Vol. 81 No. 1 January 1996

ORAL SURGERY
ORAL MEDICINE
ORAL PATHOLOGY

ENDODONTICS

Editor: Richard E. Walton

Types and incidence of human periapical lesions obtained with extracted teeth

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Objectives. To determine (1) the frequency of the incidence of abscess, granuloma, and radicular cyst among human periapical lesions obtained with extracted teeth; and (2) whether periapical cysts occur in two categories when histologically analyzed in relation to the root canals.
Study design. A total of 256 lesions were analyzed. The specimens were decalcified and embedded in plastic. Serial sections or step-serial sections were prepared, and the sections were evaluated on the basis of predefined histopathologic criteria.
Results. The 256 specimens consisted of 35% periapical abscess, 50% granuloma, and 15% cysts. The latter occurred in two categories, the *apical true cysts* and the *apical pocket cysts.*
Conclusions. These results show (1) the low incidence of radicular cysts among periapical lesions as against the widely held view that almost half of all periapical lesions are cysts; and (2) the occurrence of two classes of radicular cysts. We are of opinion that the pocket cysts may heal after root canal therapy but the true cysts are less likely to be resolved by conventional root canal treatment.
(ORAL SURG ORAL MED ORAL PATHOL ORAL RADIOL ENDOD 1996;81:93-102)

Apical periodontitis is primarily initiated and in most cases maintained by microorganisms living in the apical root canals of the affected teeth.[1-6] Some of these lesions contain epithelial cells[7-18] that are believed to be derived from the cell rests of Malassez.[7, 19] It is postulated that these cells serve as the source of the epithelium that line the cavities of lesions that have developed into radicular cysts. Studies indicate[20-23] that conventional root canal treatment leads to the radiographic disappearance of 85% to 90% of apical radiolucencies or to a marked reduction in the size. On the basis of these clinical observations and some histopathologic diagnostic studies,[24-27] it has been assumed that most cystic lesions at the periapex heal after conventional endodontic treatment. In contrast, some oral surgeons maintain that cysts do not heal and have to be surgically removed.[28]

The histopathologic structure of the apical cysts in relation to the root canal of the affected teeth is of particular importance. Simon[29] described the morphologic aspect and the clinical relevance of certain types of periapical cysts. He discovered two distinct categories of radicular cysts, namely those containing cavities completely enclosed in epithelial lining or *true cysts*, and those containing epithelium-lined cavities that are open to the root canals. Simon[29] designated the latter *bay cysts*. Apparently, he encountered only the larger variety of such lesions with large cavities into which the root apices of the affected teeth appeared to protrude. This might have been only coincidence because of the small sample-size of his study (n = 35). Further, the published photomicrographs reveal severe damage of the topographic rela-

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Received for publication April 27, 1995; returned for revision June 28, 1995 and June 21, 1995; accepted for publication Aug. 24, 1995.

1079-2104/96/$5.00 + 0 **7/15/68938**

Table I. Incidence of radicular cysts among periapical lesions

Reference	*Cysts (%)*	*Granuloma (%)*	*Others (%)*	*Total lesions (n)*
Sommer[35]	6	84	10	170
Block et al.[48]	6	94	—	230
Sonnabend and Oh[11]	7	93	—	237
Winstock[28]	8	83	9	9804*
Linenberg et al.[40]	9	80	11	110
Wais[39]	14	84	2	50
Patterson et al.[49]	14	84	2	510
Simon[29]	17	54	23	35
Stockdale & Chandler[50]	17	77	6	1108
Lin et al.[36]	19	—	81	150
Nobuhara and Del Rio[51]	22	59	19	150
Baumann and Rossman[38]	26	74	—	121
Mortensen et al.[42]	41	59	—	396
Bhaskar[25]	42	48	10	2308
Spatafore et al.[52]	42	52	6	1659
Lalonde and Luebke[27]	44	45	11	800
Seltzer et al.[26]	51	45	4	87
Priebe et al.[24]	55	46	—	101

*Number of operations performed. The author does not explicitly say whether all the 9804 biopsies were subjected to histopathologic diagnosis.

tionship between the root apices and the cyst-epithelia that might have influenced critics to wonder whether the concept of bay cyst[29] was based on histologic artifacts. Simon's findings have not hitherto been confirmed by independent researchers. Also, the prevalence of radicular cysts among periapical lesions continues to be a point of disagreement among clinicians and investigators (Table I), probably because of different methods of obtaining samples and of varying histologic interpretations.

The objectives of this study therefore were (1) to determine the frequency of incidence of abscess, granuloma, and radicular cysts among human periapical lesions obtained with extracted teeth, and (2) to determine whether or not periapical cysts occur in two morphologically distinct categories when histologically analyzed in relation to the root canals of the affected teeth.

MATERIAL AND METHODS

The specimens

The material consisted of 256 human periapical lesions obtained together with carefully extracted teeth that were radiographically diagnosed as presenting apical periodontitis with nonvital pulps. They originated from the Dental Surgical Polyclinic of the University of Zurich primarily during the period of 1993 and 1994 and were obtained by consecutive collection of all extracted teeth with attached periapical lesions. The 256 specimens represented an unknown fraction of all the teeth extracted with radiolucent periapices during the period of collection of the specimens. Most of the teeth were extracted because of indications such as extensive caries and coronal damage, breakdown of the marginal periodontium, and nonstrategic value of the teeth. However, all the marginal periodontitis-influenced periapical lesions were excluded from the study. Few teeth were recorded as symptomatic (pain, swelling, and sensitivity to percussion); this is explainable because most of the specimens originated from teeth with carious crowns and open pulp chambers.

Tissue processing

Immediately after extraction, the teeth with the attached periapical lesions were fixed by immersion for several weeks in half-strength Karnovsky's[30] fixative (2% paraformaldehyde and 2.5% glutaraldehyde buffered in 0.02 M (molar) sodium cacodylate). Thereafter the apical third of the affected roots with the lesions were severed with a diamond-coated disk operated on a custom-made miniature lathe. The specimens were further processed either by embedding in Epon or in 2-hydroxypropyl methacrylate (HPMA). The two methods were adopted because the former would allow the specimens to be investigated by transmission electron microscopy, but the latter would not. However, no such investigation became necessary to achieve the aims of this study.

Epon embedding and processing. The smaller of the lesions with the root apices were decalcified in a solution of 0.15 M ethylenediamine tetraacetic acid (Titriplex, Merck, Darmstadt, Germany) and 4% glutaraldehyde supplemented with sucrose for several weeks. After decalcification the lesions were subdivided into about 0.5-mm slices in the axial plane of the tooth, with a sharp razor blade and a Wild M-5 stereomicroscope (Wild, Heerbrugg, Switzerland). The tissue blocks were then washed overnight in 0.185 M sodium cacodylate buffer (pH 7.4; 360 mOsm) and treated for 3 hours in 1.33% of osmium tetroxide buffered in 0.067 s-collidine,[31] dehydrated in ascending grades of ethanol and embedded in Epon.[32] From each Epon block, 1 to 2 μm thick survey sections and from selected blocks serial sections were prepared with glass or histodiamond knives and the Ultracut E microtome (Reichert Jung, Vienna, Austria). The sections were stained in periodic acid-Schiff and methylene blue-Azur II stains.[33]

HPMA embedding and processing. The larger lesions were demineralized in an aqueous solution consisting of a mixture of 22.5% (vol/vol) formic acid and 10% (wt/vol) of sodium citrate for about 2 weeks, washed thoroughly in cold running tap water, and

Table II. Classification and incidence of the periapical lesions

	Class of lesion	*HPMA**	*EPON†*	*Total*	*%*
I	Periapical abscess	—	—	—	35
	Epithelialized abscess	20	16	36	14
	Nonepithelialized abscess	24	30	54	21
II	Periapical granuloma	—	—	—	50
	Epithelialized granuloma	22	36	58	23
	Nonepithelialized granuloma	33	36	69	27
III	Periapical cysts	—	—	—	15
	Apical true cyst	10	14	24	9
	Apical pocket cyst	8	7	15	6
Total		117	139	256	100

*Embedded in HPMA and meticulously serial sectioned.
†Embedded in EPON and step-serial sectioned.

stored overnight in 0.185 M sodium cacodylate buffer. The specimens were then divided into two halves in the axial plane, dehydrated in ascending grades of ethanol, and embedded in HPMA.[34] [HPMA should be acid-free or of the low-acid variety (SPI supplies, Division of Structure Probe Inc, West Chester, Pa.)]. Polymerization was optimized in an atmosphere of nitrogen gas at 4° C in a pressure-container. Thereafter, each HPMA-embedded tissue block was serial sectioned into 5 to 7 μm thick sections with glass knives and the Supercut 2050 microtome (Reichert Jung, Vienna, Austria). From the smaller of the HPMA-embedded lesions every 10th and 11th sections and from the larger of the lesions every 15th and 16th sections were selected and stained in Toluidine blue.

Criteria of classification

The histologic categorizations of the lesions were based on the distribution of inflammatory cells within the lesions and presence or absence of epithelial cells. Also determined was whether the lesions had developed into cysts and, if so, what was the relationship of the cyst-cavities to the apical foramina and canals.

Nomenclature and definitions

Both the Epon and HPMA sections were evaluated with light microscopy; the inflammatory lesions were diagnosed and classified according to the following histopathologic definitions: *Periapical abscess* is a focus of acute inflammation characterized by the presence of a distinct collection of polymorphonuclear leukocytes (PMN) within an already existing chronic granuloma. Depending on the presence or absence of epithelial strands, these lesions were further subdivided into epithelialized and nonepithelialized abscesses. *Periapical granuloma* is chronic inflammation that consists of a granulomatous tissue that is predominantly infiltrated with lymphocytes, plasma cells, and macrophages. These lesions may be epithelialized or nonepithelialized.

Periapical cysts. Periapical true cyst is an apical inflammatory lesion with a distinct pathologic cavity completely enclosed in an epithelial lining so that no communication to the root canal exists. *Periapical pocket cyst* is an apical inflammatory lesion that contains a sac-like, epithelium-lined cavity that is open to and continuous with the root canal.

RESULTS

The 256 periapical lesions revealed 35% were periapical abscesses, 50% were periapical granulomas, and 15% were periapical cysts (Table II). Irrespective of the histologic status of the specimens, 52% of the lesions were epithelialized and the remaining 48% were non-epithelialized.

Periapical abscess

A total of 90 lesions were found to be abscessed; 36 (40%) were epithelialized and 54 (60%) were nonepithelialized (Fig. 1). In almost all cases that were classified as apical abscess, the areas of acute inflammation were embedded in preformed granulomas that predominantly contained lymphocytes and plasma cells.

Periapical granuloma

A total of 127 of the 256 lesions were granulomas (Table II); 69 (55%) were nonepithelialized (Fig. 2, *A*), and 58 (45%) were epithelialized (Fig. 2, *B*). In epithelialized granulomas, strands of epithelium could be observed to exist at random throughout the lesions. In some instances the epithelium appeared to grow into the canals so as to form epithelial plug-like structures at the apical foramina (Fig. 2, *B* and *C*). The arcading epithelium within the body of the lesion usually enclosed islands of granulomatous tissue that

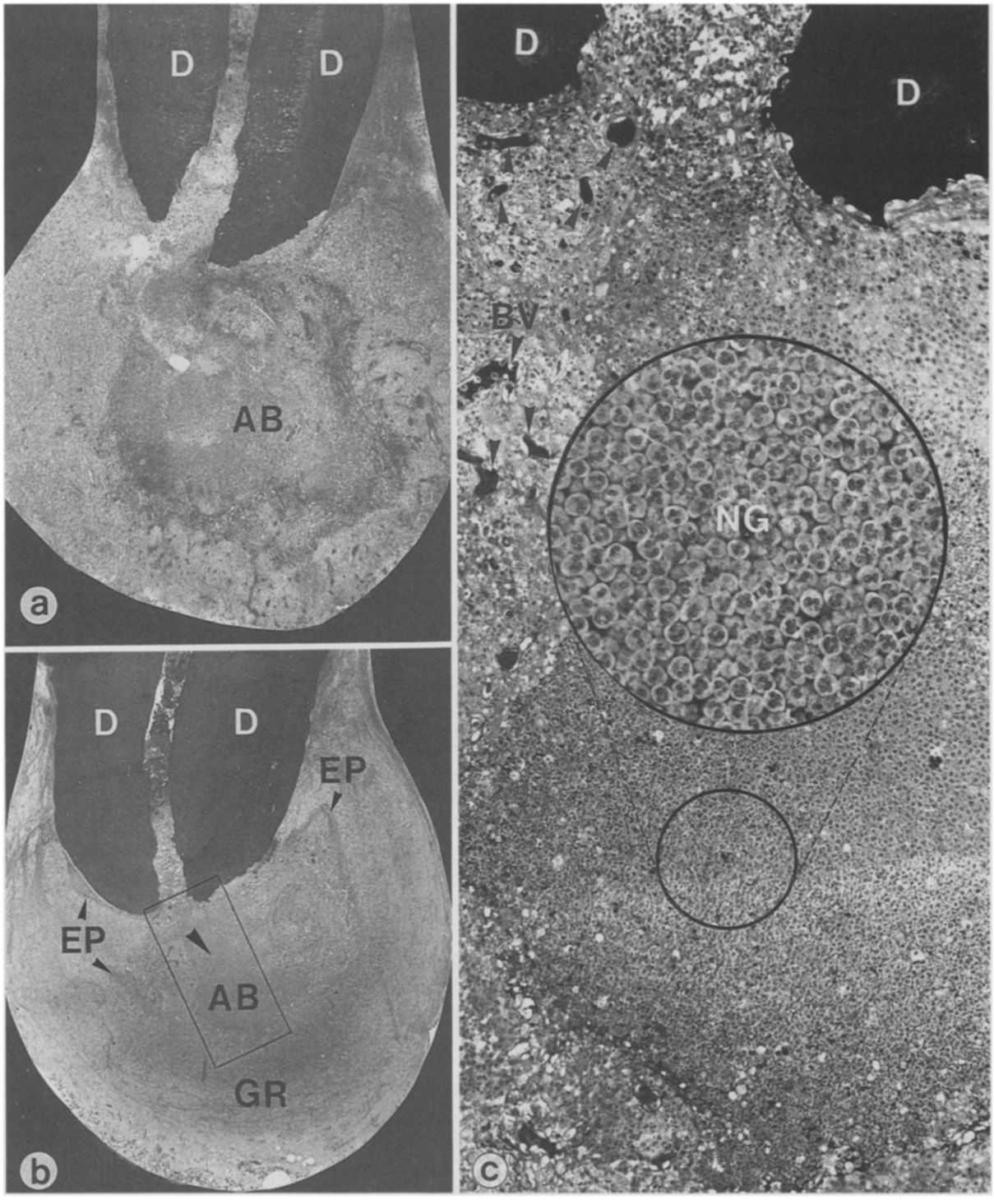

Fig. 1. A, Nonepithelialized and **b,** epithelialized microabscess at periapex. Demarcated area in **B** is magnified in **C** and as is the *inset* in **C**. Note the microabscess *(AB)* consisting of dense accumulation of neutrophilic granulocytes *(NG)*. (D = dentin, GR = granuloma, BV = blood vessels, EP = epithelium.) (Original magnifications: **A,** ×25, B × 20, C × 130, *inset* × 660.)

contained numerous lymphocytes and plasma cells. These islands were usually rich in vasculature as evidenced from the presence of numerous profiles of sectioned blood vessels (Fig. 2, *B*). Although the infiltrated tissue of the granulomas seldom revealed the presence of extravascular PMN, the epithelial strands of the lesions invariably contained numerous transmigrating PMN.

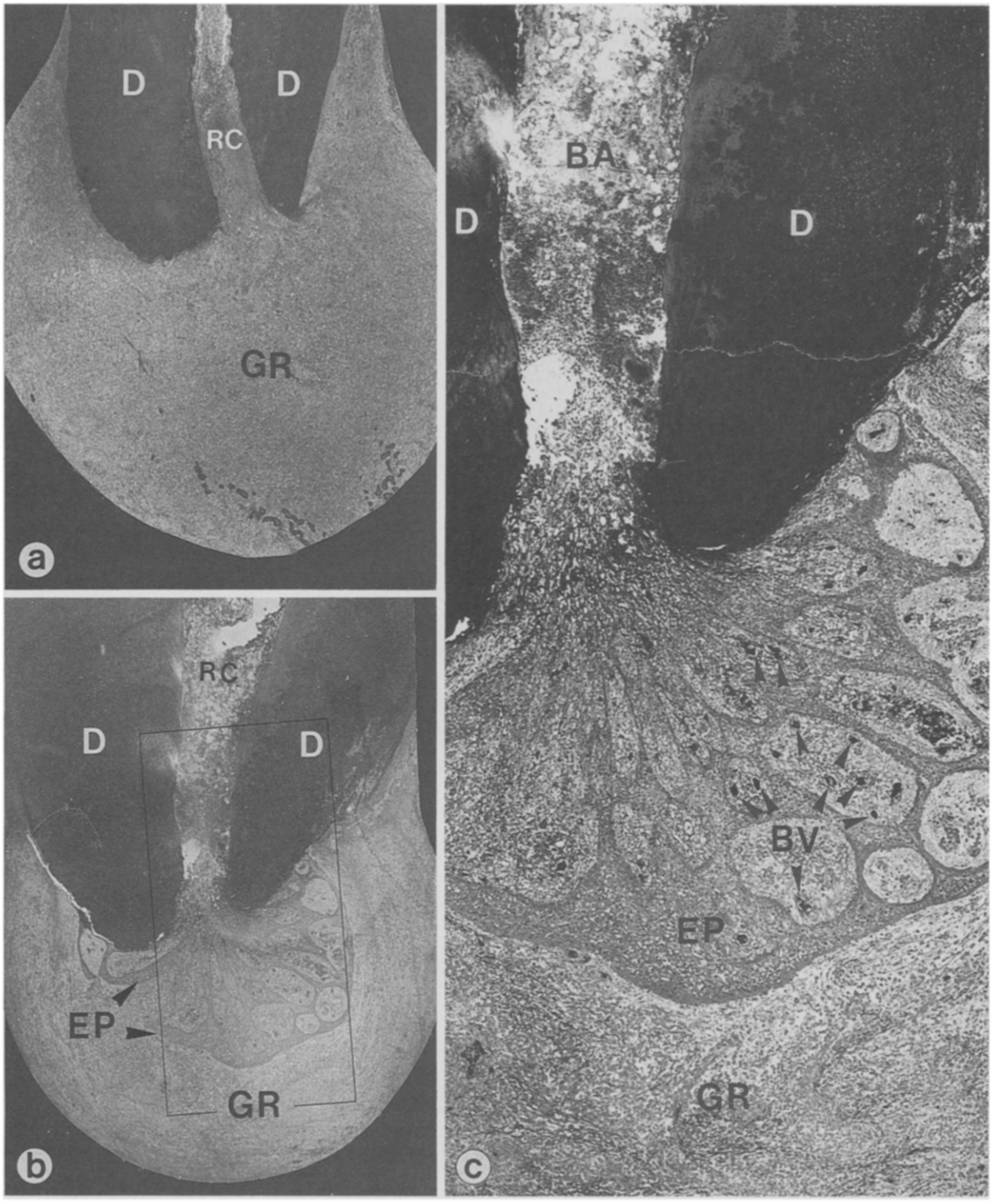

Fig. 2. A, Nonepithelialized and **B** epithelialized granulomas *(GR)* at periapex. Note the epithelial strands *(EP)* in the latter. Demarcated area in **B** is magnified in **C**. (RC = root canal, BA = bacteria, D = dentin, BV = blood vessels.) (Original magnifications: **A** × 25, **B** × 20, **C** × 60.)

Periapical cysts

Of the 256 lesions, a total of 39 (15%) were classified as cysts. Twenty-four (61%) of the cystic lesions fulfilled the criteria for true cysts; the remaining 15 (39%) revealed structural features that would characterize them as periapical pocket cysts.

True cysts

The cyst cavities contained necrotic cells in varying stages of degradation (Fig. 3, *A* and *B*) and in some instances the presence of cholesterol clefts were observed (Fig. 3, *C*). The epithelial walls of the cyst-cavities showed great regional variation in thick-

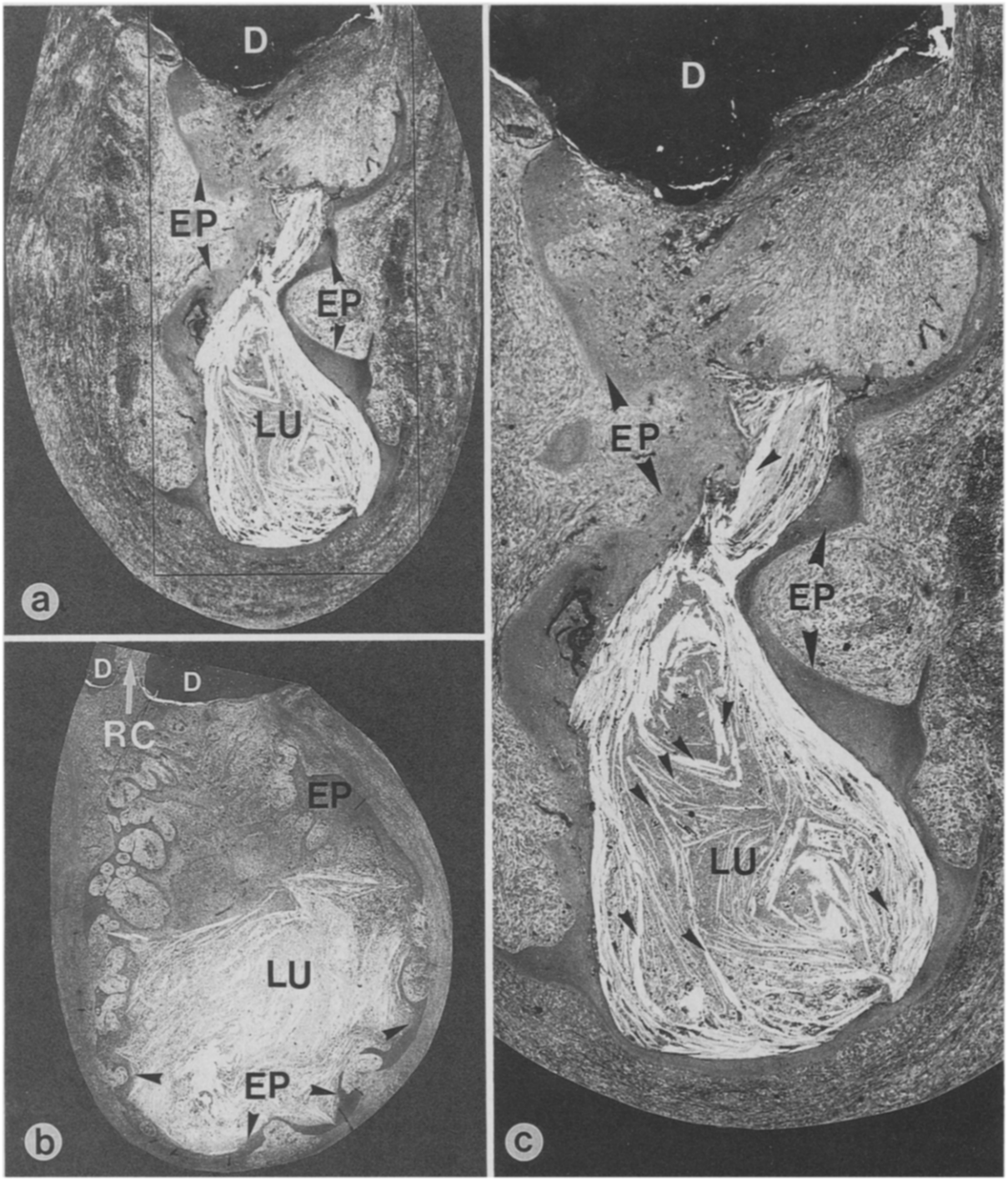

Fig. 3. A and **B,** Periapical true cysts. Cyst lumina *(LU)* are completely enclosed in stratified squamous epithelium *(EP).* Note absence of any communication of the cyst lumen with the root canal (*RC* in **B**). Demarcated area in **A** is magnified in **C.** *Arrowheads* in **C** indicate cholesterol clefts. (Original magnifications: **A** × 30, **B** × 17, **C** × 60.)

ness (Fig. 3, *C*), contained numerous transmigrating PMN, and were surrounded by narrow rims of connective tissue that blended with the collagenous capsules.

Pocket cysts

In some pocket cysts (Fig. 4, *A, inset*) the lumina were small and appeared as bubble-like extensions of the root canal spaces into the periapical region. The

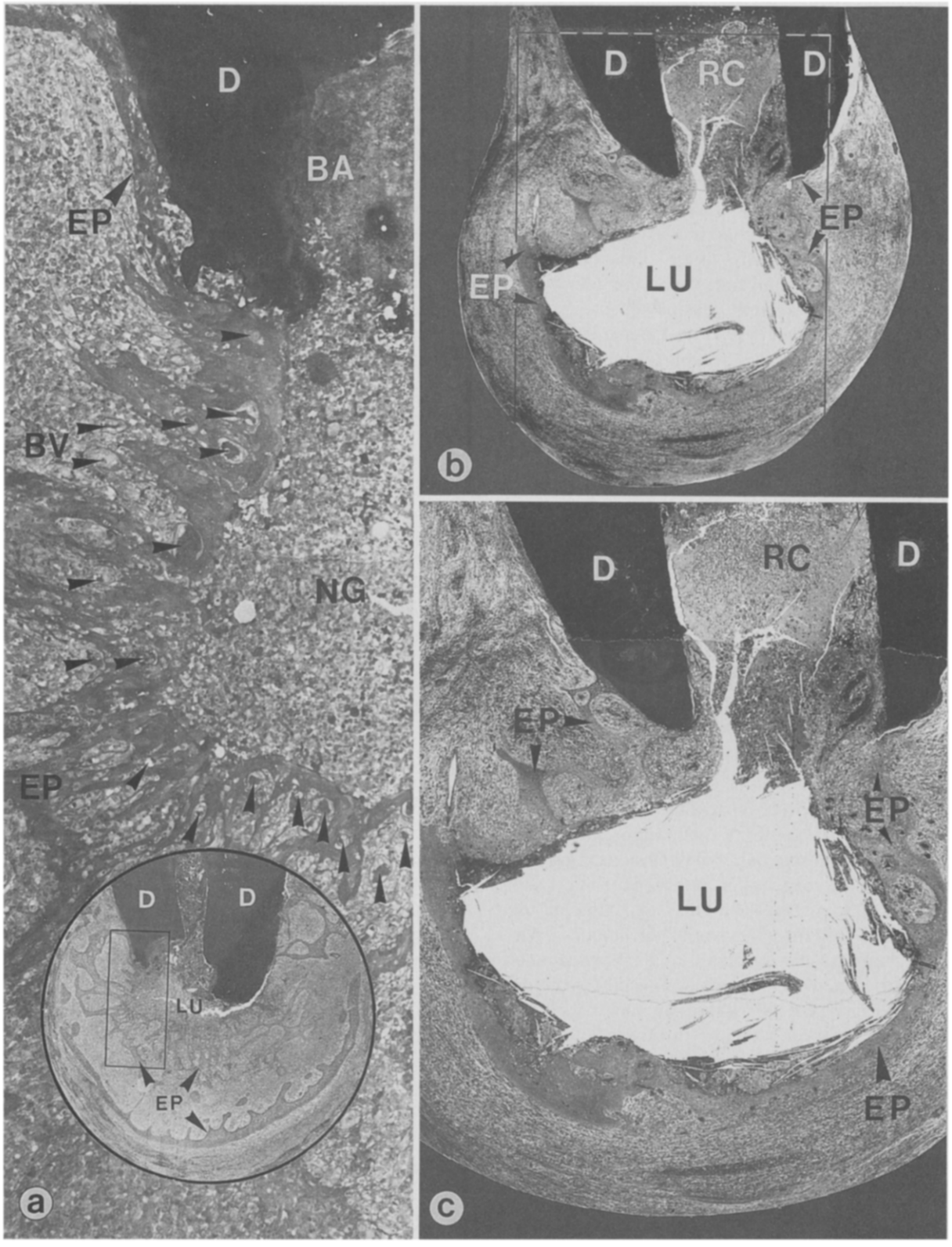

Fig. 4. Periapical pocket cysts. An initial (inset in **A**) and an established **(B)** apical pocket cyst. Composites **A** and **C** are magnified views of the demarcated areas in the *inset* in **A** and in **B,** respectively. Note the continuity of the root canals *(RC)* with the cyst lumina *(LU)* that are surrounded by epthelial linings *(EP)*. (D = Dentin, BV = blood vessels, BA = bacteria.) (Original magnifications: **A** × 132, *inset* × 10, **B** × 25, **C** × 42.)

microluminal spaces were enclosed by epithelial linings that grew onto the outer surface of the root-tip (Fig. 4, *A*) to form epithelial collars. The latter appeared to adhere closely to the root tip so as to seal off the lumen from the rest of the periapex. The stratified squamous epithelial walls of the microcavities formed folds of evaginations on the basal-cell side to form a rete ridge-like pattern. The ridges often branched and reunited to form epithelial networks enclosing islands of granulomatous tissue. These islands and the subepithelial tissue were richly vascularized and densely infiltrated with nongranulocytic leukocytes, predominantly plasma cells.

Some apical pocket cysts (Fig. 4, *B* and *C*) revealed large central cavities that occupied a substantial volume of the lesions. The epithelium-lined lumen was clearly continuous to the root canal and was always sealed off from the rest of the periapical lesion by a distinct epithelial collar attached to the root tip.

DISCUSSION

This study provides new data on the prevalence of cysts among human periapical lesions obtained with extracted teeth that would challenge the notion perpetuated by several authors that nearly half of all periapical lesions are radicular cysts. It also provides morphologic evidence in support of the existence of two distinct classes of radicular cysts namely, the periapical true cysts and the periapical pocket cysts.

The reported incidence of radicular cysts among human periapical lesions varies from 6% to 55% (Table I). An accurate histopathologic diagnosis of radicular cysts is possible only through serial sectioning or step-serial sectioning of the lesions removed in toto. From the long list of authors in Table I, only Sommer,[35] Sonnabend and Oh,[11] and Simon[29] used either one of those essential techniques. Most investigators (Table I) analyzed biopsy specimens obtained from wide sources for routine histologic reports. The statistically impressive number of 2308 lesions in Bhaskar's study[25] originated from 314 contributors and the 800 biopsies of Lalonde and Luebke[27] were obtained from 134 sources. Such diagnostic specimens, often derived through apical curettage, do not represent lesions in toto. For routine histologic diagnosis there may be fiscal restrictions to subject the specimens to complete serial or step-serial sectioning procedures. In random or a limited number of serial sections[36] from fragmented and epithelialized lesions, parts of the specimens can give the appearance of epithelium-lined cavities that might not exist in reality. For instance, Seltzer et al.[26] described a typical radicular cyst as one in which "a real or imagined lumen was lined with stratified squamous epithelium." It is relevant that the illustrations provided by Bhaskar[25] and several other investigators are only high-power views of small segments of epithelialized lesions. Low-power magnifications are missing. The vast discrepancy in the reported incidence of periapical cysts is probably because of the difference in the microscopic interpretation of the specimens. In the absence of serial or step-serial sectioning of the specimens, a substantial number of epithelialized periapical lesions might have been inappropriately categorized as radicular cysts. This possibility is strongly supported by the present data (Table II) that shows that 52% of the lesions were epithelialized but only 15% were actually periapical cysts.

These observations have significant relevance in clinical endodontics and oral surgery. Contrary to a recent claim,[37] periapical lesions cannot be differentially diagnosed into cystic and noncystic lesions on the basis of radiographs alone.[24, 25, 38-42] Nevertheless, many clinicians maintain that most cysts heal after conventional root canal therapy.[43] This notion depends largely on deductive logic. Several studies (Table I) have reported more than 40% of cyst-incidence among periapical lesions. As has been pointed out earlier, a success rate of 85% to 90% has been recorded by many clinicians and endodontic investigators.[20-23] But the histologic status of any apical radiolucent lesion at the time of treatment is unknown, and the clinician is unaware of the differential diagnostic status of the successful and failed cases. However, most of the cystic lesions must heal to account for the high success rate after conventional endodontic treatment and the observed high incidence of radicular cysts. We have already discussed how Bhaskar[25] and several other investigators listed in Table I reached the erroneous conclusion on the high incidence of cysts on the basis of incorrect categorization of epithelialized periapical lesions.

The apical pocket cysts presented in this study were microanatomically intact with perfect continuity among the various structural components of the diseased periapices. The observed size gradient in the lumina of the cysts and the structural details of the lining epithelia are suggestive of different stages in the pathogenesis of these lesions. For instance, the one with a miniature lumen around the apical foramen (Fig. 4, *A*) may be in its initial stages of cystogenesis, whereas the lesion with a large cavity (Fig. 4, *B* and *C*) may be in its advanced stage of development. From the pathogenic, structural, tissue-dynamic, and host-beneficial standpoints, the pouch-like extension of the root canal space into the periapex appears to have

much in common with marginal periodontal pockets. It has been shown that the epithelium that comes in contact with the apical root surface forms an epithelial attachment[17] that seems to seal off the infected root canal and its apical pouch from the periapical milieu. Therefore, *periapical pocket cyst* may be a more appropriate term than the bay cyst originally used by Simon.[29] In this context it is interesting to note that cystic lesions with morphologic features identical to that of the pocket cysts described here have been experimentally induced in monkeys by Valderhaug[44, 45] in the 1970s. However, he neither differentiated nor interpreted the lesions in relation to the root canals of the involved teeth.

The influence should be considered as to the structural difference between the apical true cysts and the apical pocket cysts. In random nonaxial sections that do not pass through the root canal, a periapical pocket cyst will appear as a true cyst and will be categorized as such. A periapical pocket cyst is more likely to heal after root canal therapy.[29] On the other hand, the tissue dynamics of a true cyst is self-sustaining; the lesion no longer depends on the presence or absence of irritants in the root canal.[46] Therefore the true cysts (particularly the large ones) may be less likely to be resolved by root canal therapy. This has been shown recently in a long-term longitudinal follow-up of a case.[47]

CONCLUSIONS

The 256 periapical lesions removed in toto could be classified into periapical abscesses, periapical granulomas, and periapical cysts with proliferating epithelium present in 52% of these periapical lesions; 15% were identified as periapical cysts, 50% as granuloma, and 35% as periapical abscess.

Two distinct morphologic categories of cysts were identified on the basis of the relationship of the cavities to the apical foramen; 61% of the cystic lesions were classified as true cysts, and 39% were categorized as periapical pocket cysts.

We thank Mrs. Pauline Bobst, Mrs. Esther Keller, and Mrs. Monica Raess for excellent technical and photographic assistance.

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