al.* 1990a, Lin *et al.* 1992). The clinician is often misled by the notion that procedural errors, such as broken instruments, perforations, overfilling, underfilling, ledges and so on are the direct cause of endodontic failure. In most cases, procedural errors do not jeopardize the outcome of endodontic treatment unless a concomitant infection is present. In truth, a procedural accident often impedes or makes it impossible to accomplish appropriate intracanal procedures. Thus, there is potential for failure

of root canal treatment when a procedural accident occurs during the treatment of infected teeth.

Nevertheless, there are some cases in which the treatment has followed the highest technical standards and yet failure results. Scientific evidence indicates that some factors may be associated with the unsatisfactory outcome of well-treated cases. They include microbial factors, comprising extraradicular and/or intraradicular infections, and intrinsic or extrinsic nonmicrobial factors (Nair *et al.* 1990a, Nair *et al.* 1990b, Lin *et al.* 1992, Nair *et al.* 1993, Sjögren 1996, Sundqvist & Figdor 1998, Lopes & Siqueira 1999, Nair *et al.* 1999).

The purpose of this paper is to discuss the probable reasons for the failure of root canal treatment, particularly in well-treated teeth.

Microbial factors

Intraradicular infection

Microorganisms colonizing the root canal system play an essential role in the pathogenesis of periradicular lesions (Fig. 1). Kakehashi *et al.* (1965) exposed the dental pulps of conventional and germ-free rats to the oral cavity and reported that pulp necrosis and

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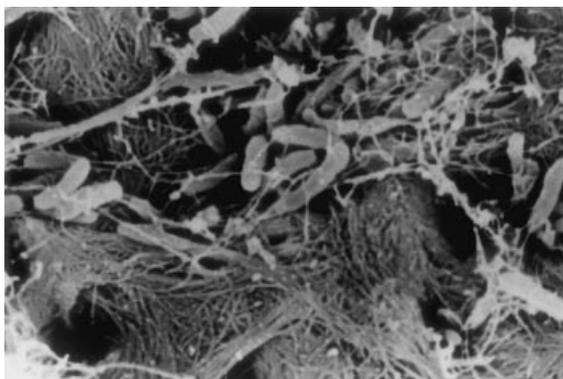
Figure 1 Scanning electron micrograph of bacterial cells colonizing the root canal wall. Bacteria infecting the root canal system are the major aetiological agents of periradicular disease (original magnification ×4500).

periradicular lesions developed only in conventional rats with an oral microbiota. In a study of monkey teeth, Möller *et al.* (1981) demonstrated that only devitalized pulps that were infected induced periradicular lesions, whereas devitalized and uninfected pulps showed absence of pathological changes in the periradicular tissues. Sundqvist (1976) confirmed the important role of bacteria in periradicular lesions in a study using human teeth, in which bacteria were only found in root canals of pulpless teeth with periradicular bone destruction.

The chances of a favourable outcome with root canal treatment are significantly higher if infection is eradicated effectively before the root canal system is obturated. However, if microorganisms persist in the root canal at the time of root filling or if they penetrate into the canal after filling, there is a higher risk that the treatment will fail (Byström *et al.* 1987, Sjögren *et al.* 1997). How high the risk of reinfection will be is dependent on the quality of the root filling and the coronal seal (Saunders & Saunders 1994). Nonetheless, in all cases where viable bacteria remain in the root canal system there is a constant risk that they may perpetuate periradicular inflammation.

In most cases, failure of endodontic treatment is a result of microorganisms persisting in the apical portion of the root canal system, even in well-treated teeth. Studies have demonstrated that part of the root canal space often remains untouched during chemomechanical preparation, regardless of the technique and instruments employed (Lin *et al.* 1991, Siqueira *et al.* 1997). Untouched areas may contain bacteria and necrotic

tissue substrate even though the root canal filling appears to be radiographically adequate (Nair *et al.* 1990a, Lin *et al.* 1991). Indeed, a radiograph of a seemingly well-treated root canal does not necessarily ensure the complete cleanliness and/or filling of the root canal system (Kersten *et al.* 1987).

Environmental influences operate in the root canal system during treatment, allowing certain microorganisms to survive and, depending on several factors, induce failure. Such influences are affected by intracanal disinfection measures (chemomechanical preparation and intracanal medication) and the low availability of nutrients within a well-treated root canal. To survive in the root-filled canal, microorganisms must withstand intracanal disinfecting measures and adapt to an environment in which there are few available nutrients. Therefore, the few microbial species that have such ability may be involved in the failure of root canal treatment.

Bacteria located in areas such as isthmuses, ramifications, deltas, irregularities and dentinal tubules may sometimes be unaffected by endodontic disinfection procedures (Lin *et al.* 1991, Siqueira *et al.* 1996, Siqueira & Uzeda 1996). It is probable that the supply of nutrients to bacteria located in ramifications and deltas will remain unaltered after root canal therapy. Nonetheless, bacteria present in areas such as dentinal tubules and isthmuses may have a drastically reduced substrate. In such anatomical regions, bacteria entombed by the root filling usually die or are prevented from gaining access to the periradicular tissues. Even interred, some bacterial species will probably survive for relatively long periods, deriving residues of nutrients from tissue remnants and dead cells. If the root canal filling fails to provide a complete seal, seepage of tissue fluids can provide substrate for bacterial growth. If growing bacteria reach a significant number and gain access to the periradicular lesion, they can continue to inflame the periradicular tissues. The fact that studies have reported the occurrence of viable microbial cells in treated teeth with a persistent periradicular lesion indicates that microorganisms derive nutrition, presumably from tissue fluid which can seep into the root canal space (Sjögren 1996, Sundqvist *et al.* 1998, Molander *et al.* 1998).

The ability to survive in such conditions is important for most bacteria because periods of starvation are commonly experienced. Several regulatory systems play essential roles in the ability of bacteria to withstand nutrient depletion. These systems are under the control of determined genes, whose transcription is activated under conditions of starvation. For instance, under conditions of nitrogen starvation, the activation of the

Ntr gene system enables bacteria that require ammonia as a nitrogen source to scavenge even small traces of ammonia. Under high concentration of ammonia, the *Ntr* gene system is uncoupled. Some facultative bacteria may activate the *Arc* system (*aerobic respiration regulatory*), composed of the *arc*A and *arc*B genes, under conditions of low concentrations of molecular oxygen. As a consequence, metabolic pathways are activated, which permit the utilization of alternate terminal electron acceptors for respiratory metabolism so that a shift can occur from aerobic to anaerobic metabolism. Under low concentrations of glucose, some bacteria can activate the catabolite repressor system, under control of the genes *cya* (adenylate cyclase) and *crp* (catabolite repressor protein), which induce the synthesis of enzymes for the utilization of various other organic carbon sources. Under conditions of phosphate starvation triggered by low concentrations of inorganic phosphate, cells turn on genes for utilization of organic phosphate compounds and for the scavenging of trace amounts of inorganic phosphate (Atlas 1997).

Depending on the availability of nutrients within the root canal system and the ability to survive in conditions with low availability of nutrients, the remaining microorganisms may either die or remain viable. In such cases, proliferation may be impeded or reduced. Failure of endodontic treatment attributed to remaining microorganisms will only occur if they possess pathogenicity, reach sufficient numbers, and gain access to the periradicular tissues to induce or maintain periradicular disease.

The microbiota associated with failed cases differs markedly from that reported in untreated teeth (primary root canal infection). Whereas the latter is typically a mixed infection, in which gram-negative anaerobic rods are dominant, the former is usually composed of one or a few bacterial species, generally gram-positive bacteria, with no apparent predominance of facultatives or anaerobes. Möller (1966), after examining failed cases, reported a mean of 1.6 bacterial species per root canal. Anaerobic bacteria corresponded to 51% of the isolates. *Enterococcus faecalis* was found in 29% of the cases. Sundqvist *et al.* (1998) observed a mean of 1.3 bacterial species per canal and 42% of the recovered strains were anaerobic bacteria. *E. faecalis* was detected in 38% of the infected root canals. Whilst this facultative bacteria is restricted to a few cases of primary root canal infections, usually in low numbers, it is frequently isolated from secondary and/or persistent root canal infections, usually as the single species of microorganism. *E. faecalis* strains have been demonstrated to be extremely resistant to several medicaments, including calcium hydroxide (Jett *et al.* 1994, Siqueira & Uzeda 1996, Siqueira & Lopes 1999). Therefore, when *E. faecalis* is established in the root canal, its eradication by conventional means may be extremely difficult (Molander *et al.* 1998).

Yeast-like microorganisms have also been found in root canals of obturated teeth in which treatment has failed (Nair *et al.* 1990a). This suggests that they may be therapy-resistant. In fact, it has been demonstrated that *Candida* spp. are resistant to some medicaments commonly used in endodontics (Waltimo *et al.* 1999).

The microbiota associated with poorly treated teeth is more likely to contain a greater number of microbial species, predominated by anaerobes, and be similar to that found in untreated teeth (primary infections) (Sundqvist *et al.* 1998, Sundqvist & Figdor 1998). This probably occurs because the microorganisms causing the initial infection persisted in the canal after inadequate cleaning of the root canal system.

Extraradicular infection

The development of periradicular lesions creates a barrier within the body to prevent further spread of microorganisms. Bone tissue is resorbed and substituted by a granulomatous tissue containing defence elements, such as cells (phagocytes) and molecules (antibodies and complement molecules) (Siqueira 1997). A dense wall composed of polymorphonuclear leucocytes, or less frequently an epithelial plug, is usually present at the apical foramen, blocking the egress of microorganisms into the periradicular tissues (Nair 1987) (Fig. 2). Very few endodontopathogens can advance through such barriers. However, microbial products can diffuse through these defence barriers and are able to induce or perpetuate periradicular pathosis.

Recently, considerable interest has been generated regarding the potential role of extraradicular persistent microorganisms in the failure of the root canal treatment. Cultural and microscopic studies have reported the occurrence of extraradicular infections in both treated and untreated root canals (Tronstad *et al.* 1987, Tronstad *et al.* 1990, Iwu *et al.* 1990, Wayman *et al.* 1992, Lomçali *et al.* 1996, Siqueira & Venturim 1997). Since microorganisms established in the periradicular tissues are inaccessible to endodontic disinfection procedures, extraradicular infection may be a factor in the failure of endodontic therapy.

Pathogens have developed mechanisms that allow them to survive in an inhospitable environment.
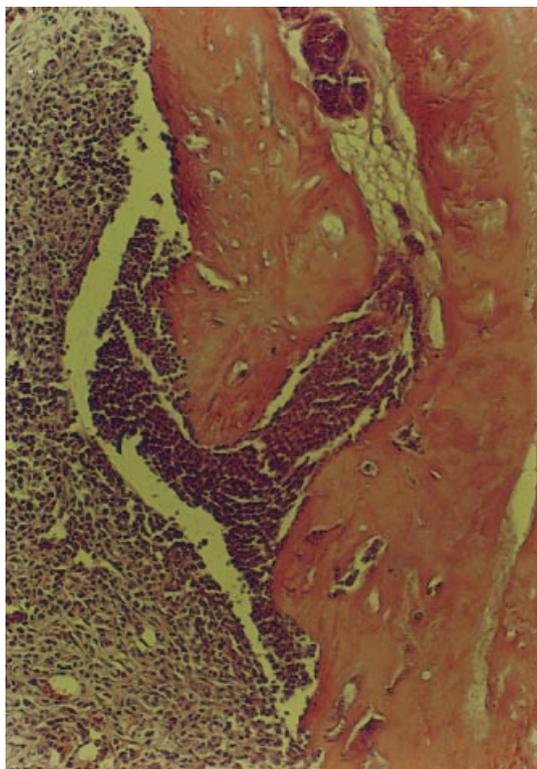
Figure 2 Host defence against endodontic infection. A dense wall composed of defence cells is observed at the apical foramen of this rat tooth associated with a periradicular lesion (original magnification ×40).

Figure 3 Scanning electron micrograph of bacterial cells arranged in a biofilm (original magnification ×3400). When organized in biofilms, microorganisms may be more resistant to both antimicrobial agents and host defence mechanisms, causing disease that is difficult to treat.

Therefore, they can escape from the action of defence cells and molecules by defending themselves against the action of the complement system, avoiding destruction by phagocytes, causing immunosuppression, changing antigenic coats, and inducing proteolysis of antibody molecules (Siqueira 1997). Nevertheless, few oral microorganisms have the ability to overcome these host defence mechanisms and thereby induce an extraradicular infection. It is currently recognized that some oral microorganisms, such as *Actinomyces* spp. and *Propionibacterium propionicum,* may be implicated in extraradicular infections (Sundqvist & Reuterving 1980, Nair 1984, Happonen 1986, Sjögren *et al.* 1988, Sakellariou 1996).

Probably, one of the most significant mechanisms of evasion from the host defence system is the microbial arrangement in a biofilm. A biofilm can be defined as a microbial population attached to an organic or inorganic substrate, surrounded by microbial extracellular products, which form an intermicrobial matrix (Costerton *et al.*
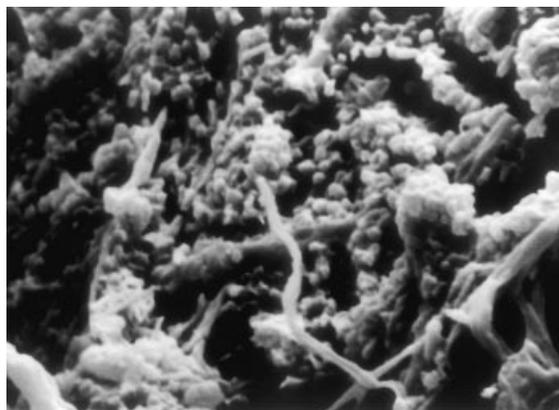
1987, Siqueira & Lopes 1998) (Fig. 3). Organized in biofilms, microorganisms show higher resistance to both antimicrobial agents and host defence mechanisms when compared with planktonic cells (Costerton *et al.* 1987, 1994, Gilbert *et al.* 1997). By examining teeth refractory to root canal treatment, Tronstad *et al.* (1990) reported the occurrence of bacterial biofilms adjacent to the apical foramen and bacterial colonies located inside periradicular granulomas. These findings suggest that bacterial organization in biofilms permits the evasion from host defenses and thereby facilitates the persistence of periradicular lesions.

Nonetheless, a low incidence of periradicular biofilms in untreated teeth with periradicular lesions (4% of the cases) has been found (Siqueira & Lopes, 2001). This finding indicated that the periradicular biofilm may occur, but in a small proportion of cases, and consequently was responsible for only a low percentage of failed cases.

The major consideration regarding treatment of periradicular biofilms is that the clinician cannot detect a biofilm in any particular clinical case. Theoretically, in a therapy-resistant clinical case a microbiological sample could inform the clinician if the root canal is bacteria free or if there are persistent intracanal microorganisms. Once root canal samples yield negative cultures, the canal is obturated. If subsequent healing does not occur, then one may suspect extraradicular infection. However, it should be emphasized that microorganisms may have been present within the root canal system but have

escaped detection in the samples that were taken. This is particularly true in retreatment cases, where microbial sampling from previously filled root canals is difficult to carry out.

It is well known that intracanal disinfection procedures or systemically administrated antibiotics can not easily affect bacteria located outside the apical foramen. The placement of endodontic medicaments into the periradicular tissues in order to eliminate microorganisms and to decompose periradicular biofilms does not appear to be an adequate procedure. First, as discussed, it is currently difficult or even impossible to clinically diagnose extraradicular infections. Secondly, most endodontic medicaments are cytotoxic and/or may have their antimicrobial effects neutralized after apical extrusion. The development of a nonsurgical strategy to combat biofilms appears questionable. Therefore, intransigent extraradicular infections, if present, must be treated by means of periradicular surgery.

Microbial involvement in special situations

Overfilling

It has been claimed that the success rate of the root canal treatment is decreased in cases of overfilling (Strindberg 1956, Engström *et al.* 1964). The toxicity of root canal filling materials has been considered to play an important role in this regard (Muruzábal *et al.* 1966). Conversely, it has been reported that the apical extent of root canal fillings has no correlation with treatment failure (Lin *et al.* 1992). Most of the materials used in root canal obturation are either biocompatible or show cytotoxicity only prior to setting (Barbosa *et al.* 1993, Spangberg 1998, Lopes & Siqueira 1999). Apart from the paraformaldehyde-containing materials, sealer toxicity is significantly reduced or even eliminated after setting. Therefore, it is highly improbable that most of the contemporary endodontic materials are able to maintain a periradicular inflammation in the absence of a concomitant endodontic infection. This statement is reinforced by the high success rate of treatment in teeth without periradicular lesions even in cases of overfilling (Lin *et al.* 1992, Sjögren *et al.* 1997). Initially, microorganisms may be either absent or present in low numbers in these cases (Sundqvist 1976, Siqueira 1997). Obviously, overfilling should be prevented as often as possible since undesirable postoperative complications such as flare-ups can develop – usually when a large amount of filling material extrudes through the apical

Figure 4 Scanning electron micrograph of extruded gutta-percha cone in an overfilled tooth. Note the voids between the cone and the root canal walls (original magnification ×90).

foramen. In truth, the role of concomitant infection as an actual cause of failure of overfilled root canals emphasizes the need to properly prevent and control endodontic infection.

Thus, failure associated with overfilled teeth is usually caused by a concomitant intraradicular and/or extraradicular infection. In most cases, apical sealing is inadequate in overfilled root canals (Fig. 4). Percolation of tissue fluids rich in glycoproteins into the root canal system can supply substrate to residual microorganisms, which can proliferate and reach sufficient number to induce or perpetuate a periradicular lesion. Another phenomenon is likely to occur in most of the overfilled
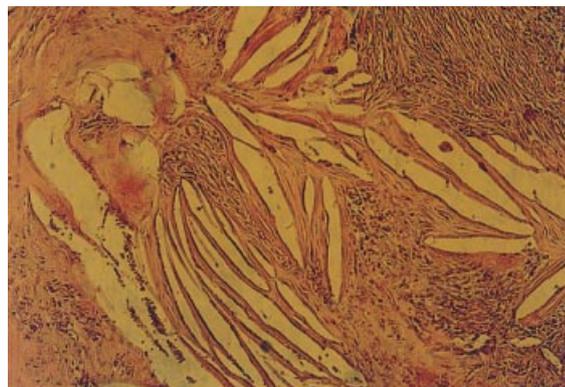

Figure 5 Cholesterol crystals in a periradicular cyst (original magnification ×40). Crystals can accumulate in a periradicular lesion and possibly sustain the inflammatory process.

teeth. It is well known that overinstrumentation usually precedes overfilling. In teeth with infected necrotic pulps overinstrumentation induces the displacement of infected dentine or debris into the periradicular tissues. In this situation, microorganisms are physically protected from the host defence mechanisms and thereby can survive within the periradicular lesion and maintain periradicular inflammation. The presence of infected dentine or cementum chips in the periradicular lesion has been associated with impaired healing (Yusuf 1982). Indeed, this is probably the most common form of extraradicular infection.

Coronal sealing

It has been stated that coronal leakage may be an important cause of failure of endodontic treatment (Saunders & Saunders 1994). There are some situations in which obturated root canals may be contaminated from the oral cavity: leakage through the temporary or permanent restorative material; breakdown, fracture or loss of the temporary/permanent restoration; fracture of the tooth structure; recurrent decay exposing the root canal filling material; or delay in the placement of permanent restorations (Siqueira *et al.* 1999). In such circumstances, if root canal obturation does not impede saliva leakage, microorganisms may invade and recolonize the root canal system. If microbial cells and their products reach the periradicular tissues, they can induce and/or perpetuate periradicular disease.

Recontamination of the root canal system by coronal leakage will occur through: sealer dissolution by saliva; percolation of saliva in the interface between sealer and root canal walls (particularly if smear layer is present) and/or between sealer and gutta-percha (Siqueira *et al.* 1999). In addition, voids and other minor flaws in the obturation, which often are not detected radiographically, may be responsible for the rapid recontamination of the root canal system.

Taken together, some studies (Torabinejad *et al.* 1991, Siqueira *et al.* 1999) have revealed that, regardless of the obturation technique or filling material employed, entire recontamination of the root canal can occur after a short period of microbial challenge. Once the coronal seal is lost, microorganisms, their products and other irritants from saliva may reach the periradicular tissues via lateral canals or apical foraminas, and thereby jeopardize the outcome of root canal treatment. Clinically, it is impossible to determine whether the entire root canal system is recontaminated after exposure to saliva. Obviously, it appears inconsistent to restore a tooth with a root canal that may be completely recontaminated. Therefore, from a clinical standpoint, coronal exposure of the root canal obturation to saliva for a relatively short period of time (30 days or more) might be considered an indication for retreatment.

When the root canal filling is completed, a temporary coronal restoration is applied until the placement of the permanent restoration. Since temporary cements are water-soluble and have low resistance to compression, the temporary restoration should be replaced as soon as possible with the definitive restoration.

Nonmicrobial factors

Although most of the cases of root canal treatment failure are associated with intraradicular and/or extraradicular infections, it has been suggested that some cases can fail because of intrinsic or extrinsic nonmicrobial factors. In these cases, no microorganisms can be found, and failures have been attributed to a foreign body reaction in the periradicular tissues.

A study reported a therapy-resistant lesion, which was surgically removed and diagnosed as a periradicular cyst by light and electron microscopy (Nair *et al.* 1993). A great number of cholesterol crystals were observed in the connective tissue around the cystic epithelial lining. Since microorganisms were not detected, the investigators attributed the failure to a foreign body reaction against cholesterol crystals. Cholesterol crystals are believed to be precipitated and accumulate as they are released from disintegrating host cells, including erythrocytes, lymphocytes, plasma cells and macrophages. These can be numerous in chronic periradicular lesions (Fig. 5). They can also originate from circulating plasma lipids. It has been demonstrated that cholesterol crystals can be an aetiological factor in nonresolving chronic inflammation (Nair *et al.* 1998). If multinucleated giant cells are ineffective in removing crystals, they continue to accumulate and can maintain the periradicular lesion.

The question of whether the development or presence of a radicular cyst is the cause of endodontic treatment failure is still a controversial issue. Although it has been revealed that the majority of periradicular cysts heal after conventional root canal therapy (Morse *et al.* 1975), it has been suggested that true cysts, which contain cavities completely enclosed by epithelial lining, do not (Nair *et al.* 1993). Such a statement is based on the theory that true cysts are self-sustaining by virtue of their independence from the presence or absence of irritants in the root canal system (Nair 1998). However, it has been theorized that the formation of the cyst cavity
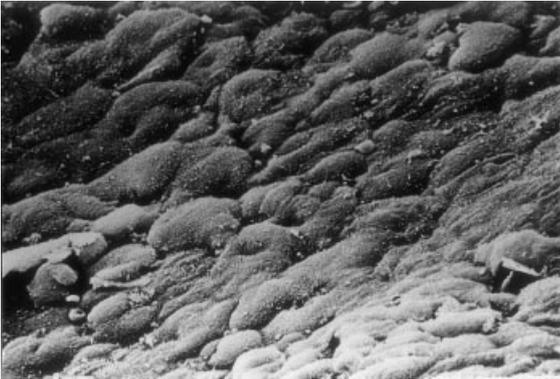
Figure 6 Scanning electron micrograph of the epithelial lining of a pocket cyst (original magnification ×700).
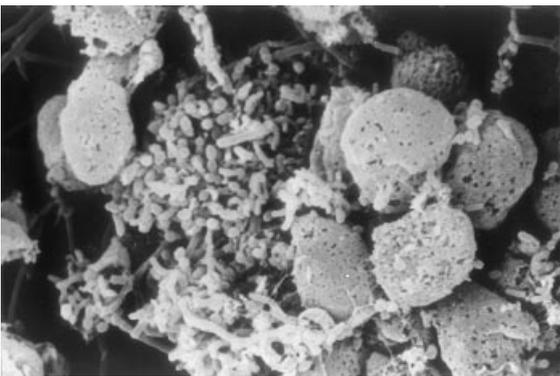

Figure 7 Phagocytes combating a bacterial colony within the cyst cavity. Scanning electron microscopy from the same specimen shown in Fig. 6 (original magnification ×3300).

is originated from immunological reactions, which attack epithelium cells in proliferation (Torabinejad 1983). If the immunological theory is true, it is probable that true cysts can also heal since the cause of epithelial proliferation, i.e. the irritants within the root canal, are eliminated. To date, despite a number of theories regarding the healing of different types of periradicular cysts, there is no significant scientific evidence that supports any theory. Furthermore, it is well known that cysts may become infected. Theoretically, cysts containing epithelial-lined cavities that are open to the root canals (bay cyst or periradicular pocket cyst) have a higher risk of becoming infected than true cysts. Within the cyst cavity, microorganisms egressing from the root canal system are combated by defence molecules (antibodies and components of the complement system) and by polymorphonuclear neutrophils that transmigrate through the epithelium into cyst lumen (Figs 6, 7). Because of the

morphological characteristics of the cyst cavity, the host defence mechanisms may not be effective in eliminating microorganisms. Persisting microbial cells and their products within the cyst lumen may maintain a periradicular inflammation in well-treated root canals. This also characterizes an extraradicular infection.

In addition to intrinsic causes, extrinsic factors may be the cause of endodontic failure. Some root filling materials contain insoluble substances, such as talc-contaminated gutta-percha cones, which can evoke foreign body reactions when protruded into the periradicular tissues and cause failure (Nair *et al*. 1990b). The cellulose component of paper points, cotton wool, and some food material of vegetable origin may also cause persistence of periradicular lesions, if placed into the periradicular tissues (Simon *et al*. 1982, Koppang *et al*. 1989). This stable polysaccharide of plant cell walls is neither digested by man nor degraded by the defence cells. As a result, cellulose can remain in the tissues for long periods and elicit a foreign body reaction. Paper points or particles thereof can be dislodged or pushed into the periradicular tissues, inducing a foreign body giant cell response or sustain the periradicular lesion (Nair 1998). The same can occur with cotton wool, which in the author's opinion has no indication for intracanal use. Particles of food material of vegetable origin (containing cellulose) may also be inadvertently pushed into the periradicular tissues of teeth with grossly damaged crowns, that have been left open for drainage, or when the temporary restoration has been lost. In addition, paper points, cotton wool and food may also carry microorganisms into the root canal system and/or the periradicular tissues. The practice of leaving a tooth open to drainage has been considered as unscientific for many years (Walker 1936). Complications rarely occur if clinical practice is based on the contemporary biological principles of endodontics. In contrast, complications arising from a tooth that has been left open to drain are usually difficult to treat (Weine *et al*. 1975).

Treatment of endodontic failure

Only one of the factors discussed above, intraradicular infection, can be managed by retreatment of the root canal. Although knowledge of the cause of failure of endodontic therapy would facilitate the choice of an appropriate therapy, at the present time such diagnoses can usually be made only after surgery. Assuming that persistent intraradicular infection is the most common cause of failure, it is worthwhile retreating failed teeth prior to surgery in order to exclude such a possibility.

Clearly, appropriate measures for the control and prevention of infection are essential to maximize the success of retreatment; including strict asepsis, complete chemomechanical preparation using antimicrobial irrigants, intracanal medication, adequate root canal filling, and proper coronal sealing. The permanent coronal restoration should be placed as rapidly as possible, ideally in the first week after treatment. The success rate of retreatment may reach approximately two-thirds of cases (Sjögren 1996). Thus, one should try to retreat a failed root canal, particularly when the previous treatment falls short of the accepted technical standards.

Periradicular surgery is indicated in the following cases: the treatment or retreatment is impossible (fractured instruments, ledges, blockages, filling material impossible to remove, etc.); failure of retreatment; where the prognosis of the nonsurgical retreatment is unfavourable; where a biopsy is needed (Gutmann & Harrison 1991, Lopes & Siqueira 1999).

Conclusion

Although it has been suggested that nonmicrobial factors may be implicated in endodontic treatment failure, the literature suggests that persistent intraradicular or secondary infections, and in some cases extraradicular infections, are the major causes of failure of both poorly treated and well-treated root canals.

Acknowledgement

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