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Review
New perspectives on radicular cysts: do they heal?

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Summary

During the past few decades several authors have perpetuated the notion that nearly half of all periapical lesions are radicular cysts. A few studies, based on meticulous serial sectioning of periapical lesions retrieved *in toto*, have shown that the actual incidence of radicular cyst is only about 15% of all periapical lesions. Equally significant was the discovery in 1980 and recent confirmation that radicular cysts exist in two structurally distinct classes namely, those containing cavities completely enclosed in epithelial lining (periapical true cysts) and those containing epithelium-lined cavities that are open to the root canals (periapical pocket cysts). From a clinical point of view a periapical pocket cyst may heal after conventional root canal therapy whereas an apical true cyst is less likely to be resolved without surgical intervention.

***Keywords*: apical periodontitis, apical pocket cysts, radicular cysts, apical true cysts.**

Introduction

Radicular cysts are inflammatory jaw cysts at the apices of teeth with infected and necrotic pulps. The term cyst is derived from the Greek word *Kystis* meaning sac or bladder. Chronic periapical lesions contain epithelial cells (Malassez 1884, Thoma 1917, McConnell 1921, Freeman 1931, Sonnabend & Oh 1966, Seltzer *et al.* 1969, Summers 1974, Summers & Papadimitriou 1975, Langeland *et al.* 1977, Yanagisawa 1980, Nair & Schroeder 1985, Nair & Schmid-Meier 1986), believed to be derived from the cell rests of Malassez (Malassez 1884), which proliferate in some lesions and are presumed to serve as the source of epithelium that lines the lumen in certain lesions that develop into radicular cysts.

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Incidence

Radicular cysts are the most common of all jaw cysts and comprise about 52 (Shear 1992) to 68% (Killey *et al.* 1977) of all the cysts affecting the human jaw. Their incidence is highest amongst patients in their third decade of life (Bhaskar 1966, Mortensen *et al.* 1970, Shear 1992) and are more common amongst men than amongst women (Bhaskar 1966, Shear 1992). Anatomically the apical cysts occur in all tooth-bearing sites of the jaw but are more frequent in maxillary than mandibular teeth. In the upper jaw the anterior region appears to be more cyst-vulnerable whereas in the lower jaw the radicular cysts occur more frequently in the premolar region (Borg *et al.* 1974).

Prevalence amongst periapical lesions

A survey of literature shows that there have been several studies on the prevalence of radicular cysts amongst human periapical lesions (Table 1). The reported incidence of cysts amongst apical periodontitis lesions varies from 6 to 55%. Accurate histopathological diagnosis of radicular cysts is possible only through serial sectioning or step-serial sectioning of the lesions removed *in toto*. There are only very few authors (Sonnabend & Oh 1966, Simon 1980, Nair *et al.* 1996) who used either one of those essential techniques. Most of the investigators (Table 1) analyzed specimens obtained from wide sources for routine histopathological reports. The 2308 lesions in Bhaskar's study (Bhaskar 1966) were from 314 contributors and the 800 biopsies of Lalonde & Luebke (1968) originated from 134 sources. Such histopathological diagnostic specimens, often derived through apical curettage, do not represent lesions *in toto*. In random sections from fragmented and

Table 1 The incidence of radicular cysts amongst periapical lesions

Reference	Cysts %	Granuloma %	Others %	Total lesions *n*
(Sommer 1966)	6	84	10	170
(Block *et al.* 1976)	6	94	–	230
(Sonnabend & Oh 1966)	7	93	–	237
(Winstock 1980)	8	83	9	9804*
(Linenberg *et al.* 1964)	9	80	11	110
(Wais 1958)	14	84	2	50
(Patterson *et al.* 1964)	14	84	2	510
(Nair *et al.* 1996)	15	50	35	256
(Simon 1980)	17	54	23	35
(Stockdale & Chandler 1988)	17	77	6	1108
(Lin *et al.* 1991)	19	–	81	150
(Nobuhara & Del Rio 1993)	22	59	19	150
(Baumann & Rossman 1956)	26	74	–	121
(Mortensen *et al.* 1970)	41	59	–	396
(Bhaskar 1966)	42	48	10	2308
(Spatafore *et al.* 1990)	42	52	6	1659
(Lalonde & Luebke 1968)	44	45	11	800
(Seltzer *et al.* 1967)	51	45	4	87
(Priebe *et al.* 1954)	55	46	–	101

Table adapted from (Nair *et al.* 1996) * Number of operations performed. The author does not explicitly say whether all the 9804 biopsies were subjected to histopathological diagnosis.

epithelialized lesions, part of the specimens can give the appearance of epithelium-lined cavities that do not exist in reality. Seltzer *et al.* (1967) defined a typical radicular cyst as one in which 'a real or imagined lumen was lined with stratified squamous epithelium'. It should be pointed out that the photomicrographic illustrations in many studies (Bhaskar 1966, Lalonde & Luebke 1968) represent only magnified views of selected small segments of epithelialized lesions. They are not supported by overview pictures of lesser magnifications of sequential sections derived from different axial planes of the lesions in question. The discrepancy in the reported incidence of periapical cysts is most probably due to the difference in the histopathological interpretation of the sections. When the histopathological diagnosis is based on random or limited number of serial sections, most epithelialized periapical lesions would be wrongly classified as radicular cysts. This assumption is strongly supported by the results of a most recent study (Nair *et al.* 1996) in which an overall 52% of the lesions (n = 256) were found to be epithelialized but only 15% were actually periapical cysts.

There are 'cysts and cysts'

In routine histopathological diagnostic work the structure of a radicular cyst in relation to the root canal of the affected teeth has not been taken into account. The major reason for this has been the nature of the biopsy itself. Apical specimens removed by curettage do not contain the root-tips of the diseased teeth. Obviously, structural reference to the root canals of the affected teeth is not possible. Simon (1980) pointed out that there are two distinct categories of radicular cysts namely, those containing cavities *completely enclosed in epithelial lining*, and those containing epithelium-lined *cavities that are open to the root canals*. Simon (1980) designated the latter 'bay cysts'. It seems that he observed only the large type of such lesions with voluminous cavities into which the root apices of the affected teeth appeared to protrude. The photomicrographs in the publication reveal severe damage of the microanatomical relationship between the root apices and the cyst-epithelia. Furthermore, they do not represent axial sections passing through the root canal. These factors might have influenced critics to wonder whether the 'bay cysts' (Simon 1980) are histological artefacts. More recently, (Nair *et al.* 1996) analyzed 256 periapical lesions obtained with extracted teeth. The specimens were processed by modern plastic-embedding technique and meticulous serial or step-serial sections were prepared and evaluated based on predefined histopathological criteria. Out of the 256 specimens 35% were found to be 'periapical abscess', 50% were periapical granulomas and only 15% were periapical cysts. Equally significant was the finding that two distinct classes of radicular cysts – the *apical true cysts*, with cavities completely enclosed in epithelial linings and the *apical pocket cysts*, with cyst-lumina open to the root canals – occur at the periapex when the lesions were analyzed in relation to the root canals. An overall 9% of the 256 lesions were apical true cysts and 6% were periapical pocket cysts.

Periapical true cyst

The periapical true cyst may be defined as a chronic inflammatory lesion at the periapex that contains an epithelium lined, closed pathological cavity (Fig. 1). The pathogenesis of radicular cysts, presumably the true cysts, has been discussed by various authors (Thoma 1917, Rohrer 1927, Gardner 1962, Shear 1963, Main 1970, Ten Cate 1972, Torabinejad 1983). An apical cyst is considered to be a direct sequel to apical granuloma, although a granuloma need not always develop into a cyst. Due to still unexplainable reasons only a small fraction (< 10%) of the periapical lesions advance

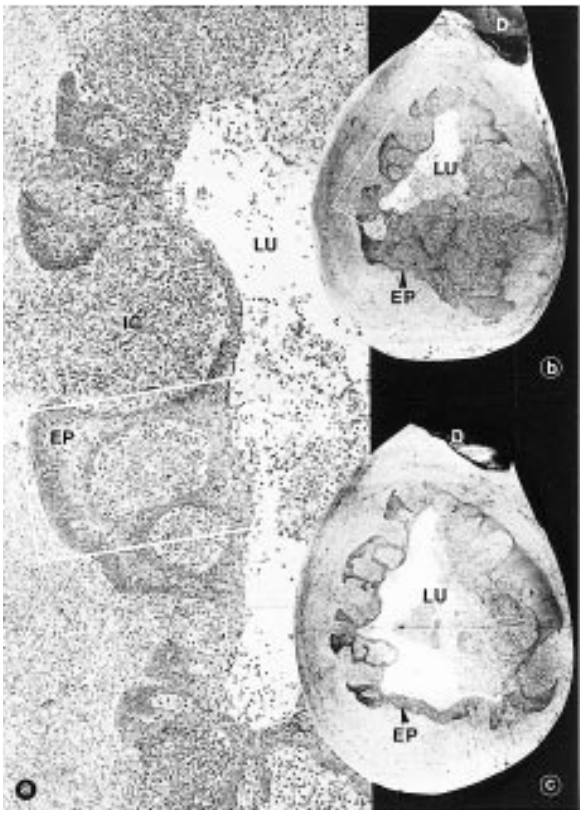

Fig. 1 (a) Periapical true cyst. Two sequential sections derived from different axial planes (b, c) from the same lesion. Note the lumen (LU) is completely enclosed in epithelium (EP). The rectangular demarcated area in (b) is magnified in (a). D dentine; IC infiltrate cells. Magnifications: a x130; b, c ×25.

into true radicular cysts (Sonnabend & Oh 1966, Simon 1980, Nair *et al.* 1996). The process of the true cyst formation has been discussed in three stages (Shear 1992). During the *first phase* the dormant cell-rests of Malassez begin to proliferate, probably under the influence of growth factors, cell mediators and metabolites that are released by various cells residing in the periapical lesion. During the *second phase* an epithelium lined cavity comes into existence. There are two main theories regarding the formation of the cyst cavity: (i) the 'nutritional deficiency theory' is based on the assumption that the central cells of the epithelial strands get removed from their source of nutrition and undergo necrosis and liquefactive degeneration (James 1926, Hill 1930, Tratman 1939, Ten Cate 1972). The accumulating products in turn attract neutrophilic granulocytes into the necrotic area. Such microcavities containing degenerating epithelial cells, infiltrating mobile cells and tissue fluid coalesce to form the cyst cavity lined by stratified epithelium, (ii) the 'abscess theory' postulates that the proliferating epithelium lines an abscess cavity formed by tissue necrosis and lysis because of the inherent nature of the epithelial cells to cover exposed connective tissue surfaces (McConnell 1921, Summers 1974). During the *third phase* the cyst grows the exact mechanism of which is still unknown. It is generally believed to be by osmosis. The presence of necrotic tissue in the cyst lumen attracts neutrophilic granulocytes, which extravasate and transmigrate through the epithelial lining (Fig. 2) into the cyst cavity where they perish. The lytic products of the dying cells in the cyst-lumen release a greater number of molecules. As a result the osmotic pressure of the cyst fluid rises to a level higher than that of the tissue fluid (Toller 1970). The latter diffuses into the cyst cavity so as to raise the intraluminal hydrostatic pressure well above the capillary pressure. The increased intracyst pressure may lead to bone resorption and expansion of the cyst. However, the fact that an apical pocket cyst with lumen open to the necrotic root canal can become larger (Nair *et al.* 1996, Nair 1997) would eliminate osmotic pressure as a potential factor in the development of radicular cysts. On the

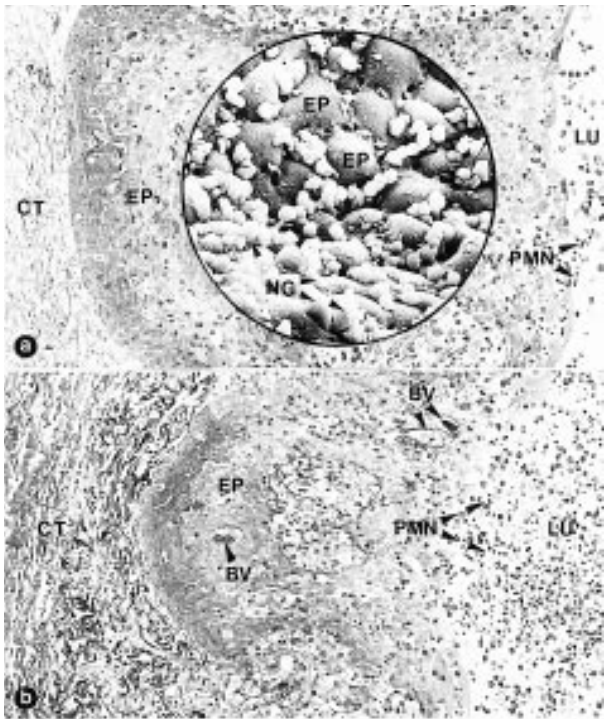

Fig. 2 Transmigration of neutrophilic granulocytes (PMN) across the epithelial wall (EP) of the cyst lumen (LU). (a) Represents magnified view of the rectangular area demarcated in Fig. 1(a). Inset in (a) is an intramural scanning electron microscopic view of a cyst wall. Note the flat epithelial cells (EP) and the globular nutrophilic granulocytes (NG). The latter emerge through the interepithelial spaces into the cyst lumen. CT, connective tissue; BV, blood vessels. Magnifications: a, b ×330; *inset* x670.

other hand, there is increasing evidence in support of a molecular mechanism for cyst expansion (Nair 1997). The macrophages (Nair 1997) and T-lymphocytes (Torabinejad & Kettering 1985) in the cyst wall may provide a continuous source of bone resorptive metabolites (Formigli *et al.* 1995) and cytokines. The presence of effector molecules such as matrix metalloproteinase-1 and –2 have also been reported in the cyst walls (Teronen *et al.* 1995).

Periapical pocket cyst

The periapical pocket cyst is a radicular cyst containing an epithelium-lined pathological cavity which is open to the root canal of the affected tooth (Fig. 3). As has been mentioned previously such lesions were originally described as 'bay cysts' (Simon 1980) and has been recently investigated in detail and renamed as the 'periapical pocket cysts' (Nair *et al.* 1996). It is postulated that a pocket cyst is initiated by a small bubble-like extension of the infected root canal space into the periapex. The microluminal space is enclosed in a stratified squamous epithelium which grows and forms an epithelial collar (Fig. 3c) around the root tip. The epithelial collar forms an 'epithelial attachment' (Nair & Schroeder 1985) to the root surface so as to seal off the infected root canal and the microcystic lumen from the periapical milieu. The presence of micro-organisms in the apical root canal attracts neutrophilic granulocytes by chemotaxis into the microlumen. However, the pouch-like lumen – biologically outside the body milieu – acts as a 'death trap' and 'garbage bag' to the externalized and dying neutrophils. As the necrotic tissue and microbial products accumulate, the sac-like lumen enlarges to accommodate the debris to form a voluminous diverticulum of the root canal space into the periapical area (Fig. 3c). It has been pointed out (Nair *et al.* 1996) that from the pathogenic, structural, tissue dynamic and host-beneficial and protective stand points, the epithelium-lined pouch-like extension of the root canal space of such lesions has much in common with a marginal periodontal pocket so as to justify the terminology of 'periapical pocket cyst' as against a biologically meaningless nomenclature of 'bay cyst' (Simon 1980).

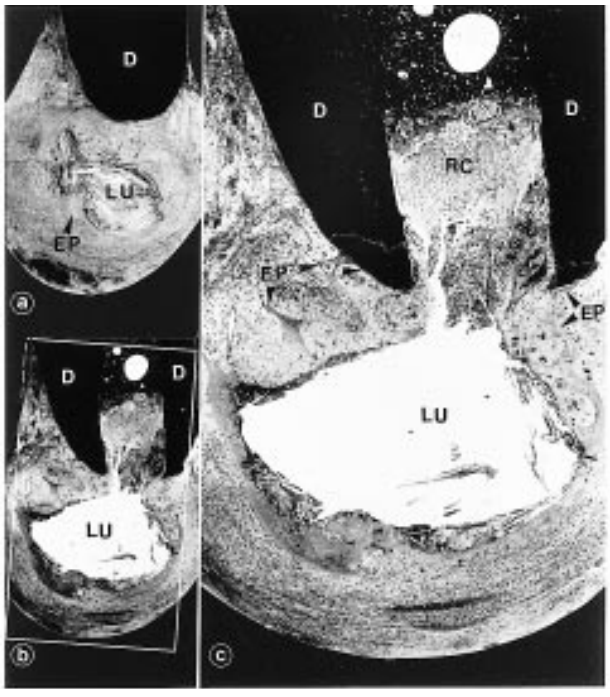

Fig. 3 Periapical pocket cyst. Axial sections passing peripheral to the root canal (a) give the false impression of the presence of a cyst lumen (LU) completely enclosed in epithelium. Sequential section passing through axial plane of the root canal (RC) clearly reveals the continuity of the cystic lumen with the root canal (RC). The rectangular area in (b) is magnified in (c). Note the pouch-like lumen (LU) of the pocket cyst with the epithelium (EP) forming a collar at the root apex. Magnifications: a, b ×21; c ×50.

Do radicular cysts heal?

The prevalence of two distinct classes of radicular cysts and the low incidence of true cysts (< 10%) amongst periapical lesions has much significance in oral surgery and clinical endodontics. Oral surgeons generally hold the view that cysts do not heal and have to be removed by surgery. It should be pointed out with emphasis that – in spite a recent claim (Shrout *et al.* 1993) – periapical lesions cannot be differentially diagnosed into cystic and noncystic lesions based on radiographic evidence alone (Priebe *et al.* 1954, Baumann & Rossman 1956, Wais 1958, Linenberg *et al.* 1964, Bhaskar 1966, Lalonde 1970, Mortensen *et al.* 1970). However, routine histopathological diagnostic laboratories and publications based on reviewing such reports perpetuate the notion that nearly half of all periapical lesions are radicular cysts. As a result a disproportionately large number of surgical interventions are done at the tooth-apex to 'enucleate' lesions that are diagnosed clinically as cysts. In fact studies based on meticulous serial sections have shown that the incidence of true radicular cysts is less than 10% of all periapical lesions (Sonnabend & Oh 1966, Simon 1980, Nair *et al.* 1996). This would imply that most of the cases in which apical surgery has been performed based on radiographic diagnosis of the presence of cysts might have resolved by conventional root canal therapy.

On the other hand, many clinicians are of the opinion that a great majority of cysts heal after conventional root-filling-therapy. A 'success rate' of 85–90% has been recorded by many practitioners and endodontic investigators (Staub 1963, Kerekes & Tronstad 1979, Barbakow *et al.* 1981, Sjögren *et al.* 1990). However, the histological status of any apical radiolucent lesion at the time of treatment is unknown to the clinician and he/she is unaware of the differential diagnostic status of the 'successful' and 'failed' cases. However, most of the cystic lesions must heal in order to account for the 'high success rate' after conventional root canal treatment and the observed 'high incidence' of radicular cysts. We have already seen how several investigators listed in Table 1 reached the erroneous conclusion of high cyst-incidence based on incorrect diagnosis of epithelialized periapical lesions.

The clinical impact of the structural difference between the apical true cysts and the apical pocket cysts should also be considered. The aim of conventional root canal therapy has been the elimination of infectious agents from the root canal and the prevention of reinfection by obturation. A periapical pocket cyst is, likely therefore, to heal after conventional root canal therapy (Simon 1980). The tissue dynamic of a true cyst is *self-sustaining* however, as the lesion is no longer dependent on the presence or absence of irritants in the root canal. Therefore, true cysts, particularly the large ones, are less likely to be resolved by conventional root canal therapy (Fig. 4). This has been clearly shown in a longitudinal follow-up of a case (Nair *et al.* 1993).

The low incidence of periapical cysts and the existence of two distinct classes of cystic lesions at the periapex call for a rethinking of the rationale behind some of the diagnostic and therapeutic procedures currently practised in oral surgery and clinical endodontics such as: (i) routine histopathological examination of periapical lesions removed by curettage, (ii) performing disproportionately large numbers of apical surgery based on radiographic diagnosis of a periapical lesion as a radicular cyst, (iii) the widely held notion amongst endodontists that a large majority of cysts heal after conventional root filling therapy and (iv) the decision to re-treat an asymptomatic, post-therapeutically persisting periapical lesion instead of adopting apical surgery as the treatment of choice under those clinical circumstances.

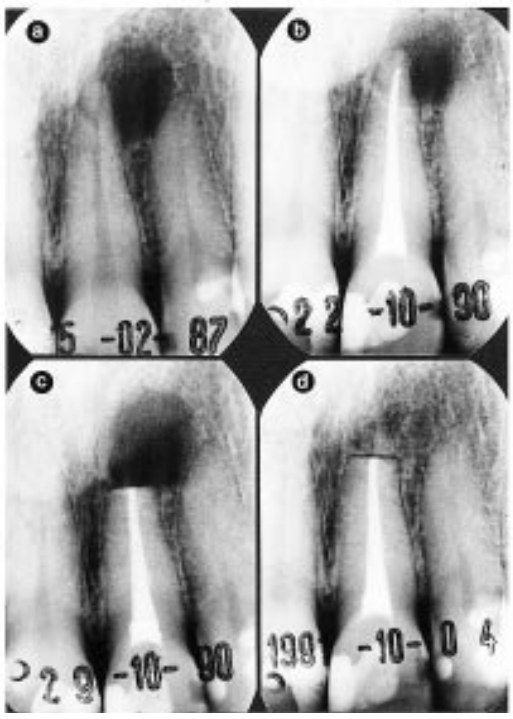

Fig. 4 Longitudinal radiographs of a periapically affected central maxillary incisor of a 37-year-old woman for a period of 4 years and 9 months. Note the large radiolucent asymptomatic lesion before (a), 44 months after root-filling (b), and immediately after periapical surgery (c). The periapical area shows distinct bone healing 1 year post-operatively. Histopathological examination of the surgical specimen by modern tissue processing and step-serial sectioning technique has confirmed that the lesion was a true radicular cyst. (Selected radiographs from P.N.R. Nair *et al.* Int Endod J 1993, **26:**225–233).

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