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The Management Approach for a Large Periapical Lesion: A Review

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ABSTRACT

Endodontic therapy of large periapical lesions presents a substantial challenge to the clinician. The destruction of periapical tissues, including bone and adjacent structures, characterizes these lesions.

A systematic approach that incorporates multiple treatment modalities for optimal healing is necessary for the effective management of such lesions.

This article discusses the management strategy for large periapical lesions in endodontics, emphasizing the significance of accurate diagnosis, appropriate treatment planning, and the application of effective therapeutic techniques. It has been reported that endodontic therapy has a more favorable prognosis for minor lesions as opposed to larger lesions.

A conservative approach, such as non-surgical root canal therapy, should be the initial course of action prior to surgical endodontic intervention.

INTRODUCTION

Apical periodontitis is an inflammation and damage of periradicular tissues resulting from endodontically derived etiological agents. Typically, it follows endodontic infection. Initial infection and necrosis of the tooth pulp are caused by oral microflora. Endodontic environments provide favorable conditions for the development of a diverse, predominately anaerobic flora. This root canal-dwelling polymicrobial community has several biological and pathogenic properties, including antigenicity, mitogenic activity, chemotaxis, enzymatic histolysis, and activation of host cells (Nair, 2004).

Invading microorganisms in the root canal can progress into the periapex, or their byproducts can egress. In response, the host mobilizes an array of cells, intercellular messengers, antibodies, and effector molecules. Various types of apical periodontitis lesions are caused by microbial factors and host defense

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forces encountering, clashing with, and destroying much of the periapical tissue. Despite its formidable defense, the body is unable to eradicate the microorganisms firmly situated in the sanctuary of the necrotic root canal, which is beyond the reach of the body's defenses. Apical periodontitis is therefore not self-healing. The treatment for apical periodontitis consists of eliminating infection from the root canal and preventing reinfection by sealing the root canal space with a suitable material (Ramachandran Nair, 1987; Stashenko, 1990; Stashenko et al., 1998).

Pathogenesis of periapical lesion

Periapical cysts are commonly believed to be the primary result of chronic apical granulomas, although not all granulomas develop into cysts (Ramachandran Nair, 1987). 6-55% of apical periodontitis lesions are reported to contain cysts (Lalonde & Luebke, 1968; Ramachandran Nair et al., 1996). Investigations based on serial sectioning and strict histopathological criteria (Ramachandran Nair et al., 1996; Simon, 1980) indicate that the incidence of cysts among these lesions may be well below 20%. The remainder of these cysts are apical pocket cysts (Ramachandran Nair et al., 1996; Simon, 1980).

There are three phases of cyst formation; 1) dormant epithelial cell rests proliferate, 2) epithelium-lined cavity established and 3) the cyst grows. The mechanism of the apical cyst arising from endodontic infection has long been a perplexing subject. Multiple hypotheses have been put forward for a considerable period of time (Lin et al., 2007; Nair, 2004).

(i) Nutritional deficiency theory: The expansion of epithelial islands results in increased distance between central epithelial cells and their nutrient supply, leading to their necrosis. As a result of liquefaction necrosis, the center of the cell mass develops a cystic cavity.
(ii) Abscess theory: A cavity for an abscess develops within the periapical connective tissues. Following this, the abscess becomes entirely encircled by epithelium due to the inherent propensity of stratified squamous epithelium to line the surfaces of exposed connective tissue.
(iii) Merging of epithelial strands theory: A three-dimensional ball mass is formed when epithelial strands merge as they continue to expand. A cyst develops because of the degeneration of the connective tissue inside the spherical mass.

Prognosis endodontic tooth with large periapical lesion

The presence and size of a periapical lesion appear to have the greatest impact on the periapical health (Ng et al., 2011; Sjögren et al., 1990). The profound change in success rates following the establishment of a periapical lesion is intriguing, as it correlates with the development of infection in the apical canal anatomy. Once the apical canal complexities become infected, it may be considerably more challenging to eradicate the infection. Large periapical lesions have a reasonable biological explanation for their deleterious impact. Greater bacterial diversity as measured by the number of species and their relative abundance is observed in teeth with more extensive periapical lesions (Sundqvist, 1992).

Endodontic infections are more likely to persist in canals that contain a greater number of bacteria preoperatively (Byström & Sundqvist, 1981). Moreover, larger lesions may indicate longer-standing root canal infections that have penetrated deeper into dentinal tubules and accessory anatomy in the complex canal system (Love & Jenkinson, 2002) where mechanical and chemical decontamination procedures may not be as effective. Cystic transformation can also occur in larger lesions (Nair, 2006). The host response may also play a role, as patients with larger lesions may have a less favorable innate response to residual bacteria (Nair et al., 2005).

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The technical quality of a root filling had a greater impact on the persistence of apical periodontitis (AP) than on its development (Kirkevang et al., 2007). This assertion is supported by a study (Fabricius et al., 2006) that investigated the influence of residual bacteria on the healing of periapical tissue in infected monkey teeth following root canal therapy. If bacteria remained after root canal treatment, nearly 80% of root canals had persisting AP, whereas if no bacteria were detected, less than 30% of AP lesions remained. In addition, healing occurred regardless of the quality of the root filling when no microbes remained in the canal. However, if the bacteria remained, the correlation between low-quality root fillings and non-healing was greater than in root fillings that were technically executed well.

Meta-analysis studies predominately based on radiographic interpretation found that root-filled teeth with adequate restorations and root canal treatment resulted in better treatment outcomes. This reaffirms the fundamental biologic principle of preventing bacterial ingress through the concerted efforts of the endodontist and the restorative dentist in providing the highest quality of care in saving functional teeth (Gillen et al., 2011).

Management approach for large periapical lesion

1. Diagnosis

Before rendering a diagnosis, it is essential to collect all pertinent information about the patient, the oral condition, and the involved teeth. From the patient's description of symptoms, the complaint's history, and the specifics of any recent treatment, provisional diagnoses of the pulp and periapical tissues should be made. The results of the diagnostic tests, along with the findings from the clinical and radiographic examinations, are evaluated in order to create a conclusive diagnosis of the tissue problems and identify which tooth is affected. Ideally, at least two signs and/or symptoms should be present to signify and confirm the disease. If there is any uncertainty and the pain is not severe, the clinician should postpone treatment until the diagnosis is apparent.

Imaging techniques such as periapical radiographs, panoramic radiographs, and cone-beam computed tomography (CBCT) provide detailed information about the lesion's size, shape, location, and proximity to vital structures. Histopathological evaluation may be necessary in certain cases to confirm the diagnosis and differentiate between inflammatory and cystic lesions.

2. Periapical lesion visibility

Within the same patient, the thickness of the cortices varies significantly. Consequently, a lesion of a particular size can be detected in a region with a thin cortex, but it cannot be detected in a region with a thicker cortex. The location of lesions within various types of bone also affects their radiographic visibility. Because cortical bone contains more minerals per unit volume than cancellous bone, the resorption or demineralization process will manifest radiolucent changes, sufficient minerals will be lost to create contrast sooner and more readily in the more calcified tissue. Several in vitro studies have addressed the issue of periapical lesion visibility. It appears that the lesion is more visible when it is close by (Bender, 1982) or within the cortex (Bender, 1982; Bender & Seltzer, 2003). It may not be (Schwartz & Foster, 1971) or is unlikely to manifest in cancellous bone (Bender, 1982). The magnitude at which a periapical lesion becomes radiologically detectable varies across the mandible. Larger than 3mm in diameter, isolated spongiosa lesions are frequently visible on the mandibular front teeth and premolars. Generally, isolated spongiosa lesions at mandibular molars are undetectable. Atypical lesions, such as discontinuities of skeletal structures, are particularly challenging to detect radiographically (Patel et al., 2012).

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Periapical radiographs may falsely suggest an area of apical periodontitis without infection of the root canal system when there is extensive periodontal disease and the pocket has extended beyond the level of the root apex. In this situation, substantial breakdown of the supporting tissues and loss of bone (either labially or lingually) creates a radiolucency, which is superimposed over the periapical region giving the appearance of apical periodontitis.(Langeland et al., 1974)

CBCT imaging can detect small areas of periapical pathosis before they are visible on 2D radiographs (Paula-Silva et al., 2009), as well as distinguish larger, indistinct periapical radiolucent areas from normal variations in bone density (Patel et al., 2012). This conclusion was supported by clinical investigations in which 20% and 48%, respectively, of patients had periapical periodontitis identified by intraoral radiography and CBCT. The same authors showed that 1 year after treatment, 2D radiographs could detect the absence of a periapical radiolucency in 93% of instances, whereas CBCT could detect it in only 74% of cases (Patel et al., 2012).

3. Non-surgical technique

Before resorting to surgery, a nonsurgical approach must always be taken. In addition, surgical treatment causes greater psychological anxiety than non-surgical treatment. During surgical procedures, one must also be aware of the dangers and complications associated with medically compromised patients.Numerous approaches have been suggested regarding the non-surgical management of periapical lesions (Fernandes & de Ataide, 2010; Hoen et al., 1990; Shah, 1988)

(i) Conservative root canal treatment without adjunctive therapy.

Nonsurgical management is often the initial approach for large periapical lesions. It involves thorough root canal treatment (RCT) to eliminate the source of infection and promote healing. The removal of any remaining bacteria in the root canal, the creation of a tight seal to stop tissue fluid from the periapical tissues feeding bacteria while still in the root canal, and the establishment of an effective blockade of any communication between the oral cavity and the periradicular tissue through high-quality endodontic and coronal restorations are all necessary for root canal treatment to be successful. (Voruganti, 2008). Techniques such as mechanical instrumentation, irrigation with antimicrobial solutions, and the use of intracanal medications aid in achieving these goals.

(ii) Decompression technique

Toller (1972) hypothesised that the growth of the cyst may be due to the increased hydrostatic pressure of the confined fluid, which stimulates additional osteoclastic activity (Toller, 1972). The techniques of decompression (Loushine et al., 1991; Shah, 1988) and aspiration-irrigation (Hoen et al., 1990) help reduce hydrostatic pressure, resulting in lesion diminution. The decompression technique entails the placement of drainage tubes (Martin, 2007). This methodology offers several benefits, including its straightforward implementation, reduced potential for harm to neighboring critical anatomical components. Inflammation of alveolar mucosa, persistence of a surgical defect at the site, development of acute or chronic infection of the lesion, submersion of the tube, and patient cooperation limit the use of this technique (Calişkan & Türkün, 1997).

(iii) Active non-surgical decompression technique

By generating a negative pressure with the Endo-eze vacuum system (Ultradent, Salt Lake City, Utah), this method decompresses huge periapical lesions. By connecting the high-volume suction

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aspirator to a micro 22-gauge needle that is inserted into the root canal and activated for a duration of 20 minutes, a negative pressure is generated, leading to the exudate being aspirated. Temporary cement is utilized to seal the access cavity when drainage ceases in part, thereby aiding in the maintenance of bacterial control. In contrast to the decompression technique, this method is performed entirely within the root canal, rendering it minimally invasive and consequently inducing reduced patient distress.

(iv) Intracanal medicament with calcium hydroxide

Calcium hydroxide is extensively used as an intracanal endodontic material due to its high alkalinity (Tronstad et al., 1981), tissue dissolving effect, induction of hard tissue formation, and bactericidal effect (Siqueira & Lopes, 1999; Sjögren et al., 1991). Its antibacterial properties are a result of its effect on bacterial cytoplasmic membranes, protein denaturation, DNA damage, carbon dioxide absorption, action on lipopolysaccharides, and hygroscopic property. In the presence of large periapical lesions, intracanal calcium hydroxide placement would have a direct effect on inflamed tissue, biofilm and epithelial cystic linings, thereby promoting periapical healing and encouraging osseous repair (Tronstad et al., 1981).

(v) Laser sterilisation and tissue repair

The Cariology Research Unit of the Niigata University School of Dentistry has developed the concept of 'Lesion Sterilisation and Tissue Repair (LSTR)' therapy, which uses a triple antibiotic paste consisting of ciprofloxacin, metronidazole, and minocycline, for disinfection of oral infectious lesions, such as dentinal, pulpal, and periradicular lesions (Sain et al., 2018; Sato et al., 1996). If lesions are disinfected, damaged tissues can be anticipated to recover (Takushige et al., 2004). Due to its broad antibacterial spectrum against anaerobes, metronidazole is the preferred option (Ingham et al., 1975). Due to the fact that certain bacteria are resistant to metronidazole, ciprofloxacin and minocycline are added to the mixture (Sato et al., 1993). It has been demonstrated that the combination of medications can effectively permeate dentine from prepared root canals, particularly ultrasonically irrigated root canals (Sato et al., 1996). The commercially available drugs are powdered and combined with macrogol-propylene glycol (3 Mix-MP) or a canal sealer (3 Mix-sealer) in a ratio of 1:3:3 or also utilised is a 1:1:1 ratio of the drug combination.

4. Surgical techniques

When nonsurgical treatment alone fails to adequately manage large periapical lesions, surgical intervention becomes necessary. Apical surgery, also known as apical microsurgery or periapical surgery, involves the removal of the lesion through an apical access and subsequent retrograde filling. The need for apical surgery arises when nonsurgical retreatment procedures have been unsuccessful or are thought to be impractical. The aetiology of a chronic pathosis must be extensively assessed prior to selecting surgical retreatment (Karabucak & Setzer, 2007).

When indicated, periradicular surgery should be viewed as an extension of nonsurgical treatment because the underlying aetiology of the disease process and treatment goals are identical: prevention or elimination of apical periodontitis. Surgical root canal treatment should not be considered distinct from nonsurgical treatment, despite the evident differences in instruments and techniques.

Histologically, most periapical lesions are inflammatory pathologies. 50% of lesions were granulomas, 35% were periapical abscesses, and 15% were pocket or genuine cysts, according to Nair et al. (1996). Pocket cysts are directly associated with the infected root canal system, whereas true cysts are independent of the root (Nair, 2006; Ramachandran Nair et al., 1996). Primary endodontic treatment or

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nonsurgical retreatment may not permit the healing of true cysts making endodontic surgery necessary (Ramachandran Nair et al., 1996). Foreign body reactions caused by gutta- percha and other filler or sealer materials, paper point remnants, and cholesterol clefts have been identified in cystic lesion (Nair, 2006). Lastly, extra-radicular infections may manifest as biofilms on an external root surface (Tronstad et al., 1990) or as Actinomyces and Propionibacterium colonies within asymptomatic lesions (Ramachandran Nair, 1987; Ricucci & Siqueira, 2008; Sjögren et al., 1988) and necessitate endodontic surgery.

Endodontic surgery may be contraindicated or compromised when the proximity of vital anatomical structures may cause temporary or irreparable harm during the surgical procedure. These structures may include the nasal or sinus cavities, mental and infra-alveolar nerves, or palatal neurovascular bundle. Systemic conditions, such as congenital bleeding disorders, may preclude surgical intervention. A history of intravenous bisphosphonate therapy is associated with a significantly increased risk of osteonecrosis of the mandible due to bisphosphonate (Setzer & Kratchman, 2022). Finally, teeth with inadequate definitive restorations, a low or doubtful crown-to-root ratio, severe periodontal disease, or increased mobility might not be a good candidate for a surgical treatment because of a less promising prognosis.

The use of surgical operating microscopes improves visualization and facilitates precise surgical procedures. Techniques like root-end resection, retrograde cavity preparation, and retrograde filling with biocompatible materials ensure a successful outcome.

5. Guided Tissue Regeneration (GTR) and endodontic surgery in complicated bony defect

Endodontic lesions with a defect size greater than 10 mm in diameter, 'through-and-through' lesions with a buccolingual defect and/or perforation to the nasal cavity, or a large maxillary sinus perforation are examples of complicated defects (Setzer & Kratchman, 2022)

GTR could potentially be advantageous for complicated defects. Membrane placement on both the buccal and lingual aspects of 'through-and-through' rat calvaria defects resulted in complete healing, whereas there was no healing in the control group without membranes (Bohning et al., 1999; Dahlin et al., 1988). In addition, Dahlin et al. (1990) found that the use of a barrier resulted in complete recovery of similar defects following endodontic surgery, as compared to controls that displayed only fibrous connective tissue (Dahlin et al., 1990). Azim et al. (2021) demonstrated that GTR techniques enhanced the quality of apical bone remodelling following endodontic surgery (Azim et al., 2021). Healing of through-and-through lesions was observed in 88% of patients with GTR placement, compared to 57% without (Taschieri et al., 2008). Together, these findings suggest that for effective recovery of through-and-through lesions, both buccal and lingual barriers should be placed (Bohning et al., 1999). Lesions larger than 10 mm in diameter healed faster and with better outcomes when GTR was used as compared to when it was not (Pecora et al., 1995; Pecora et al., 2001), including radiographic, clinical, and histologic outcomes (Pecora et al., 1995; Rankow & Krasner, 1996; Tobón et al., 2002).

Current study by Zubizarreta- Macho et al. (2022) evaluating the clinical evidence on the efficacy of GTR techniques and included 11 randomised clinical trials comparing six GRT techniques, such as bone graft, membrane, membrane plus bone graft, platelet- rich plasma, and membrane plus platelet- rich plasma. Both membrane and membrane plus bone graft techniques exhibited statistically significant likelihood ratios when compared to procedures without GTR (Zubizarreta-Macho et al., 2022).

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CONCLUSION

In summary, the management of large periapical lesions necessitates precise diagnosis, efficacious root canal treatment, and surgical interventions, when warranted. Essential elements for success encompass meticulous disinfection, root canal sealing, and appropriate restorative procedures. While non-surgical approaches should be prioritized, surgical modalities such as apical microsurgery may be requisite. The synergistic collaboration between endodontists and restorative and oral maxillofacial surgeon assumes paramount importance in ensuring optimal care provision. Noteworthy advancements in diagnostic methodologies and treatment modalities have significantly enhanced the prognostic outlook, promoted the preservation of functional dentition, and rendered improved long-term outcomes for patients afflicted with large periapical lesions.

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CONFLICT OF INTEREST STATEMENT

The authors agree that this research was conducted in the absence of any self-benefits, commercial or financial conflicts and declare the absence of conflicting interests with the funders.

AUTHORS' CONTRIBUTIONS

Nazrin Mohd Isa carried out the research, wrote and revised the article. Afzan Adilah Ayoub conceptualised the central research idea and provided the theoretical framework. Afzan Adilah and Nurul Ain Ramlan designed the research, supervised research progress; Afzan Adilah and Nurul Ain Ramlan anchored the review, revisions and approved the article submission.

REFERENCES

Azim, A. A., Albanyan, H., Azim, K. A., & Piasecki, L. (2021). The Buffalo study: Outcome and associated predictors in endodontic microsurgery- a cohort study. *International endodontic journal*, *54*(3), 301–318. https://doi.org/ 10.1111/iej.13419.

Bender, I. B. (1982). Factors influencing the radiographic appearance of bony lesions. *Journal of endodontics*, *8*(4), 161–170. https://doi.org/ 10.1016/S0099-2399(97)80199-9.

Bender, I. B., & Seltzer, S. (2003). Roentgenographic and direct observation of experimental lesions in bone: II. 1961. *Journal of endodontics, 29*(11), 707–12; discussion 701. https://doi.org/10.1097/00004770-200311000-00006.

Bohning, B. P., Davenport, W. D., & Jeansonne, B. G. (1999). The effect of guided tissue regeneration on the healing of osseous defects in rat calvaria. *Journal of endodontics, 25*(2), 81–84. United States. https://doi.org/10.1016/S0099-2399(99)80001-6.

Byström, A., & Sundqvist, G. (1981). Bacteriologic evaluation of the efficacy of mechanical root canal instrumentation in endodontic therapy. *Scandinavian journal of dental research, 89*(4), 321–328. https://doi.org/10.1111/j.1600-0722.1981.tb01689.x.

https://doi.org/10.24191/cos.v11i2.27499

Byström, A., & Sundqvist, G. (1981). Bacteriologic evaluation of the efficacy of mechanical root canal instrumentation in endodontic therapy. *Scandinavian journal of dental research*, *89*(4), 321–328. Denmark. https://doi.org/10.1111/j.1600-0722.1981.tb01689.x

Calişkan, M. K., & Türkün, M. (1997). Periapical repair and apical closure of a pulpless tooth using calcium hydroxide. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, *84*(6), 683–687. United States. https://doi.org/10.1016/s1079-2104(97)90373-5.

Dahlin, C., Gottlow, J., Linde, A., & Nyman, S. (1990). Healing of maxillary and mandibular bone defects using a membrane technique. An experimental study in monkeys. *Scandinavian journal of plastic and reconstructive surgery and hand surgery*, *24*(1), 13–19. England. https://doi.org/10.3109/02844319009004514.

Dahlin, C., Linde, A., Gottlow, J., & Nyman, S. (1988). Healing of bone defects by guided tissue regeneration. *Plastic and reconstructive surgery*, *81*(5), 672–676. United States. https://doi.org/10.1097/00006534-198805000-00004.

Fabricius, L., Dahlén, G., Sundqvist, G., Happonen, R.-P., & Möller, A. J. R. (2006). Influence of residual bacteria on periapical tissue healing after chemomechanical treatment and root filling of experimentally infected monkey teeth. *European journal of oral sciences*, *114*(4), 278–285. England. https://doi.org/10.1111/j.1600-0722.2006.00380.x.

Fernandes, M., & de Ataide, I. (2010). Nonsurgical management of periapical lesions. *Journal of conservative dentistry : JCD*, *13*(4), 240–245. India. https://doi.org/10.4103/0972-0707.73384.

Gillen, B. M., Looney, S. W., Gu, L.-S., Loushine, B. A., Weller, R. N., Loushine, R. J., Pashley, D. H., et al. (2011). Impact of the quality of coronal restoration versus the quality of root canal fillings on success of root canal treatment: a systematic review and meta-analysis. *Journal of endodontics*, *37*(7), 895–902. United States. https://doi.org/10.1016/j.joen.2011.04.002.

Hoen, M. M., LaBounty, G. L., & Strittmatter, E. J. (1990). Conservative treatment of persistent periradicular lesions using aspiration and irrigation. *Journal of endodontics*, *16*(4), 182–186. United States. https://doi.org/10.1016/S0099-2399(06)81968-0.

Ingham, H. R., Selkon, J. B., & Hale, J. H. (1975). The antibacterial activity of netronidazole. *The Journal of antimicrobial chemotherapy*, *1*(4), 355–361. England. https://doi.org/10.1093/jac/1.4.355.

Karabucak, B., & Setzer, F. (2007). Criteria for the ideal treatment option for failed endodontics: surgical or nonsurgical? *Compendium of continuing education in dentistry (Jamesburg, N.J. : 1995), 28*(6), 304–10, quiz 311, 332. United States.

Kirkevang, L.-L., Vaeth, M., Hörsted-Bindslev, P., Bahrami, G., & Wenzel, A. (2007). Risk factors for developing apical periodontitis in a general population. *International endodontic journal*, *40*(4), 290–299. England. https://doi.org/10.1111/j.1365-2591.2007.01224.x.

Lalonde, E. R., & Luebke, R. G. (1968). The frequency and distribution of periapical cysts and granulomas. An evaluation of 800 specimens. *Oral surgery, oral medicine, and oral pathology, 25*(6), 861–868. United States. https://doi.org/10.1016/0030-4220(68)90163-1.

https://doi.org/10.24191/cos.v11i2.27499

Langeland, K., Rodrigues, H., & Dowden, W. (1974). Periodontal disease, bacteria, and pulpal histopathology. *Oral surgery, oral medicine, and oral pathology*, *37*(2), 257–270. United States. https://doi.org/10.1016/0030-4220(74)90421-6.

Lin, L. M., Huang, G. T.-J., & Rosenberg, P. A. (2007). Proliferation of epithelial cell rests, formation of apical cysts, and regression of apical cysts after periapical wound healing. *Journal of endodontics*, *33*(8), 908–916. United States. https://doi.org/10.1016/j.joen.2007.02.006.

Loushine, R. J., Weller, R. N., Bellizzi, R., & Kulild, J. C. (1991). A 2-day decompression: A case report of a maxillary first molar. *Journal of endodontics*, *17*(2), 85–87. United States. https://doi.org/10.1016/S0099-2399(06)81614-6.

Love, R. M., & Jenkinson, H. F. (2002). Invasion of Dentinal Tubules by Oral Bacteria. *Critical Reviews in Oral Biology \& Medicine*, *13*(2), 171–183. https://doi.org/10.1177/154411130201300207.

Martin, S. A. (2007). Conventional endodontic therapy of upper central incisor combined with cyst decompression: A case report. *Journal of endodontics, 33*(6), 753–757. United States. https://doi.org/10.1016/j.joen.2007.01.013.

Nair, P. N.R. (2006). On the causes of persistent apical periodontitis: A review. *International Endodontic Journal*, *39*(4), 249–281. https://doi.org/10.1111/j.1365-2591.2006.01099.x

Nair, P N R. (2004). Pathogenesis of apical periodontitis and the causes of endodontic failures. *Critical reviews in oral biology and medicine : An official publication of the American Association of Oral Biologists*, *15*(6), 348–381. United States. https://doi.org/10.1177/154411130401500604.

Nair, P N R, Henry, S., Cano, V., & Vera, J. (2005). Microbial status of apical root canal system of human mandibular first molars with primary apical periodontitis after "one-visit" endodontic treatment. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, *99*(2), 231–252. United States. https://doi.org/10.1016/j.tripleo.2004.10.005.

Nair, P N Ramachandran. (1997). Apical periodontitis: A dynamic encounter between root canal infection and host response. *Periodontology 2000*, *13*(1), 121–148. Wiley Online Library. https://doi.org/10.1111/j.1600-0757.1997.tb00098.x.

Ng, Y. L., Mann, V., & Gulabivala, K. (2011). A prospective study of the factors affecting outcomes of nonsurgical root canal treatment: Part 1: Periapical health. *International Endodontic Journal, 44*(7), 583–609. https://doi.org/10.1111/j.1365-2591.2011.01872.x.

Patel, S., Wilson, R., Dawood, A., Foschi, F., & Mannocci, F. (2012). The detection of periapical pathosis using digital periapical radiography and cone beam computed tomography - part 2: A 1-year post-treatment follow-up. *International endodontic journal*, *45*(8), 711–723. England. https://doi.org/10.1111/j.1365-2591.2012.02076.x.

Patel, S., Wilson, R., Dawood, A., & Mannocci, F. (2012). The detection of periapical pathosis using periapical radiography and cone beam computed tomography - part 1: Pre-operative status. *International endodontic journal*, *45*(8), 711–723. England. https://doi.org/10.1111/j.1365-2591.2012.02076.x.

Paula-Silva, F. W. G. de, Wu, M. K., Leonardo, M. R., Bezerra da Silva, L. A., & Wesselink, P. R. (2009). Accuracy of Periapical Radiography and Cone-Beam Computed Tomography Scans in Diagnosing Apical Periodontitis Using Histopathological Findings as a Gold Standard. *Journal of Endodontics, 35*(7), 1009–1012. https://doi.org/10.1016/j.joen.2009.04.006.

Pecora, G., Kim, S., Celletti, R., & Davarpanah, M. (1995). The guided tissue regeneration principle in endodontic surgery: One-year postoperative results of large periapical lesions. *International endodontic journal, 28*(1), 41–46. England. https://doi.org/10.1111/j.1365-2591.1995.tb00155.x.

Pecora, G., De Leonardis, D., Ibrahim, N., Bovi, M., & Cornelini, R. (2001). The use of calcium sulphate in the surgical treatment of a "through and through" periradicular lesion. *International endodontic journal*, *34*(3), 189–197. England. https://doi.org/10.1046/j.1365-2591.2001.00369.x.

Ramachandran Nair, P. N. (1987). Light and electron microscopic studies of root canal flora and periapical lesions. *Journal of endodontics*, *13*(1), 29–39. United States. https://doi.org/10.1016/S0099-2399(87)80089-4.

Ramachandran Nair, P. N., Pajarola, G., & Schroeder, H. E. (1996). Types and incidence of human periapical lesions obtained with extracted teeth. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, *81*(1), 93–102. United States. https://doi.org/10.1016/s1079-2104(96)80156-9.

Rankow, H. J., & Krasner, P. R. (1996). Endodontic applications of guided tissue regeneration in endodontic surgery. *Journal of endodontics*, *22*(1), 34–43. United States. https://doi.org/10.1016/S0099-2399(96)80234-2.

Ricucci, D., & Siqueira, J. F. J. (2008). Anatomic and microbiologic challenges to achieving success with endodontic treatment: A case report. *Journal of endodontics*, *34*(10), 1249–1254. United States. https://doi.org/10.1016/j.joen.2008.07.002.

Sain, S., Reshmi, J., Anandaraj, S., George, S., Issac, J. S., & John, S. A. (2018). Lesion Sterilization and Tissue Repair-Current Concepts and Practices. *International journal of clinical pediatric dentistry, 11*(5), 446–450. India. https://doi.org/10.5005/jp-journals-10005-1555.

Sato, I., Ando-Kurihara, N., Kota, K., Iwaku, M., & Hoshino, E. (1996). Sterilization of infected root-canal dentine by topical application of a mixture of ciprofloxacin, metronidazole and minocycline in situ. *International endodontic journal, 29*(2), 118–124. England. https://doi.org/10.1111/j.1365-2591.1996.tb01172.x.

Sato, T., Hoshino, E., Uematsu, H., & Noda, T. (1993). In vitro antimicrobial susceptibility to combinations of drugs on bacteria from carious and endodontic lesions of human deciduous teeth. *Oral microbiology and immunology, 8*(3), 172–176. Denmark. https://doi.org/10.1111/j.1399-302x.1993.tb00661.x.

Schwartz, S. F., & Foster, J. K. J. (1971). Roentgenographic interpretation of experimentally produced bony lesions. I. *Oral surgery, oral medicine, and oral pathology*, *32*(4), 606–612. United States. https://doi.org/10.1016/0030-4220(71)90326-4.

https://doi.org/10.24191/cos.v11i2.27499

Setzer, F. C., & Kratchman, S. I. (2022). Present status and future directions: Surgical endodontics. *International Endodontic Journal*, *55*(S4), 1020–1058. https://doi.org/10.1111/iej.13783.

Shah, N. (1988). Nonsurgical management of periapical lesions: A prospective study. *Oral surgery, oral medicine, and oral pathology*, *66*(3), 365–371. United States. https://doi.org/10.1016/0030-4220(88)90247-2.

Simon, J. H. (1980). Incidence of periapical cysts in relation to the root canal. *Journal of endodontics, 6*(11), 845–848. United States. https://doi.org/10.1016/S0099-2399(80)80039-2.

Siqueira, J. F. J., & Lopes, H. P. (1999). Mechanisms of antimicrobial activity of calcium hydroxide: A critical review. *International endodontic journal*, *32*(5), 361–369. England. https://doi.org/10.1046/j.1365-2591.1999.00275.x.

Sjögren, U, Figdor, D., Spångberg, L., & Sundqvist, G. (1991). The antimicrobial effect of calcium hydroxide as a short-term intracanal dressing. *International endodontic journal*, *24*(3), 119–125. England. https://doi.org/10.1111/j.1365-2591.1991.tb00117.x.

Sjögren, U, Happonen, R. P., Kahnberg, K. E., & Sundqvist, G. (1988). Survival of Arachnia propionica in periapical tissue. *International endodontic journal*, *21*(4), 277–282. England. https://doi.org/10.1111/j.1365-2591.1988.tb01012.x.

Sjögren, Ulf, Hägglund, B., Sundqvist, G., & Wing, K. (1990). Factors affecting the long-term results of endodontic treatment. *Journal of Endodontics, 16*(10), 498–504. https://doi.org/10.1016/S0099-2399(07)80180-4.

Stashenko, P. (1990). Role of immune cytokines in the pathogenesis of periapical lesions. *Endodontics & dental traumatology, 6*(3), 89–96. Denmark. https://doi.org/10.1111/j.1600-9657.1990.tb00400.x.

Stashenko, P., Teles, R., & d'Souza, R. (1998). Periapical inflammatory responses and their modulation. *Critical Reviews in Oral Biology & Medicine, 9*(4), 498–521. International and American Associations for Dental Research. https://doi.org/10.1177/10454411980090040701.

Sundqvist, G. (1992). Ecology of the root canal flora. *Journal of Endodontics, 18*(9), 427–430. https://doi.org/10.1016/S0099-2399(06)80842-3.

Takushige, T., Cruz, E. V, Asgor Moral, A., & Hoshino, E. (2004). Endodontic treatment of primary teeth using a combination of antibacterial drugs. *International endodontic journal, 37*(2), 132–138. England. https://doi.org/10.1111/j.0143-2885.2004.00771.x.

Taschieri, S., Del Fabbro, M., Testori, T., Saita, M., & Weinstein, R. (2008). Efficacy of guided tissue regeneration in the management of through-and-through lesions following surgical endodontics: A preliminary study. *The International journal of periodontics & restorative dentistry*, *28*(3), 265–271. United States.

Tobón, S. I., Arismendi, J. A., Marín, M. L., Mesa, A. L., & Valencia, J. A. (2002). Comparison between a conventional technique and two bone regeneration techniques in periradicular surgery. *International endodontic journal*, *35*(7), 635–641. England.

Toller, P. A. (1972). Newer concepts of odontogenic cysts. *International journal of oral surgery, 1*(1), 3–16. Denmark. https://doi.org/10.1016/S0300-9785(72)80031-0.

Tronstad, L, Andreasen, J. O., Hasselgren, G., Kristerson, L., & Riis, I. (1981). pH changes in dental tissues after root canal filling with calcium hydroxide. *Journal of endodontics*, *7*(1), 17–21. United States. https://doi.org/10.1016/S0099-2399(81)80262-2.

Tronstad, Leif, Barnett, F., & Cervone, F. (1990). Periapical bacterial plaque in teeth refractory to endodontic treatment. *Dental Traumatology, 6*(2), 73–77. https://doi.org/10.1111/j.1600-9657.1990.tb00394.x.

Voruganti, K. (2008). *Essential endodontology - prevention and treatment of apical periodontitis* (2nd edition). British Dental Journal, 204(9), 536.

Zubizarreta-Macho, Á., Tosin, R., Tosin, F., Velasco Bohórquez, P., San Hipólito Marín, L., Montiel-Company, J. M., Mena-Álvarez, J., & Montero, S. H. (2022). Influence of guided tissue regeneration techniques on the success rate of healing of surgical endodontic treatment: A systematic review and network meta-analysis. *Journal of clinical medicine*, *11*(4). Switzerland. https://doi.org/10.3390/jcm11041062.