Prognosis of initial endodontic therapy

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'Prognosis' is the forecast of the course of a disease. In the context of apical periodontitis, therefore, this term applies to both the time course and chances of healing.

Over the past 80 years, an extensive volume of studies has been amassed that focuses on the prognosis of apical periodontitis after endodontic therapy. Cumulatively, the authors of these studies have recorded, grouped, and analyzed data from thousands of treated cases. Two major reviews had summarized the state-of-the-art knowledge at different times – Strindberg (1) reviewed studies reported in the first half of the 20th century, and Friedman (2) reviewed studies reported from 1956 up to 1997. From those comprehensive reviews it has become obvious that the data pertaining to the prognosis of apical periodontitis after endodontic therapy is inconsistent and largely variable (2). Apparently, the wealth of available information is somewhat confused by the lack of standardization among the studies, with respect to material composition, treatment procedures, and methodology (2). Furthermore, certain clinical procedures performed in specific studies may no longer be relevant to the current practice of endodontics. Clearly, therefore, *undiscerning review of all the existing studies can be ineffective and even misleading.* For a review to yield reliable and valid information, it must focus on studies selected according to well-defined criteria. The purpose of this article is to review and discuss selected articles on the prognosis of initial endodontic therapy of apical periodontitis.

Diversity of studies

Studies that include teeth with apical periodontitis treated by initial endodontic therapy (1, 3–52) are listed in Table 1. As stated in the most recent review by Friedman (2), direct comparisons of the different studies are precluded by their diversity with regards to the following factors.

Composition of study material

Tooth type and number of roots

Several studies include only anterior or single-rooted teeth (5, 10, 12, 14, 29, 36, 43, 52), whereas others pool single- and multirooted teeth together. Results of a study can differ between single- and multirooted teeth, not just because of the increased difficulty of management but also because of differences in the definition of the unit of evaluation, the root or the whole tooth. When a multirooted tooth is evaluated as one unit and judged by the worst appearing root, the chance of observing persistent apical periodontitis is multiplied (40), whereas when each root is evaluated as an independent unit, the contribution of multirooted teeth to the total sample is multiplied (Fig. 1).

Sample size

Sample size determines the power of a clinical study, and thus the ability to substantiate statistically signifi-

cant differences among groups. The smaller the difference between compared outcomes, the larger is the sample required in each group to achieve sufficient power (53). According to the power analysis calculated by Trope et al. (44), over 350 subjects are required for each group to substantiate a 10% difference

Table 1. Follow-up studies on the outcome of initial endodontic therapy in teeth with apical periodontitis, appraised for inclusion/exclusion in this review

	Cases observed	Follow-up (years)	Appraisal categories				Outcome (%)		
			cohort	exposure	assessment	analysis	healed	healing	functional*
Strindberg 1956	**60[a]**	**0.5–10**	**y**	**y**	**n**	**y**	**80**		
Grahnén & Hansson 1961	105[a, c]	4–5	y	n	n	y	81[d]		
Seltzer et al. 1963	1223[a]	0.5	n	n	n	n			76
Bender et al. 1964	410[a, b]	2	n	n	n	n			77
Grossman et al. 1964	98[a]	1–5	n	n	n	n	62	24	86
Engström et al. 1964	**147[a]**	**4–5**	**y**	**y**	**n**	**y**	**73[d]**		
Oliet & Sorin 1969	220[a]	not given	n	n	n	n			86
Storms 1969	102[a]	1	n	n	n	n	81		93
Harty et al. 1970	879[a]	0.5–2	n	n	n	n	91		
Heling & Tamshe 1970	78[a]	1–5	n	n	n	n	53		
Tamse & Heling 1973	83[a]	1–6	n	y	n	n	81		
Selden 1974	481[a]	0.5–1.5	n	n	n	n			93
Adenubi & Rule 1976	271[a]	0.5–7	n	n	n	y	82	8	90
Heling & Shapira 1978	65[a]	1–5	n	y	n	y	74		
Jokinen et al. 1978	2459[a, c]	2–7	y	n	n	n	38	20	58
Kerekes & Tronstad 1979	**172[a, c]**	**3–5**	**y**	**y**	**n**	**y**	**90[d]**		
Barbakow et al. 1980	112[a]	≥1	n	n	n	n	91[d]		
Barbakow et al. 1981	124[b]	1–9	n	n	n	y	59	29	88
Nelson 1982	144[a]	2–30	n	n	n	n			72
Cvek et al. 1982	45	4	y	n	n	n	88[e, g]		
Oliet 1983	192[a]	≥1.5	n	y	n	n	90		
Klevant & Eggink 1983	260[a]	2	n	n	n	n			91
Morse et al. 1983	127[a]	1	n	n	n	y			95
Swartz et al. 1983	714[a]	≥1	n	n	n	n			83
Pekruhn 1986	285[a]	1	n	y	n	n	89		
Halse & Molven 1987	96[a]	10–17	n	n	y	y	65		
Safavi et al. 1987	199[a]	0.5–2	n	y	y	n	17	not interpretable	
Byström et al. 1987	**79[c]**	**2–5**	**y**	**y**	**y**	**n**	**85**	**9**	**94**
Matsumoto et al. 1987	52[a]	2–3	n	y	n	n			67
Åkerblom & Hasselgren 1988	16[a, c]	2–12	n	y	n	n	63[g]		
Molven & Halse 1988	96[a, b, c]	10–17	n	n	y	y	65		
Shah 1988	93	0.5–2	n	n	n	n			84

Table 1. Continued

	Cases observed	Follow-up (years)	Appraisal categories				Outcome (%)		
			cohort	exposure	assessment	analysis	healed	healing	functional*
Eriksen et al. 1988	**121[c]**	**3**	**n**	**y**	**y**	**y**	**82**	**9**	**91**
Augsburger & Peters 1990	50[a]	0.3–5	n	y	n	n			96
Sjögren et al. 1990	**204[a, c]**	**8–10**	**y**	**y**	**y**	**y**	**86**		
Murphy et al. 1991	89	0.3–2	n	n	n	n	46	48	94
Ørstavik & Hörsted-Bindslev 1993	**133[a]**	**4**	**n**	**y**	**y**	**y**	**not interpretable**		
Smith et al. 1993	481[a]	2–5	n	n	n	y			81
Friedman et al. 1995	113[a]	0.5–1.5	y	y	n	n	63	28	91
Caliskan & Sen 1996	172	2–5	y	y	n	n	81	8	89
Ørstavik 1996	**126[a, c]**	**4**	**n**	**y**	**y**	**y**	**75**	**13**	**88**
Sjögren et al. 1997	**53**	**≤5**	**y**	**y**	**y**	**y**	**83**		
Trope et al. 1999	**76**	**1**	**n**	**y**	**y**	**y**	**80[h]**		
Weiger et al. 2000	**67**	**1–5**	**y**	**y**	**n**	**y**	**78**	**16**	**94**
Chugal et al. 2001	177[a, c]	4	n	n	y	y	63[d]		
Abitbol 2001	**72[a]**	**4–6**	**y**	**n**	**y**	**y**	**74**	**4**	**96**
Peak et al. 2001	280[a]	≤1	n	n	n	n			87
Pettiette et al. 2001	40	1	n	y	n	n			60
Heling et al. 2001	319	1–12	n	y	y	n			65
Cheung 2002	**107**	**4–10**	**y**	**n**	**y**	**y**			**80[i]**
Peters & Wesselink 2002	**38**	**1–4.5**	**y**	**y**	**y**	**y**	**76**	**21**	**97**

*Asymptomatic, without or with residual radiolucency (reduced or unchanged in size).
[a]Data extracted from larger study material that includes also teeth without apical periodontitis.
[b]Repeated material.
[c]Roots considered as unit of evaluation, rather than teeth.
[d]Recalculated after exclusion of cases classified as 'uncertain'.
[e]Cases with procedural errors excluded.
[f]Cases with prepared but unfilled canals excluded.
[g]All canals obliterated to some extent.
[h]Teeth treated in two sessions without intracanal medication excluded.
[i]True survival, based on survival analysis
y satisfies criteria of acceptable quality
n does not satisfy criteria of acceptable quality.
Studies selected for review are highlighted in bold font.

in healing after treatment in one or two sessions (with 80% power). Because in the majority of studies the sample size is considerably smaller (Table 1), specific variables may emerge as insignificant, whereas in larger studies the same variables may significantly influence the prognosis.

Case selection criteria

Case selection is the process of discriminating cases according to their prognosis and, as such, it determines the results of a clinical study (54). In some studies, cases judged to have an unfavorable prog-

nosis are excluded (10, 24). In stark contrast, one of the studies (31) includes only teeth with obstructed canals, in which the ability to fulfill the technical objectives of treatment is doubtful. In other studies, all treated teeth are included, even those compromised by advanced periodontal disease or procedural errors (40, 47) (Fig. 2).

Intra-operative procedures

Treatment providers

Experienced and skillful operators are less likely to perform procedural errors that might compromise the prognosis (54); therefore, study results may vary according to the providers of treatment and their expertise. As providers of treatment in the different studies varied from undergraduate students to qualified endodontists (2), the reported results vary accordingly.

Asepsis

In at least two of the studies (16, 19), treatment was performed routinely without rubber dam. It can be assumed that in these and several other studies, asep-sis was not strictly observed; compromised asepsis would impair the results in a given study.

Intracanal procedures

Specific root canal preparation techniques (17) and filling materials (32, 55) have been associated with poorer prognosis of endodontic treatment than other techniques and materials. Several studies (16, 17, 23, 29, 31, 32, 36, 39, 43) have used those reportedly ineffective materials, such as root filling with kloroperka N-Ø and rosin-chloroform (32, 55), whereas other studies have used techniques alleged to be very effective, such as the 'Schilder technique' (26). The variability with regards to the intracanal procedures is indeed striking; however, the effect of this variability on the results is subject to speculation (1).

Also, intracanal medicaments used in the studies may have been ineffective. Intracanal medicaments are critical for controlling root canal infection (29, 56–61), but not all are equally effective. The antimicrobial efficacy of 'classical' medicaments, such as camphorated phenol and paramonochlorophenol, iodine potassium iodide and formocresol, is short-lived (62–64), and may be insufficient for in-between-sessions disinfection of canals associated with
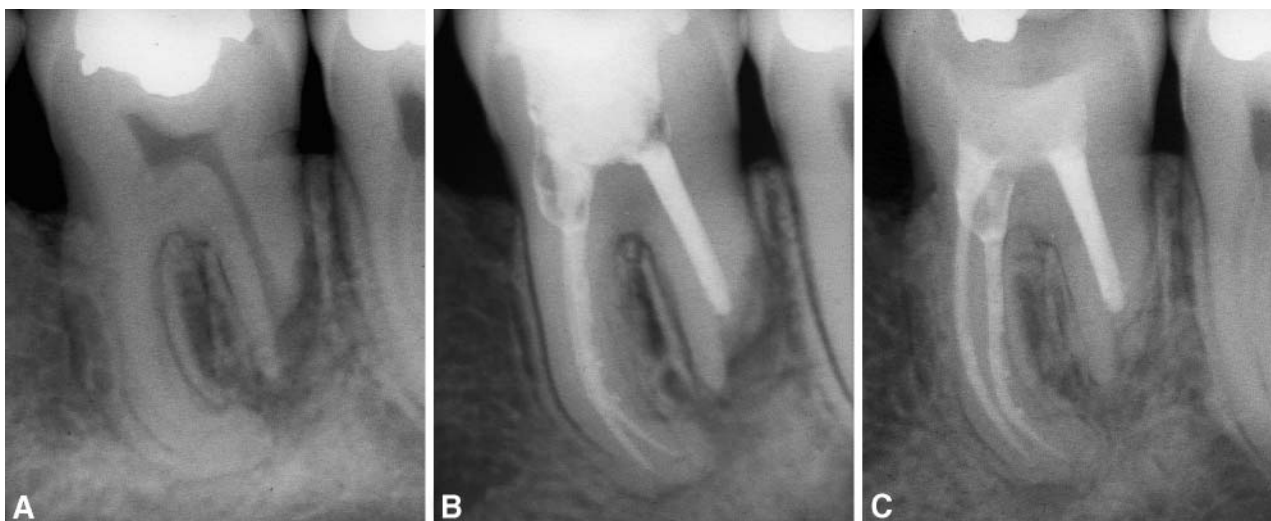

Fig. 1. Multi-rooted teeth – consideration of individual roots vs. the whole tooth as the unit of evaluation. A. Mandibular first molar with apical periodontitis about both the mesial and distal roots. Note the apical external root resorption of the distal root. B. Immediate post-operative radiograph. C. At 3 years, the original lesions have healed, but a new lesion has emerged about the mesial root. The tooth as a whole was considered the unit of evaluation in the original study (40 – reprinted with permission); it contributed one unit to the study sample and it was recorded as "failure". In contrast, if each root were considered an independent unit of evaluation, the tooth would have contributed two units to the sample, one recorded as healed and the other as having disease.

apical periodontitis (59). These 'classical' medicaments have been used in many studies (3, 9–12, 14, 15, 17–19, 24), where they may have compromised the results. The more effective calcium hydroxide dressing was used in other studies (29, 34, 36, 40–42, 44–47, 52, 55, 61). In selected studies (26, 43) treatment was completed in one session, without the use of any intracanal medicament.

Bacterial culturing

In several studies a negative bacterial culture was a prerequisite for root filling (7, 23, 29, 36). If indeed the culturing procedures were reliable, the negative culture would have been a confirmation of effective disinfection; such has been associated with an improved prognosis relative to teeth with a positive culture (7, 43).

Post-operative restoration

The influence of the definitive restoration (type and timing of placement) on the prognosis after endodontic treatment is, at best, vague. The majority of the studies do not elaborate on the restoration of the treated teeth. Occasionally, it is indicated that a considerable proportion of the teeth had not been restored (11, 15). A compromised restoration (Fig. 2c and Fig. 3) may impair the prognosis (15, 25), and the result of any study is likely to be influenced by this factor.

Methodology

In recent years, the academic community has become aware of the need to differentiate clinical studies by their relative importance, and of the critical role that
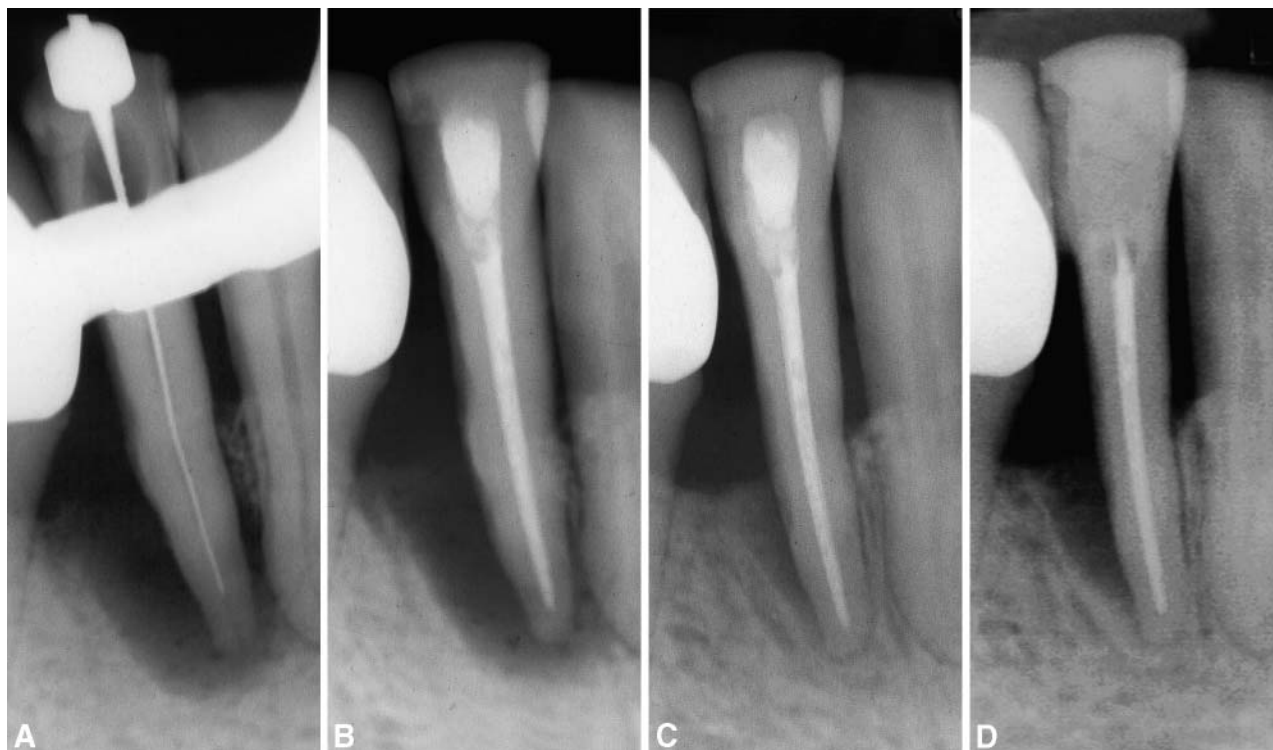

Fig. 2. Case selection – inclusion of a tooth compromised by advanced periodontal disease in the study sample. A. Mandibular lateral incisor with apical periodontitis and advanced marginal periodontitis, being treated as part of a clinical study (40 – reprinted with permission). Note extensive bone loss of combined endodontic and periodontal etiology. B. Immediate post-operative radiograph. C. At 8 months, healing is impressive albeit incomplete (classified as "incomplete healing" in the original study). Tooth is still restored with a temporary filling. D. At 3 years, deterioration at the coronal aspect of the lesion indicates further advancement of periodontal disease.

proper methodology and reporting play in this process. Among the endodontic follow-up studies, there is considerable variability in the methods of collecting, recording, processing and reporting data. Consequently, some studies may be assigned less importance than others (see section on 'Best evidence' below).

Study design

Retrospective studies differ greatly from prospective ones, and the generated results may differ accordingly. Frequently, in retrospective studies (8, 11, 13, 22, 25) and occasionally in prospective ones (31), important pre-, intra- and postoperative data is lacking, including composition of the material, treatment procedures and complications. The results of studies lacking such important information cannot be utilized as a basis for assessing the prognosis in specific clinical conditions, but, at the most only for generating hypotheses.

Specific studies were designed to answer one main research question (43–45, 49, 52); they may not be utilized for comparisons with other studies in regard to general results.

Recall rate

When many subjects included in the inception cohort of a study are not available for follow-up, the unknown treatment outcome invalidates the results and renders them subject to speculation (1, 26, 53). For example, it has been speculated that a low recall rate may skew the results towards an unfavorable outcome (54) unless it results from objective factors, such as deceased or relocated subjects who cannot be reached (1, 53). As the recall rates in the different studies vary from 12% (13) to close to 100% (43, 52), and in some studies it is not even reported (5, 6, 9, 14, 25), the prognosis reported in the studies is also inconsistent.

Interpretation of radiographs

Radiographs have been used invariably as the principal measure for assessing the outcome of endodontic therapy. Radiographs are subject to changes in angulation and contrast, as well as interpretation (65–70). Because inconsistent radiographs and biased interpretation may undermine the reliability of the results, blinded examiners, standardized in interpretation of

Fig. 3. Lack of definitive restoration. A. Maxillary lateral incisor with extensive apical periodontitis. B. Immediate postoperative radiograph. Tooth is temporarily restored with reinforced zinc-oxide eugenol (IRM). C. At 3 years, the temporary restoration has not been replaced for a definitive one, and persistent apical periodontitis is clearly evident.

radiographs, are an essential component of the evaluative process (55, 68, 70).

Follow-up period

Healing of apical periodontitis is a dynamic process, and sufficient time is required to evaluate its progression and completion (1, 29, 42). Observations after a short follow-up may demonstrate only signs of healing (1, 37, 40, 42) (Fig. 4). Therefore, results of studies with short follow-up periods (Table 1) may be skewed and not reflect the true prognosis (1, 54, 55, 71). Follow-up of at least 1 year is required to reveal meaningful changes (34, 42), but extension of the follow-up to 3 or 4 years (Fig. 5) may be required to record a stable treatment outcome (1, 17, 29, 42, 55). Because with time, endodontically treated teeth are subject to adverse effects of periodontal and restorative deterioration, extensive follow-up periods are more likely to reveal the influence of those effects on the outcome. Comparing the 4-year and the final follow-up, Strindberg (1) observes a difference in healing rates of 16%.

Analysis

The nature of statistical analyses used, or the lack thereof, has greatly confused the issue in respect to prognostic factors. In many studies mostly univariate analyses are used to assess the influence of specific factors (9, 16, 17, 20, 23–25, 29, 30, 32, 36, 39, 40, 43, 54, 55), that ignore coincidental influences by other factors (1). For example, Halse & Molven (27) conclude that teeth in which overfilling occured have a poorer prognosis than teeth filled without overfilling. Careful analysis of the study reveals that overfilling occurred more frequently in teeth with apical periodontitis. Clearly, then, the poorer prognosis can be 'blamed' on the infection, but not necessarily on the overfilling.

Unit of evaluation

Comparisons among studies are certainly facilitated when each root is considered an independent unit of evaluation (2). However, this strategy raises some concerns with regards to multirooted teeth. Counting roots as the evaluated unit assigns more weight to studies that include a large proportion of multirooted teeth than to studies that include mostly single-rooted teeth. Also, the healing rate becomes higher than if the teeth were evaluated as a whole (1, 7, 24, 25, 40) (Fig. 1). This fact is clearly demonstrated in the most recent cross-sectional study by Boucher *et al.* (72), who report the prevalence of apical periodontitis separately for endodontically treated teeth
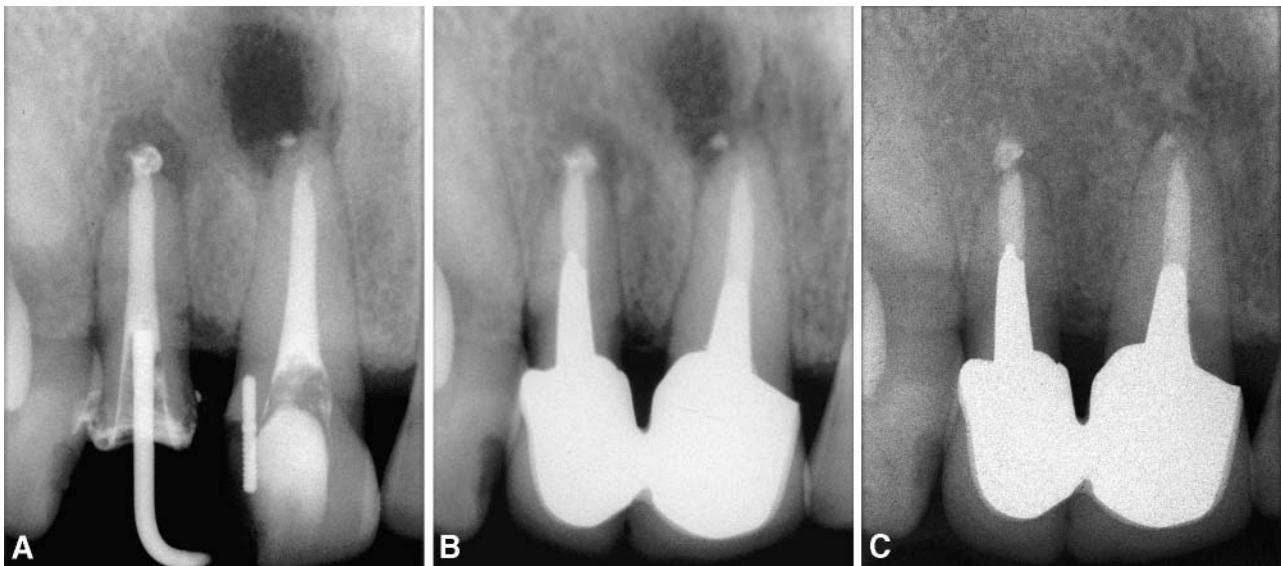

Fig. 4. Extent of the follow-up period. A. Immediate post-operative radiograph of two maxillary incisors with apical periodontitis. B. At 9 months, both teeth demonstrate reduced radiolucencies. Termination of a study at this end-point would result in both teeth being recorded as showing signs of healing. C. At 18 months, both teeth are healed. Termination of a study at this end-point would result in both teeth being recorded as completely healed.

(29.7%) and roots (24.4%) for the same French sub-population.

Outcome measures and criteria

The lack of standardized criteria for measuring the outcome in clinical studies in endodontics is clearly the main cause for the inconsistent reports on prognosis. In many studies the radiographic appearance is used as the only outcome measure (4, 10, 11, 13, 17, 23, 32, 37–39, 42, 44, 49–51, 55). Because in those studies any symptomatic but radiographically normal teeth are unnoted, the results are usually skewed towards higher healing rates (73). Likewise, a bias occurs when incompletely healed lesions are grouped together with completely healed ones (4, 5, 10, 13, 24, 30, 33, 39, 50). This issue of outcome measures and criteria is debated in detail in the following sections.

Outcome classification: 'Success', 'Healing', 'Function'

One of the main causes for the variability of reported outcomes in follow-up studies on endodontic therapy is the inconsistent definition of 'success' and use of different outcome criteria (2). The following are some of the outcome criteria used.

Radiographic and clinical normalcy

In the majority of the studies in Table 1, a strict definition of 'success' is used, requiring a combination of normal radiographic and clinical presentation (1, 9, 12, 14–19, 22, 23, 26, 29, 31, 32, 36, 40, 41, 43, 45–47, 52). Within this strict definition, a small radiolucency is accepted if it appears around extruded filling materials (1, 7), but otherwise incomplete healing, or any remaining radiolucency is excluded

Clinical normalcy

In contrast to the strict definition described above, in several of the studies in Table 1 the researchers define 'success' primarily as the absence of clinical signs and symptoms. As for the radiographic appearance, in several studies a decrease in the size of the radiolucency is required (4, 13, 24, 30, 39, 49), while in others, all that is required is that the radiolucency is not increased in size (10, 25, 33).

'Uncertain', 'questionable' or 'doubtful'

This category of outcome introduces an additional inconsistency. Several researchers (1, 3, 7, 17–19, 23, 46) use these terms strictly for cases they could not assess because of insufficient radiographic infor-
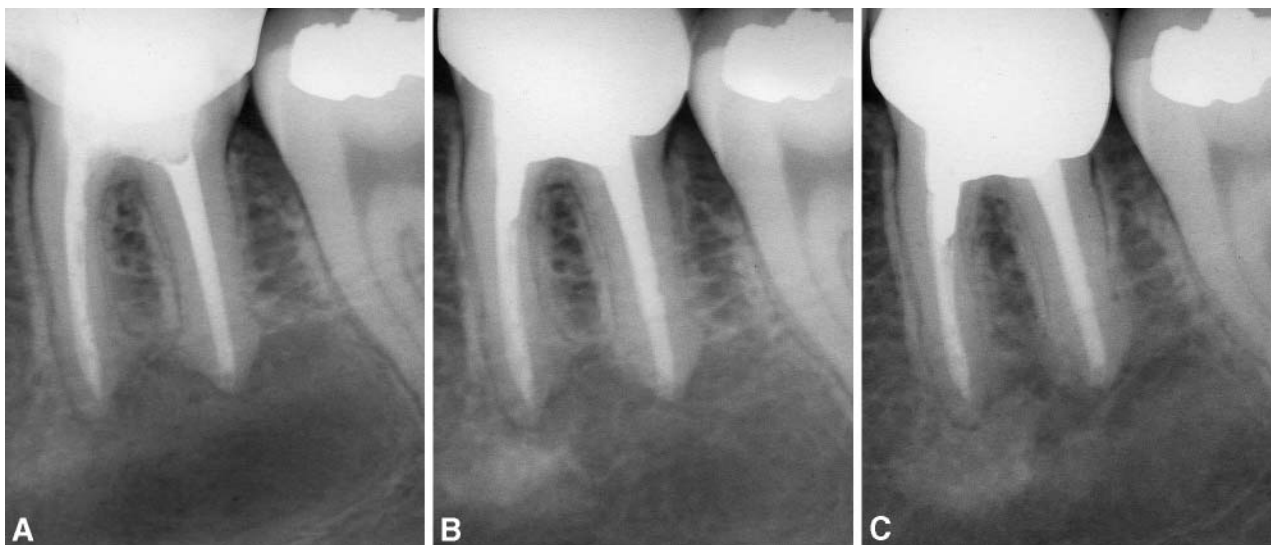

Fig. 5. Extention of the follow-up period beyond one year. **A.** Immediate post-operative radiograph of mandibular first molar with extensive apical periodontitis, included in a clinical study (40). **B.** At 18 months, most of the original lesion has healed, but a small radiolucency remained about the mesial root tip. As the study was terminated at this end-point, the tooth was recorded as "incomplete healing". **C.** Two years later (at 3.5 years) the entire lesion has completely healed. If the follow-up period were extended to 4 years, this tooth would have been recorded as healed.

mation. Others (6, 14, 16, 31, 32, 40, 41, 52) use them to describe incomplete healing characterized by decreased radiolucency (not considered as success by the former group). Using the former classification, the success rate is somewhat lowered; recalculation of success after elimination of the 'questionable' cases in the relevant studies yields success rates that are approximately 5% higher (3, 7, 17, 46). Using the latter classification, the success rate is not affected, but the failure rate is lowered in comparison with the former classification.

The Periapical Index

Apart from the considerable difference between the 'strict' and 'lenient' definitions of success, the very assessment of radiographic images is associated with bias (66–70). To address this concern, Ørstavik et al. (74) introduced the Periapical Index (PAI) for the radiographic appraisal of endodontically treated teeth. The PAI relies on the comparison of the evaluated radiographs with a set of five radiographic images, which represent histologically confirmed periapical conditions (65). These reference images represent a healthy periapex (scores 1 and 2), and increasing extent and severity of apical periodontitis (scores 3–5). To avoid bias, the examiner is calibrated until reaching a level of sufficient consistency. Each radiograph is then assessed independently in a 'blind' manner, and assigned a score according to which of the five reference images it appears to match best. This method permits unbiased interpretation of the radiographs, and therefore also reproducible comparisons (74). However, it has been used in a minority of the studies listed in Table 1 (38, 42, 44). Results obtained with the PAI cannot be directly interpreted as measures of 'success' or 'failure'; originally, the researchers reported on the extent of increase or decrease in mean scores within compared groups. However, in recent studies (44, 72, 75), PAI scores are dichotomized, with scores 1 and 2 representing 'healthy' periapical tissues, and scores of 3 and above representing 'disease'.

Clearly, the definition of 'success' requiring only clinical normalcy but allowing leniency with regards to the radiographic appearance, increases the success rate in comparison with the more strict definition requiring combined clinical and radiographic normalcy. For example, Friedman et al. (40) report 63% com-

plete healing and 28% incomplete healing; by the strict criteria, their success rate is 63%, whereas by the more lenient criteria, the success rate would be 91%. The discrepancy would be even larger if these researchers included unchanged, persisting lesions in the criteria for success. The main dilemma with the more lenient criteria, however, is the fact that apical periodontitis is frequently asymptomatic, whether it is affecting an untreated tooth or persists after therapy (2, 26, 47, 76). With regard to untreated teeth, apical periodontitis is universally considered a disease requiring therapy, regardless of the presence or absence of symptoms. By the same token, persisting apical periodontitis after therapy cannot be regarded as 'success' only because it is asymptomatic; *it is the same disease, still requiring management.*

The ambiguity of 'success' when referring to endodontic therapy is a concern, because it may confuse communication within the profession and with patients. Patients may be even more confused by the different meaning of 'success' when referring to other dental treatment procedures, such as periodontal therapy or implants. Therefore, there is the risk that undiscerning use of the term 'success' may mislead the patients when they consider alternative treatments, and particularly when they are expected to select between endodontic therapy and extraction, followed by tooth replacement with an implant. The definition of 'success' in implantology is different from that used in endodontics, and it excludes cases associated with iatrogenic and other complications (77). Based on that definition, the reported 'success' rates for single-tooth implants are considerably higher than those reported for endodontic therapy (78). The patient weighing one 'success' rate against the other may erroneously assume their definitions are comparable, and select the treatment alternative with the "higher number" – that appears to suggest a better chance of 'success'.

In most follow-up studies after endodontic therapy, an unfavorable outcome is normally called *'treatment failure'.* This term also is ambiguous; furthermore, it has a negative connotation (79), and it fails to imply the necessity to pursue any course of action. In fact, both 'success' and 'failure' are value-laden terms that should be substituted for more neutral expressions such as 'chance of healing' and 'risk of inflammation' in order to facilitate communication with patients (42).

The goal of initial endodontic therapy is to cure apical periodontitis (80). When radiolucency is still present at follow-up, it is an expression of apical periodontitis – the same disease the initial therapy aimed to cure. To promote effective communication within the profession and with patients, it is most appropriate to describe the outcome in direct relation to the goal of therapy, the curing of disease. Accordingly, endodontic treatment outcomes should be reported in reference to *'healing'* (2, 29, 42), as follows:

• *Healing, healed, disease.* When follow-up reveals a combined clinical and radiographic normalcy, the tooth and surrounding tissues are classified as having *healed* (Fig. 6 and 7). When the radiolucency has persisted without change, that is an expression of *disease* (Fig. 8) even when there is clinical normalcy. To accommodate the fact that healing processes may require considerable time, reduced radiolucency combined with clinical normalcy can be interpreted as a suggestion of *healing* in progress (Fig. 9). The terms
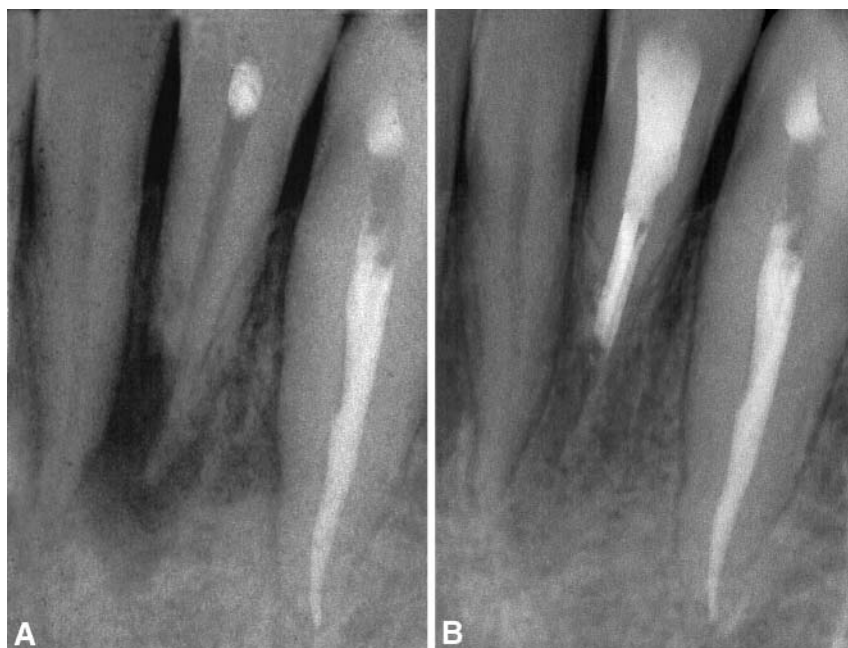

Fig. 6. Outcome classification as "healed". A. Mandibular lateral incisor with apical periodontitis and associated apical external resorption. B. At one year, the radiolucency is completely resolved and the tooth is symptom free, indicating it has healed.

Fig. 7. Outcome classification as "healed". A. Maxillary second molar with apical periodontitis extending along the mesial root surface, and associated sinus tract (traced with a gutta-percha cone). B. At one year, the radiolucency is completely resolved and the tooth is symptom free, indicating it has healed.

'healed', 'healing' and 'disease' better describe the actual observation, and the dependence on definitions of 'success' and 'failure' is avoided.

Although curing apical periodontitis is the ultimate goal of therapy, there are clinical conditions that suggest an unfavorable prognosis. This is particularly true of teeth that have been compromised by procedural errors, such as perforation, transportation, or by extensive loss of supporting bone, because of periodontal disease, a crack or a developmental groove. If a patient is still keen to attempt therapy with the hope of retaining the tooth in a functional, asymptomatic state, tooth survival then becomes the goal of therapy. Accordingly, endodontic treatment outcome in these
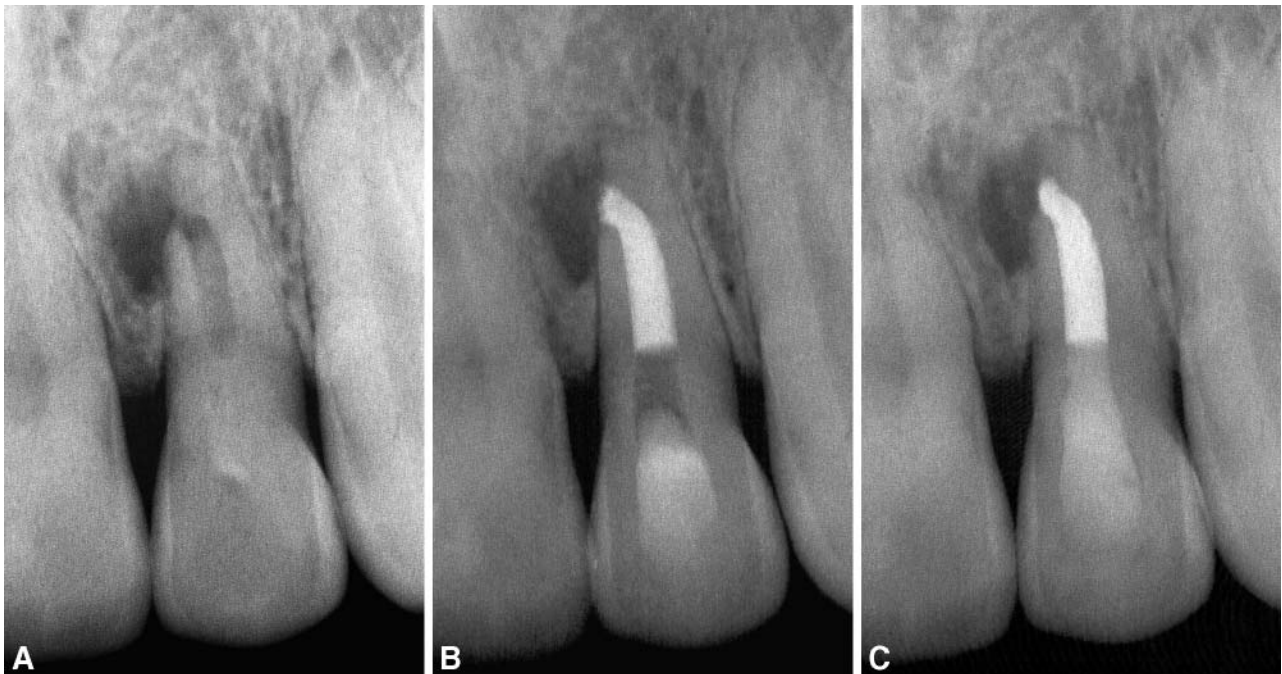

Fig. 8. Outcome classification as "disease". A. Maxillary lateral incisor with apical periodontitis. B. Immediate post-operative radiograph. C. At 1 year, the tooth is symptom free but the radiolucency has not been reduced, indicating persistence of the original disease.
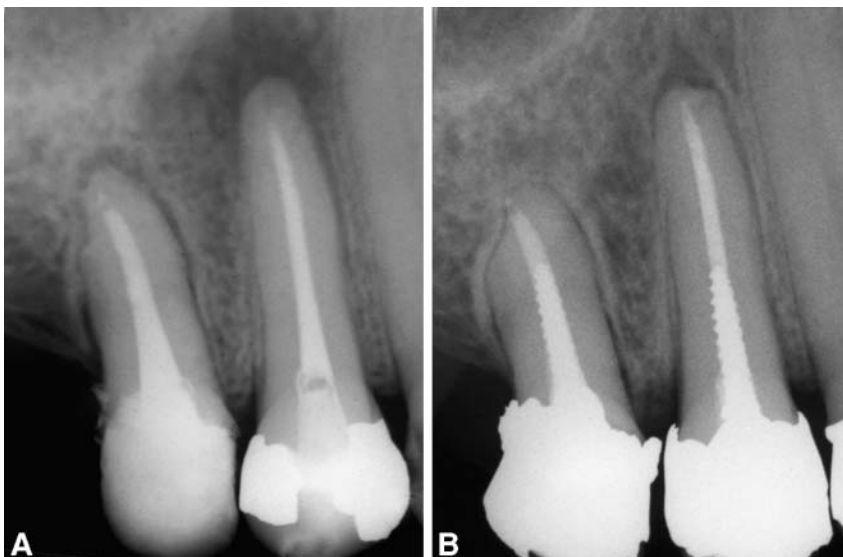

Fig. 9. Outcome classification as "healed" vs. "healing". A. Immediate post-operative radiograph of maxillary first and second premolars with apical periodontitis. B. At 1 year, both teeth are symptom free. While the second premolar is classified as healed (see Figs. 6 and 7), the reduction of the radiolucency in the first premolar is indicative of healing being in progress (see also Figs. 4 and 5). Regrettably, both the restorations are inadequate.

circumstances could be reported in reference to 'survival'. This term, however, has been widely used in health care professions with a very specific meaning, to differentiate retention from loss of the assessed subject (51, 81, 82). In order to avoid confusion in this article, surviving teeth will be defined as follows:

• *Functional:* When follow-up reveals a residual radiolucency combined with clinical normalcy, the tooth is classified as being *functional*. The residual radiolucency can be either reduced or unchanged in size (Figs. 10 and 11).

In the further sections of this article, the term 'disease' is used in lieu of 'treatment failure', and the terms 'healing' and 'functional' are used in lieu of 'success', as appropriate. Because of the inconsistency among studies, comparisons are impractical and inappropriate (2, 32, 39), and grouping studies to calculate the average healing or functional rates would be misleading. However, depending on the degree of detail provided in any given study, it is occasionally possible to 're-calculate' the treatment outcome according to set criteria, so as to facilitate and possibly validate some comparisons and grouping of data from several studies.

Best evidence for the prognosis of endodontic therapy of apical periodontitis

As demonstrated above, the studies on the prognosis of endodontic therapy are rather diverse in composition, treatment procedures and methodology. Consequently, the reported prognosis is also diverse. This can be most confusing for the conscientious dentist, who is seeking evidence of the benefits of endodontic therapy, to support clinical decision-making and prognostication of clinical cases. However, because of the aforementioned diversity, not all published studies are equally valuable as sources of valid and clinically relevant information.

In recent years, the development of the concept of evidence-based health care has resulted in the recognition that clinical studies vary with regard to the level of evidence they provide. A consensus has emerged that an evidence base to support clinical decision-making cannot be derived from indiscriminate browsing of all available studies (83). Consequently, strategies have been suggested for differentiation of

clinical studies according to the level of evidence (83). In view of the diversity among studies on the prognosis of endodontic therapy, it is most appropriate to apply those appraisal strategies to select for review those studies that provide the best evidence.

Appraisal of studies

There are several methods for appraisal of clinical studies to determine the level of evidence and clinical relevance (83). The most commonly applied criteria are those developed for inclusion/exclusion of studies in systematic reviews of the literature (84). Those criteria also determine the following hierarchy of evidence, from top to bottom:

• High quality randomized controlled trial (RCT) and systematic review (SR) or meta-analysis of same.
• High quality observational cohort study, SR of same and lower quality RCT.
• High quality observational case-control study and SR of same.
• Lower quality cohort and case-control studies, and case series.
• Expert opinion, case reports, unstructured literature review.

Appraisal of studies on the prognosis of endodontic therapy using strict criteria would most frequently result in exclusion, and the purpose (searching for evidence) would be defeated. To avoid such scenario, it should be remembered that evidence-based practice is defined as '...the conscientious, explicit and judicious use of *current best evidence* in making decisions about the care of individual patients' (85). Reviews should therefore focus on the best evidence available, even if it does not comply with the highest hierarchy. Inasmuch as observational studies should not be used for comparing benefits of different treatments, they can be very helpful for learning the course of disease (prognosis) and for identifying prognostic factors (86). Furthermore, recent reports in the medical literature suggest that structured reviews of well-designed observational studies can yield conclusions that are consistent with those of systematic reviews or meta-analyses of RCT's (87, 88). Although these recent reports are controversial, they highlight the fact that the quality of a clinical study is a most critical consideration (89) – high quality ob-
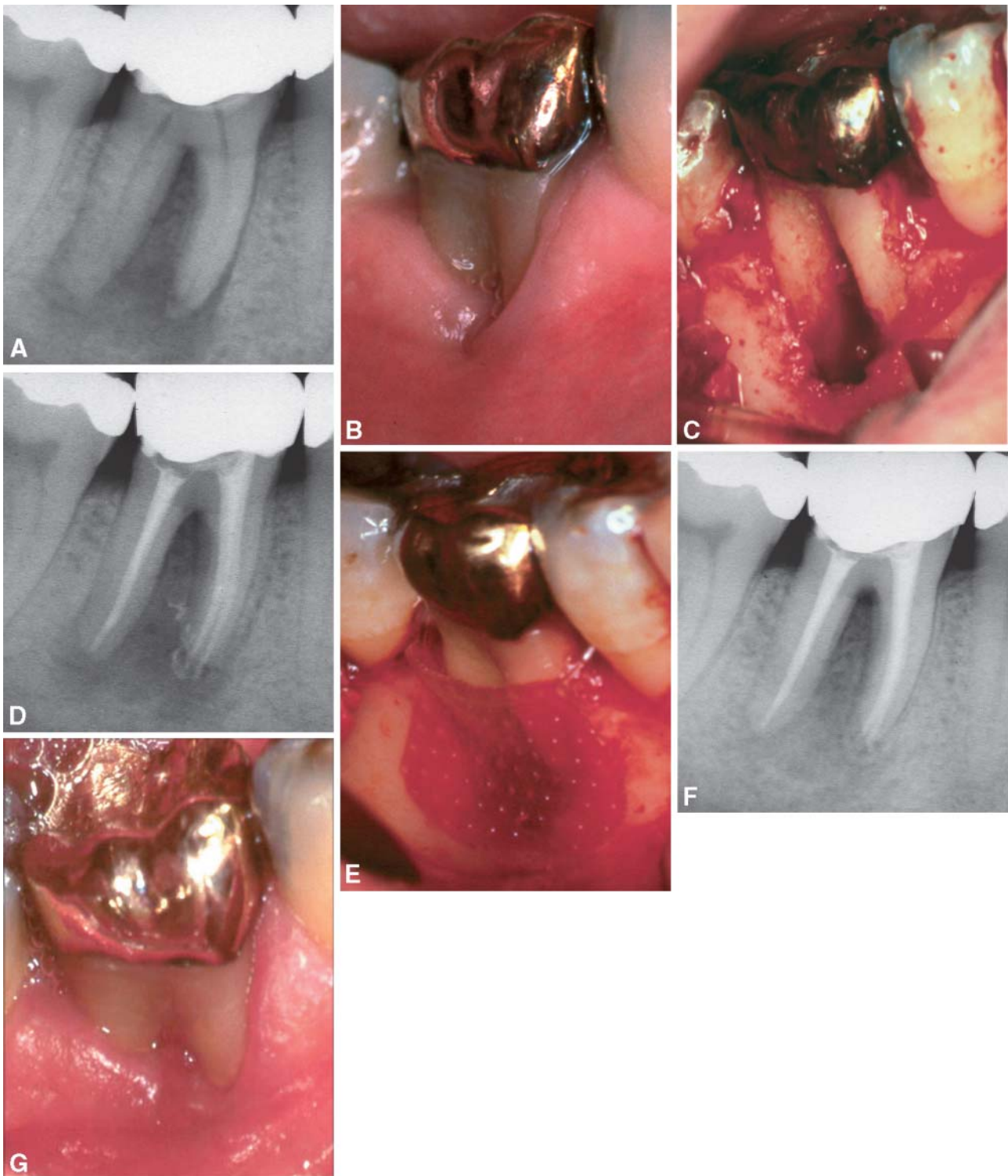
Fig. 10. Outcome classification as "functional". A. Mandibular first molar with extensive apical periodontitis. B. Clinical view of gingival recession, coupled with probing depth apical to the root tips, suggests total loss of the buccal bone plate. Prognosis is poor. C. Clinical view after reflection of a full-thickness flap, revealing the extent of bone loss. Advised of the poor prognosis, the patient decided to proceed with treatment in an attempt to retain the tooth in function as long as possible. D and E. Immediate post-operative radiograph after root canal therapy (root filling with vertical compaction of warm gutta-percha), followed by placement of a resorbable guided tissue regeneration membrane. F and G. At 6 months, the radiolucency is considerably reduced and the gingival tissue appears to be healed. Although the prognosis remains poor, the tooth being functional achieves the goals of therapy as set by the patient. (See also Fig. 2).
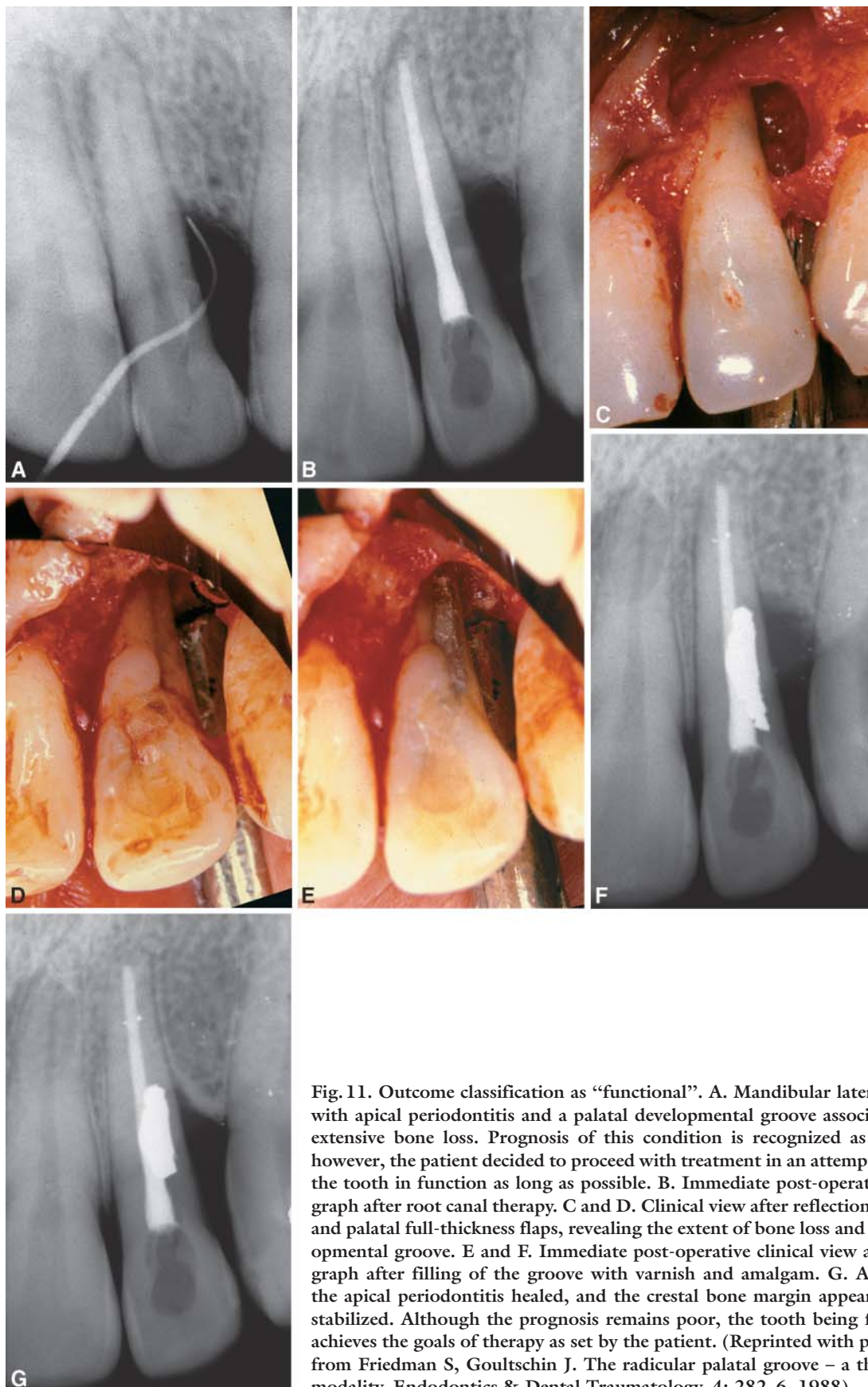
Fig. 11. Outcome classification as "functional". A. Mandibular lateral incisor with apical periodontitis and a palatal developmental groove associated with extensive bone loss. Prognosis of this condition is recognized as hopeless; however, the patient decided to proceed with treatment in an attempt to retain the tooth in function as long as possible. B. Immediate post-operative radiograph after root canal therapy. C and D. Clinical view after reflection of buccal and palatal full-thickness flaps, revealing the extent of bone loss and the developmental groove. E and F. Immediate post-operative clinical view and radiograph after filling of the groove with varnish and amalgam. G. At 4 years, the apical periodontitis healed, and the crestal bone margin appears to have stabilized. Although the prognosis remains poor, the tooth being functional achieves the goals of therapy as set by the patient. (Reprinted with permission from Friedman S, Goultschin J. The radicular palatal groove – a therapeutic modality. Endodontics & Dental Traumatology, 4: 282–6, 1988).

servational studies can outweigh poor quality RCT's. Thus several of the studies on the prognosis of endodontic therapy can be relevant to this review. Because the purpose of this review is to report on the prognosis of endodontic therapy, and not to conduct a systematic review of the literature or to compare the benefits of endodontic therapy with that of an alternative treatment (e.g. extraction and tooth replacement), the appraisal is oriented towards inclusion of all studies with at least mid-range level of evidence.

Appraisal strategies of clinical studies are primarily concerned with validity and relevance (84). A close examination of different appraisal criteria, and particularly the guidelines recommended by McMaster University Health Sciences Centre in Hamilton, Ontario, Canada (90), reveals that they can be grouped into general categories:
- study cohort;
- exposure (intervention, treatment);
- assessment of outcome;
- data analysis and reporting.

Therefore, these four categories are used below as the basis for appraisal of the studies on the prognosis of endodontic therapy.

Cohort, at inception and end-point of study

The best evidence is derived from a *prospective* design, with the *inception cohort* defined before the study is initiated, and then observed over time. Depending on the rigor of the design, selection bias can be avoided. Not only should the cohort be defined, it should also be *clearly described* in the report to ascertain unbiased interpretations. The *pattern of referral* of the treated cohort should also be described, including the type of patients being treated and the case selection criteria used, to determine the external validity (generalizability) of the reported results (53). Assuming that not all treated subjects are available for follow-up, the entire inception cohort should be *accounted for at the end-point of the study*, to allow identification of patient 'dropouts' (who do not present for follow-up at their own volition) and 'discontinuers' (who are excluded from the study by the investigator for accountable reasons, e.g. death or relocation). This distinction allows accurate calculation of the recall rate. Most importantly, it allows estimation of migration bias that can affect the internal validity of the results (53). Finally, the *sample size*, or extent of the treated cohort,

may be required to exceed a certain threshold as determined by the reviewer.

Exposure (treatment, intervention)

The *treatment procedures* should be clearly described, to avoid the need for interpretation. The characteristics of the *treatment providers*, e.g. students, general dentists, specialists, also should be clearly defined to establish the external validity of the results (53). The reviewer may choose to exclude studies if the treatment procedures described are irrelevant to the review, or otherwise considered unacceptable.

Outcome assessment

One of the concerns in observational studies is measurement bias (53). To avoid such a bias, outcome dimensions and measures should be *clearly defined*. Bader & Shugars (91) define four dimensions of dental outcomes:
- physical/physiological – pathosis, pain and function;
- psychological – perceived aesthetics, level of oral health and satisfaction with oral health status;
- economic – direct and indirect cost;
- longevity/survival – pulp death/tooth loss and time until repeat treatment for same or new condition.

Of these four dimensions, the endodontic prognosis studies assess the first, the last, or both. The outcome measures used to assess these dimensions should be as *objective* as possible, and *applied consistently* throughout the study. Therefore, examiners should be *properly calibrated* and the level of *reliability established*. Outcome assessment should be *blinded or masked*. Therefore, the examiner(s) measuring the outcome should be different from the provider(s) of treatment, and direct comparisons of radiographs, e.g. preoperative and at follow-up, should be avoided. Another consideration is the follow-up period – it should be *long enough* to capture the completion of the healing processes in the majority of the study sample. According to Ørstavik (42), 1 year would be an adequate follow-up period.

Analysis and reporting of data

The analysis in observational studies should take into account *dominant prognostic factors* that may con-

found the results by influencing or even determining the outcome studied. The main concern here is to avoid selection or assembly bias, from selecting of subjects with a preferential capacity to benefit from therapy, as well as confounding bias (53). In many observational studies the prognostic factors are not controlled by the investigator(s); at the least they should be observed and recorded, to allow judicious analysis of the outcomes.

Table 1 lists all the observational studies on the prognosis of initial endodontic therapy of apical periodontitis published in the past 50 years. In many instances, the data was extracted from larger material that included treatment of teeth without apical periodontitis. Only data pertinent to this review is presented; for additional information, see the more comprehensive tables in the previous review by Friedman (2). The outcome is interpreted from that reported by the original authors, as follows:

- combined clinical and radiographic normalcy is classified as 'healed';
- whenever the rate of reduced radiolucency combined with clinical normalcy is given, this is classified as 'healing';
- the rate of teeth with no signs and symptoms is classified as 'functional' – for several studies this is simply the sum of 'healed' and 'healing' (when both are available), while for others it includes also teeth where the radiolucency remained unchanged.

True 'survival' is not used as an outcome category, because in all the studies but one (51), the outcome is calculated after extracted teeth are excluded from the sample. The listed studies are related to the general categories of appraisal criteria outlined above, and notation is made of their compliance with those criteria. Studies that satisfy three out of the four categories are selected for this review; they are set in bold font type for easy identification.

Initial therapy of apical periodontitis

Teeth that present with apical periodontitis may have a primary infection of the pulp and root canal system, or a residual or subsequent infection after endodontic treatment. Accordingly, they undergo initial therapy, retreatment, apical surgery, intentional replantation or a combination thereof. This review covers only the prognosis of initial therapy of apical periodontitis.

Although the appraisal process of the many studies listed in Table 1 resulted in a shortlist of only 14 studies, there is still considerable variability in the reported outcome of initial therapy of apical periodontitis. From six of the studies (29, 34, 42, 45, 47, 52) it is quite clear that over 88% of the teeth are 'functional' at the follow-up examination (Table 1). In fact, the 'functional' rates entered in the table include only teeth where the initial radiolucency disappeared (healed) or became reduced (healing). It can be assumed that additional teeth were clinically normal but with the radiolucency unchanged; however, their numbers were not reported in any one of the selected studies. Thus the rate of asymptomatic, functional teeth after initial endodontic therapy of apical periodontitis probably approaches or even exceeds 95%. Inasmuch as all the functional teeth are clearly surviving very nicely, the rate of 'functional' teeth is not synonymous with 'survival' rate, because it does not take into account all lost teeth. The latter is usually derived from survival analyses (51, 81, 82). However, survival analyses of endodontically treated teeth also include a bias and may not be correlated with endodontic 'success' – occasionally, teeth are extracted because of treatment planning considerations although they may still be functional, while in other instances a functional tooth may require further treatment, i.e. restorative or periodontal, and the patient decides to forego treatment and extract the tooth (82). Even so, the reported 80% survival rate after endodontic therapy of teeth with apical periodontitis (51) is quite high. Combined with the very high rate of functional teeth, there is a strong indication of the potential of teeth with apical periodontitis to remain in a functional, asymptomatic state after endodontic therapy. This potential is at par with the 'success' rate reported for single-tooth implant-supported replacement (78). It suggests that, for restorable teeth with reasonable periodontal prognosis and apical periodontitis, *conservative endodontic therapy is definitely justified and should be attempted;* tooth extraction and replacement should not be contemplated.

The greatest variability in the reported outcomes among the studies selected for review exists for the 'healed' rate, or complete healing, ranging from 73% (7) to 90% (17). This range is considerably smaller than that observed across all studies (46% to 91%), as can be expected from the selection of only those studies that satisfy the appraisal criteria. Because in

the studies selected for review the criteria for complete healing are usually well-defined and rather uniform, this variability must be related to other factors, as discussed in the first section (Diversity of studies) of this review:

- The variability may have resulted from differences in tooth types and the tooth or root being the unit of evaluation (2). The studies that report higher 'healed' rates include only single-rooted teeth (29, 43), or calculate the outcome for each root (17, 36), which usually enhances the outcome compared to inclusion of all tooth types and use of the whole tooth as the unit of evaluation in the other studies (2) (Fig. 1). However, this argument appears to be undermined by the fact that there are other selected studies where the root is considered the unit of evaluation, and yet the 'healed' rates are lower (34, 42, 52).
- The variability may have resulted from differences in case selection (54). While cases treated by undergraduate students (7, 17, 29, 34, 36, 38) can be assumed to have been relatively uncomplicated, in one of the studies (47) it is clearly stated that some treated cases were complicated by anatomy, advanced periodontal diseases or procedural errors that occurred before referral for treatment (Fig. 2).

- The variability may have resulted from the prerequisite in several but not all studies (17, 29, 36) of a negative bacterial culture before root filling. As shown by Sjögren et al. (43) the 'healed' rate for teeth filled with a negative culture is significantly higher than for teeth with a positive culture (94% and 68%, respectively).
- The variability may also have resulted from differences in restoration. It has been stated (personal communication) that in the studies reported by the Umeå, Sweden group (29, 36, 43) all teeth had been restored in optimal conditions – each received a definitive restoration immediately after endodontic treatment, using an antimicrobial layer of zinc-oxide eugenol to seal the canal orifices. Similarly, teeth included in the study by Peters & Wesselink (52) were all well restored. In contrast, in another study (47) it is apparent that 7% of the teeth had not received definitive restoration by the time of the follow-up examination (Fig. 3). As lack of a definitive restoration can be the cause of microbial ingress into the filled canals (92), it may have resulted in persistence of apical periodontitis in some of the teeth.

When reported, the rate of 'healing' varies from 4% to 21%. The rate of incomplete healing is assumed to
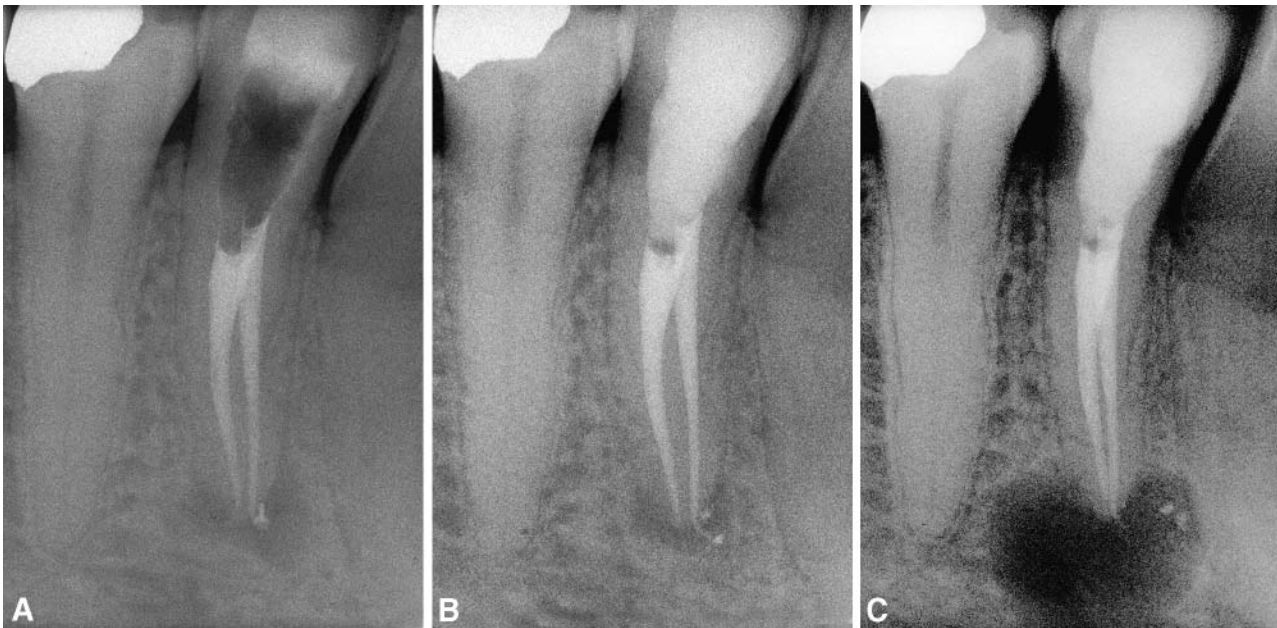

Fig. 12. Reversal or regression in healing of apical periodontitis. A. Immediate post-operative radiograph of mandibular first premolar with apical periodontitis. B. At 7 months, the clearly reduced radiolucency is indicative of the healing in progress. C. At 2 years, the radiolucency has grown larger again beyond its original size, indicative of reversal of the healing process and subsequent regression.

correlate to the follow-up period (2, 40) – in a short time frame, the 'healed' rate is not expected to be definitive. However, this assumption cannot be supported on the basis of the selected studies reviewed herein.

Dynamics of healing

Healing of apical periodontitis peaks within the first year after treatment (71). By 1 year, close to 90% of the teeth that heal eventually demonstrate signs of healing (42), and almost 50% are already completely healed (14). At two years, the majority of the teeth are healed (29, 55), while the others demonstrate further reduction of the radiolucency (23, 29, 36, 42, 55). Reduction of the radiolucency occasionally continues for 4–5 years (14, 29, 36, 42, 55). However, in fewer cases reduction continues even longer (1) – while at 4 years about 13% of the teeth still show reduction (42), closer to 6 years this rate falls down to about 4% (47). Overall, a demonstrated continuous reduction of the radiolucency (comparing at least two follow-up examinations) can be considered as a forecast of complete healing at a later time (29).

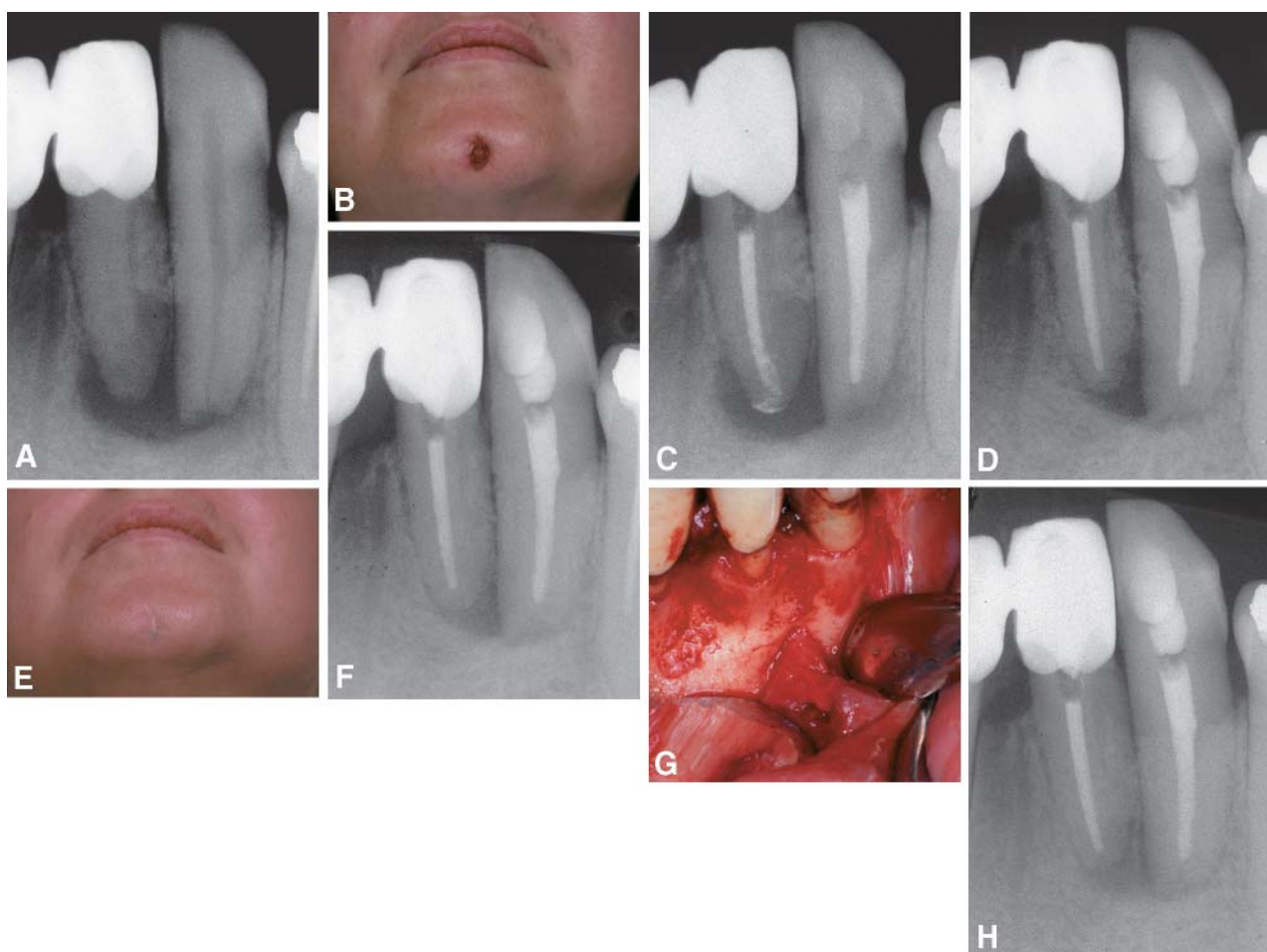Reversal of the healing process (Fig. 12) is believed to be rare (1, 42). Based on this observation, it has

Fig. 13. Scar tissue interfering with complete bone regeneration after therapy of apical periodontitis. A and B. Mandibular lateral incisor and canine with apical periodontitis associated with an oro-facial tract. C. Immediate post-operative radiograph after root canal therapy. D and E. At 1 year, the radiolucency has become considerably reduced and the tract has healed with minimal scarring of the skin. F. At 2 years, no further reduction in the size of the radiolucency is evident. This could be interpreted as persistence of apical periodontitis. G. Clinical view after reflection of a full thickness flap reveals a thick bundle of fibrous tissue connecting the periapical lesion and the soft tissues over the chin. This bundle was dissected out of the periapical cavity and the soft tissue; histological examination confirmed it to be fibrous (scar) tissue. H. At 6 months after surgery, the radiolucency appears to be further reduced and with better definition of the periodontal ligament space, indicative of healing in progress.

been suggested that extended follow-up of teeth that demonstrate signs of healing at one year may be unnecessary (42). However, it should be taken into account that, because all endodontically treated teeth remain constantly challenged by intraoral microorganisms, development of apical periodontitis in the future remains a possibility for all teeth, even those that are completely healed at one point after therapy. Therefore, periodic follow-up of endodontically treated teeth is advocated as a viable routine.

A somewhat different pattern can be observed following apexification – about 8% of healed teeth revert to disease 2–3 years after definitive root filling, and 66% of non-healing teeth do heal after the definitive root filling (93).

Healing of apical periodontitis is expected to eventually become complete; therefore, in the long term, a residual radiolucency is interpreted as persistent or recurrent disease (1, 32, 71). Seldom, however, healing of very extensive apical periodontitis lesions can be completed without total resolution of the radiolucency. In the very few such cases that have been reported, there was fibrous periapical tissue (apical scar) found, rather than a pathological lesion (29, 94–96) (Fig. 13).

Persistence of disease

Persistence of apical periodontitis after initial endodontic therapy (Fig. 14) is most frequently the result of residual infection in the root canal system (97). That is not to say that the etiology is invariably mi-crobial. Foreign materials and true cysts have been shown to cause apical periodontitis-like pathosis in the absence of root canal microorganisms (98, 99); however, this occurrence may be uncommon. The three specimens where this finding occurred represented one third of nine teeth, subjected to biopsy because of persistent disease after endodontic therapy that employed strict microbiological monitoring to verify eradication of intracanal microorganisms before root filling (36). In routine endodontic therapy, however, exclusion of microorganisms is not commonly confirmed before root filling; therefore, the proportion of the non-microbial etiology of persistent disease is likely to be much lower than that suggested by Nair et al. (98, 99).

In contrast, there is consistent evidence that persistent apical periodontitis is primarily caused by infection (100). The microbial sites can differ, as follows:

- Most frequently the microorganisms are harbored in the root canal system (76, 101–108), after having persisted despite the treatment (43), or invaded the filled canal space after treatment, possibly by way of coronal leakage (92).

- Specific microorganisms, particularly *Actinomyces israelii and Arachnia propionica,* can become established in the periapical tissues and sustain the disease process even after root canal microorganisms are eliminated (109–116).

- Recent evidence confirms that microorganisms of other species can be harbored outside the root canal, harbored within the periapical tissue (117–119). They may also survive on the root surface in

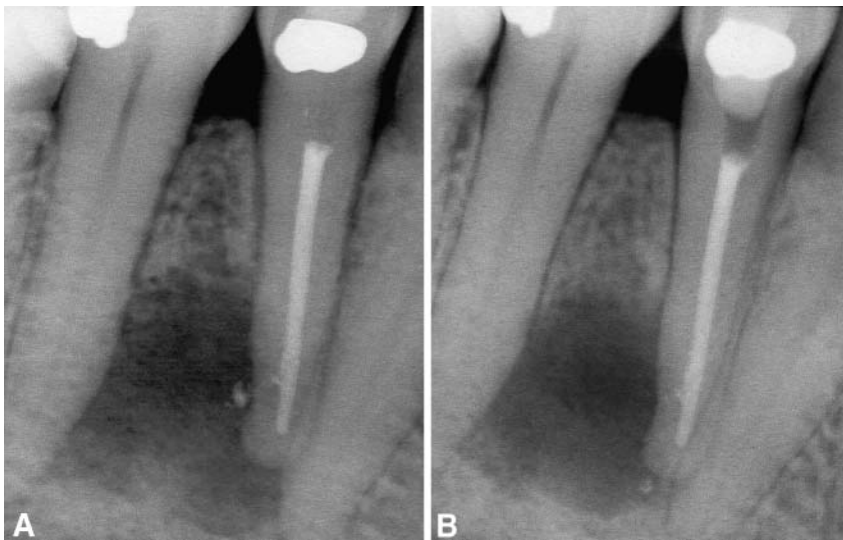Fig. 14. Persisting apical periodontitis. A. Immediate post-oeparative radiograph of mandibular first premolar with apical periodontitis. Note sealer extrusion through lateral canal corresponding to the lateral extension of the radiolucency. B. At 2 years, the minimal reduction of the radiolucency and the tooth being tender to pressure are indicative of persistent apical periodontitis. (See also Figs. 2 and 8).

cementum lacunae (120, 121), plaque-like microbial films (122–125), or in dentin debris inadvertently extruded periapically during treatment (126). However, it cannot be established with certainty to what extent any such extra-radicular (harbored outside the root canal) microorganisms can sustain persistent apical periodontitis without dependence on microbial presence in the root canal. This question still requires clarification; *the answer will have an important bearing on treatment strategies for persistent apical periodontitis.* For the time being, current knowledge suggests that the dominant cause of persistent apical periodontitis is root canal infection, while exclusively extra-radicular infection should be regarded as a far less common occurrence (97).

Prognostic factors in endodontic therapy of teeth with apical periodontitis

In a comprehensive review of the studies on the outcome of initial endodontic treatment, Friedman (2) has concluded that preoperative presence of apical periodontitis has the most decisive influence on the outcome. Other factors appear to influence the outcome to a lesser extent, and therefore their potential prognostic value may be more difficult to demonstrate. Furthermore, because in several of the reviewed studies the information on teeth with apical periodontitis is extracted from a larger material (Table 1), the findings regarding most of the prognostic factors relate to the whole material, but not necessarily to the teeth with apical periodontitis. Clear conclusions can be drawn only from those studies in which the entire sample consisted of teeth with apical periodontitis (Table 1), or where specific analysis was performed for teeth with apical periodontitis (36, 47). For easy identification in the following section, the reference numbers for these studies are highlighted by bold font type. The earlier review (2) discussed most of the pre-, intra-, and postoperative factors, and this review will follow a similar strategy. However, because root canal microorganisms are critically important as the etiological factor in persistent apical periodontitis, their elimination is reviewed as a separate entity for greater emphasis.

Pre-operative factors

Age, gender

In all of the selected studies that examined the patients' age and gender (17, **36**, 38, **47**), these factors do not significantly influence the prognosis of apical periodontitis after endodontic therapy.

Tooth location

Kerekes & Tronstad (17) observe that certain teeth (maxillary canines and second premolars, mandibular canines) have a better prognosis than other teeth, but otherwise have not observed differences between anterior and posterior teeth. Other studies (38, **45**, **47**) also do not demonstrate a specific pattern. Single-rooted teeth have demonstrated a better prognosis in one study (7); however, this may be related to the fact that the whole tooth was considered the unit of evaluation, multiplying the chances of persistent disease by the number of roots. Interestingly, a survival analysis of teeth after endodontic therapy (51) reveals a significantly lower chance of survival for mandibular molars than for other teeth.

Symptoms

Pre-operative symptoms may be a reflection of the microbial types and numbers in the root canal system (127). Nevertheless, the 'healed' rate is comparable for teeth presenting with preoperative symptoms and for asymptomatic teeth (**29**, **36**, **45**, **47**).

Lesion size

A better prognosis of endodontic therapy has been reported for small lesions, up to 5 mm in diameter, than for larger lesions (1, **45**). However, in other studies that examined this factor, differences in prognosis between small and large lesions are not statistically significant (**29**, **36**, 38, **43**, **47**) (Fig. 15). Nevertheless, there appears to be a correlation between the size of the lesion and the number of root canal microorganisms (**29**); this could possibly affect differences in prognosis.

Periodontal condition

The preoperative periodontal condition of the tooth undergoing endodontic therapy has received little

consideration with regard to the prognosis of apical periodontitis. According to Sjögren et al. (**36**), it does not influence the prognosis. Clearly, if periodontal disease is present, it continues into the follow-up period – it may advance with time so that tooth loss becomes imminent. Indeed, Abitbol (**47**) observes that of the total of 21 lost teeth, 52% had been extracted because of periodontal disease.

Systemic health

The influence of this factor on the prognosis has not been elucidated in any of the studies selected for this review. Although the patient's health was one of the research questions in Strindberg's study (1), it is not mentioned in the results; an assumption can be made that this factor was not found to significantly influence the prognosis.

Intra-operative factors

Apical extent of treatment

It would be appropriate to distinguish between the apical extent of the canal preparation and that of the root filling (1, 7); however, the majority of the studies

selected for this review refer only to the extent of the root filling. This factor has been shown to influence the prognosis in four of the reviewed studies (1, 7, **36**, 38), but not in three other studies (**29**, **45**, **47**).

Extrusion of filling materials beyond the root end generally results in a poorer prognosis (1, 7, **36**, 38). Because gutta-percha is well tolerated by the tissue, the impaired prognosis is more likely to result from over-instrumentation and periapical displacement of infected debris than from the extrusion of root filling materials *per se* (**36**, 126) (Fig. 16). Extruded root filling materials can be totally or partially removed during the healing process (1, 27, 35).

Sjögren et al. (**36**) observe that inability to instrument the canal to the apical constriction and an excessively short root filling (2 mm or shorter) impairs the prognosis relative to an adequate filling (0–2 mm short); however, this finding is not corroborated in a previous study by the same group of researchers (**29**).

Apical enlargement

Only two of the selected studies examine this factor – Strindberg (1) observes that a larger apical preparation is associated with a poorer prognosis, whereas Kerekes & Tronstad (17) observe a comparable prog-
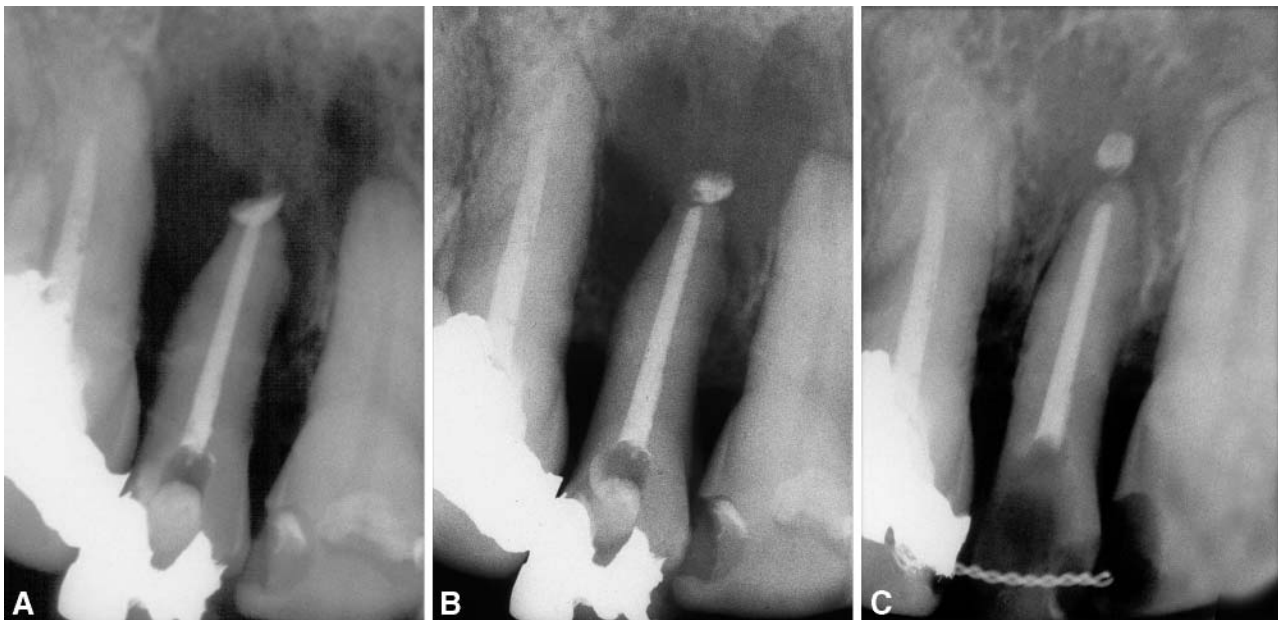
Fig. 15. Healing of a large lesion. A. Maxillary lateral incisor with extensive apical periodontitis and advanced periodontal disease, leaving the tooth with very little bone support. B. Immediate post-operative radiograph. C. At 4 years, the large apical periodontitis lesion has healed; the ongoing periodontal disease has resulted in further marginal bone loss. (For further examples of healing of large lesions see also Figs. 5 and 9).

Fig. 16. Periapically extruded gutta-percha. Maxillary first molar with 2 gutta-percha cones extruded at least 10 mm beyond the terminus of both the buccal roots. Although the same conditions apparently exist in both roots, the mesio-buccal root is associated with apical periodontitis while the disto-buccal root is not, suggesting that the cause of apical periodontitis is not the extruded gutta-percha.

to a depth of 150–250 μm (129–131), where they may be protected from irrigants and medicaments (132). Only enlargement of the canal to sizes 300–500 μm larger than its original diameter (for example, final file ISO size 50–70 if the first file that binds is size 20) can remove the infected dentin. Extensive apical enlargement is thus believed to enhance the removal of infected dentin and the disinfection of the apical portion of the canal (127, 133, 134), and it should translate into an improved prognosis. However, carrying out extensive apical enlargement is frequently associated with canal transportation that may jeopardize canal disinfection and impair the prognosis. Clearly, the procedure of extensive apical enlargement is technique-sensitive, and it requires considerable skill, particularly when performed with stainless steel hand files. It is possible that the inability to demonstrate differences in prognosis in relation to extensive or minimal apical enlargement is the reflection of the problems associated with both alternatives − extensive apical enlargement (Fig. 17B), *if not carried out skillfully,* may transport the canal, whereas minimal enlargement (actually, no enlargement (Fig. 17A)) may leave infected dentin behind. Both effects would compromise the prognosis to some extent (2).

nosis for apical enlargement to ISO sizes 20–40 and 45–100 (Fig. 17). These findings appear to be in conflict with the conceptual importance of removing infected dentin in endodontic therapy. Root dentin is penetrated by intracanal microorganisms (121, 128)

Culturing

The original study that correlated a negative culture obtained before root filling with a better prognosis (7) utilized microbiological techniques that did not ad-

Fig. 17. Extent of apical enlargement in two mandibular first molars with apical periodontitis. A. Minimal enlargement, to ISO size 30 in both the mesial canals, and to size 45 in the distal canal. B. Extensive enlargement, to size 60 in both the mesial canals and the disto-lingual canal (not seen), and to size 80 in the disto-buccal canal. These canals were enlarged with stainless steel files; however, canal transportation is more likely to be avoided if nickel-titanium files are used to enlarge the apical portion of the canal.

equately address the anaerobic bacteria that are the major endodontic pathogens (**43**). Using an advanced anaerobic bacteriological technique, Sjögren et al. (**43**) have observed complete healing in 94% of teeth in which the cultures were negative before root filling, in contrast to only 68% in teeth with positive cultures. This finding clearly demonstrates the potential value of reliable culturing in prognostication of endodontic therapy, even though it is apparently disputed by a most recent study (**52**). Furthermore, it appears that the microbial species that infect the canal also may influence the prognosis (**43**). Nevertheless, state-of-the-art culturing techniques are not readily available for use in the day-to-day practice of endodontic therapy (**43**).

Treatment sessions

When treatment is performed in two sessions or more, the prognosis may not be influenced by the number of sessions (17). However, a survival analysis reveals that teeth treated in two sessions or less have a better chance of surviving than teeth treated in multiple sessions (51). This finding appears to parallel that of Sirén et al. (135), who suggest that teeth treated in multiple visits are at a greater risk of becoming infected with *E. faecalis*, and developing persistent apical periodontitis.

The 'hottest' question in endodontics today is whether the prognosis differs for treatment in one session or two. Sjögren et al. (**43**) clearly demonstrate that intracanal infection cannot be reliably eliminated in a single treatment session. To maximize disinfection, application of intracanal medication is required (56–61). Therefore, an improved prognosis is expected to be improved when treatment is performed in two sessions and an effective intracanal medication is used in between. This hypothesis is not clearly supported in the clinical studies selected for this review (Table 2). Consistently, differences in healing rates shown in the relevant reviewed studies for treatment in one or two sessions have not been statistically significant (**44**, **45**, **47**, **52**). The main reason for the lack of significance is the insufficient power of these studies – the differences observed in healing rates are too small for significance to be established with the limited sample included in the studies. Undoubtedly, treatment in one session can have a very good prognosis (**43**).

Flare-up

Only three studies from those reviewed herein (17, **29**, **36**) examine this factor. They all conclude that the occurrence of flare-up or pain between treatment sessions does not influence the prognosis of apical periodontitis after completion of endodontic therapy.

Materials and technique

Clinical study-based information on the impact of the treatment technique or the materials used on the prognosis is sparse. This issue can be divided into the following:

- *Intracanal medicament:* Cheung's (51) survival analysis reveals that teeth medicated with calcium hydroxide have a better chance to survive than teeth that are not medicated or medicated with other materials.
- *Instrumentation technique:* Kerekes & Tronstad (17) suggest that the prognosis may be better using the 'standardized' technique than with the 'serial' technique.
- *Root-filling technique:* Abitbol (**47**) observes a comparable prognosis for lateral and vertical condensation.
- *Sealer:* When studying a large sample of teeth without and with apical periodontitis, Ørstavik et al. (55) suggest that the choice of sealer may influence the prognosis. However, in a smaller sample of teeth with apical periodontitis (**34**) and in another study of a larger population (38) the sealer had no impact on the prognosis.

Complications

Mid-treatment complications, such as perforation of the pulp chamber or root, file breakage at a stage that prevents cleaning of the canal, and massive extrusion of filling materials (Fig. 18), all impair the prognosis (1, 17, **36**). Overall, however, these complications appear to be infrequent (136).

Post-operative factors

Restoration

Friedman et al. (92) clearly demonstrate that root canal infection and associated apical periodontitis can

Table 2. Selected follow-up studies on the outcome of initial endodontic therapy in teeth with apical periodontitis, performed in one or two sessions

	Follow-up (years)	One session		Two sessions	
		n	healed	*n*	healed
Sjögren et al. 1990	8–10	204	86%	–	–
Sjögren et al. 1997	≤5	–	–	53	83%
Trope et al. 1999	1	22[a]	64%	19[a]	74%
Weiger et al. 2000	1–5	36	83%	31	71%
Abitbol 2001	4–6	12	58%	60	76%
Peters & Wesselink 2002	1–4.5	21	81%	12	71%

[a]Only teeth with extensive apical periodontitis (PAI > 3) included.

occur subsequent to endodontic treatment, when microorganisms become established in the coronal portion of the tooth, e.g. the pulp chamber. This finding corroborates earlier indications of microbial proliferation in the filled root canal *in vitro* (137–141). Nevertheless, correlation of the prognosis with the status of the restoration has not been clearly established. The type of the restoration (temporary, de-finitive, filling, cast) does not appear to influence the prognosis (**43**, **47**), with the exception of one study (**36**) where teeth restored with crowns or serving as bridge abutments show a poorer prognosis than teeth restored with fillings. Regarding posts, their presence or absence may influence the prognosis if the remaining root filling is reduced to less than 3 mm (142). In a recent cross-sectional study (**72**), the presence of

Fig. 18. Massive extrusion of root canal sealer. A. Immediate post-operative radiograph of mandibular first premolar with extensive apical periodontitis. Note large mass of sealer (glass ionomer cement) extruded beyond the root end. B. At 9 months, the radiolucency had become larger. The tooth is restored with a post-core and a temporary crown. The patient was advised to undergo apical surgery. C. At 3 years, it is apparent that the patient has not had surgery as advised, and the temporary crown has not been replaced for a permanent one. Nevertheless, the radiolucency has become reduced to approximately half its original size.

posts has been associated with an increased prevalence of apical periodontitis.

Although there is insufficient data to examine the prognostic value of the restoration, it is clear that the restoration, and particularly restorative failure, plays an important role in the survival or loss of endodontically treated teeth (136). Abitbol (47) reports that of the total of 21 lost teeth, 29% were extracted because of restorative considerations, compared to 19% that were extracted for other causes including persistent apical periodontitis. Posts clearly present a risk to endodontically treated teeth (Fig. 19) – they have been identified as the cause of vertical root fracture and tooth loss in approximately 9% of cases (136). Also, root perforation associated with a post impairs the prognosis (143). In a survival analysis, Cheung (51) reports that 53% of teeth lost after endodontic therapy were extracted because of fracture (root or crown is not specified), with additional teeth extracted because of a 'prosthetic need'.
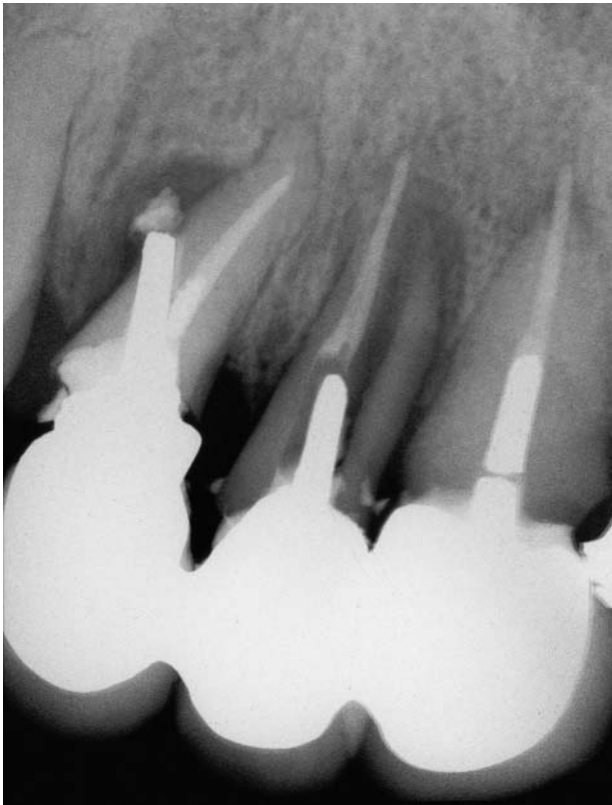

Fig. 19. Risks associated with post-retained restoration of endodontically-treated teeth (from left to right) – perforation, root fracture and post fracture.

Summary of prognostic factors – microbial elimination

When initial endodontic treatment is reviewed in general, there is a consensus among most studies that preoperative apical periodontitis is by far the most dominant factor that influences the prognosis, but no such consensus exists with regards to the prognostic value of other factors (2). Because apical periodontitis is caused and sustained primarily by root canal infection, it can be argued that *the extent to which root canal infection is eliminated is, in itself, a prognostic factor* (43). Therefore, use of means that enhance microbial elimination should be considered as enhancing the prognosis.

Irrigation

The first critically important step in elimination of root canal microorganisms is irrigation with effective bactericidal solutions. Byström & Sundqvist (56), and more recently Dalton et al. (60), have observed that root canal instrumentation coupled with inactive irrigants does not predictably eliminate microorganisms, regardless of whether it is carried out with stainless-steel hand instruments or with nickel-titanium engine-driven ones. The chances to eliminate microorganisms and obtain a negative culture using filing and inactive irrigants are about 30% (60). In contrast, irrigation with sodium hypochlorite, even if it is diluted to 0.5% or 1.25%, considerably improves the efficiency of microbial elimination (57, 58, 61). The chances to obtain a negative culture then increase to about 60% (61).

Dressing

The next step in elimination of root canal microorganisms is dressing with an effective medicament, which requires completion of treatment at a subsequent session. Apparently, there has been some controversy about the importance of this step. Byström and coworkers (29, 59) have clearly demonstrated the superior efficiency of intracanal dressing with calcium hydroxide in microbial elimination. According to Shuping et al. (61), the chances of obtaining a negative culture after such dressing are about 90%. However, the most recent findings of Peters et al. (144) did not corroborate this conclusion – in

fact, they observed an increase in microbial counts after root canal dressing with calcium hydroxide. It is difficult to reconcile those contrary findings. Some concern has been voiced regarding the calcium hydroxide application technique used by Peters et al. (144) – the dressing was plugged with paper points, which could have excessively dried the calcium hydroxide mix. A similar technique was used in the clinical study (51), where teeth dressed with calcium hydroxide and treated in two sessions have healed slightly less frequently than those filled in one session. Nevertheless, placement of calcium hydroxide is not recognized as being highly technique-sensitive, and the aforementioned concerns may be unfounded. Clearly, more research is required to irrefutably establish whether dressing with calcium hydroxide, or another effective medicament, is critical in the elimination of root canal microorganisms.

Enlargement

Microbial elimination appears to improve with progressive enlargement of the root canal. Even without the use of sodium hypochlorite, microbial counts are somewhat reduced when the canal is enlarged from ISO size 45 (size 25 in curved canals) to size 50 and 60 (size 30 and 35 in curved canals) (60). This reduction is even more pronounced when sodium hypochlorite is used (61). However, when the apical portion of the canal is enlarged to even larger sizes with the use of nickel-titanium instruments, a further reduction is clearly demonstrated (134), supporting the premise that enlargement does promote microbial elimination.

From the data presented above, a clear picture emerges – the combination of abundant use of sodium hypochlorite (with a small gauge needle that allows its penetration into the apical portions of the root canal), extensive apical enlargement (to sizes approximating those listed by Kerekes & Tronstad (145–147)), and dressing with an effective intracanal medicament such as calcium hydroxide, has the best potential to maximize elimination of root canal microorganisms. Because microorganisms are the primary cause of persistent apical periodontitis, the ability to maximize microbial elimination by meticulously applying the aforementioned combination of therapeutic means enhances the prognosis of endodontic therapy of apical periodontitis.

Case selection

Selection of cases for endodontic therapy takes into consideration the prognosis of the endodontic, restorative and periodontal procedures, but also health and socio-economic factors. Contraindications to treatment include non-restorable and periodontally hopeless teeth, patients with extensive dental problems and restricted resources (which have to be utilized so to benefit as many teeth as possible), and medically compromised patients at high-risk for infection.

From the endodontic perspective, none of the preoperative clinical factors truly contraindicates therapy. The prognosis of endodontic therapy of apical periodontitis is good – the chances of complete healing are reasonably high, and the chances for the tooth remaining asymptomatic and functional over time are truly excellent, provided that the tooth is promptly and well restored. Therefore, whenever feasible, endodontic therapy should be attempted before considering tooth extraction and replacement.

References

1. Strindberg LZ. The dependence of the results of pulp therapy on certain factors. An analytic study based on radiographic and clinical follow-up examination. *Acta Odontol Scand* 1956: **14**: Suppl. 21.
2. Friedman S. Treatment outcome and prognosis of endodontic therapy. In: Ørstavik D, Pitt Ford TR, eds. *Essential endodontology: Prevention and treatment of apical periodontitis*. Oxford: Blackwell Science, 1998.
3. Grahnén H, Hansson L. The prognosis of pulp and root canal therapy. *Odontol Revy* 1961: **12**: 146–165.
4. Seltzer S, Bender IB, Turkenkopf S. Factors affecting successful repair after root canal therapy. *J Am Dent Assoc* 1963: **52**: 651–662.
5. Bender IB, Seltzer S. To culture or not to culture?. *Oral Surg Oral Med Oral Pathol* 1964: **18**: 527–540.
6. Grossman LI, Shepard LI, Pearson LA. Roentgenologic and clinical evaluation of endodontically treated teeth. *Oral Surg Oral Med Oral Pathol* 1964: **17**: 368–374.
7. Engström B, Hard AF, Segerstad L, Ramstrom G, Frostell G. Correlation of positive cultures with the prognosis for root canal treatment. *Odontol Revy* 1964: **15**: 257–270.
8. Oliet S, Sorin SM. Evaluation of clinical results based upon culturing root canals. *J Br Endod Soc* 1969: **3**: 3–6.
9. Storms JL. Factors that influence the success of endodontic treatment. *J Can Dent Assoc* 1969: **35**: 83–97.
10. Harty FJ, Parkins BJ, Wengraf AM. Success rate in root canal therapy. *Br Dent J* 1970: **128**: 65–70.
11. Heling B, Tamshe A. Evaluation of the success of endodontically treated teeth. *Oral Surg Oral Med Oral Pathol* 1970: **30**: 533–536.

12. Tamse A, Heling B. Success of endodontically treated anterior teeth in young and adult patients. *Ann Dent* 1973: **32**: 20–27.

13. Selden HS. Pulpoperiapical disease: diagnosis and healing. *Oral Surg Oral Med Oral Pathol* 1974: **37**: 271–283.

14. Adenubi JO, Rule DC. Success rate for root fillings in young patients. *Br Dent J* 1976: **141**: 237–241.

15. Heling B, Shapira J. Roentgenologic and clinical evaluation of endodontically treated teeth, with or without negative culture. *Quintessence Int* 1978: **11**: 79–84.

16. Jokinen MA, Kotilainen R, Poikkeus P, Poikkeus R, Sarkki L. Clinical and radiographic study of pulpectomy and root canal therapy. *Scand J Dent Res* 1978: **86**: 366–373.

17. Kerekes K, Tronstad L. Long-term results of endodontic treatment performed with a standardized technique. *J Endod* 1979: **5**: 83–90.

18. Barbakow FH, Cleaton-Jones P, Friedman D. An evaluation of 566 cases of root canal therapy in general dental practice. 2. Postoperative observations. *J Endod* 1980: **6**: 485–489.

19. Barbakow FH, Cleaton-Jones PE, Friedman D. Endodontic treatment of teeth with periapical radiolucent areas in a general dental practice. *Oral Surg Oral Med Oral Pathol* 1981: **51**: 552–559.

20. Nelson JA. Endodontics in general practice – a retrospective study. *Int Endod J* 1982: **15**: 168–172.

21. Cvek M, Granath L, Lundberg M. Failures and healing in endodontically treated non-vital anterior teeth with post-traumatically reduced pulpal lumen. *Acta Odontol Scand* 1982: **40**: 223–228.

22. Oliet S. Single-visit endodontics: a clinical study. *J Endod* 1983: **9**: 147–152.

23. Klevant FJH, Eggink CO. The effect of canal preparation on periapical disease. *Int Endod J* 1983: **16**: 68–75.

24. Morse DR, Esposito JV, Pike C, Furst ML. A radiographic evaluation of the periapical status of teeth treated by the gutta-percha – eucapherca endodontic method. A one-year follow-up study of 458 root canals. *Oral Surg Oral Med Oral Pathol* 1983: **55**: 56, 89–96; 190–197.

25. Swartz DB, Skidmore AE, Griffin JA. Twenty years of endodontic success and failure. *J Endod* 1983: **9**: 198–202.

26. Pekruhn RB. The incidence of failure following single-visit endodontic therapy. *J Endod* 1986: **12**: 68–72.

27. Halse A, Molven O. Overextended gutta-percha and Kloroperka N-Ø root canal fillings. *Acta Odontol Scand* 1987: **45**: 171–177.

28. Safavi KE, Dowden WE, Langeland K. Influence of delayed coronal permanent restoration on endodontic prognosis. *Endod Dent Traumatol* 1987: **3**: 187–191.

29. Byström A, Happonen RP, Sjögren U, Sundqvist G. Healing of periapical lesions of pulpless teeth after endodontic treatment with controlled asepsis. *Endod Dent Traumatol* 1987: **3**: 58–63.

30. Matsumoto T, Nagai T, Ida K, Ito M, Kawai Y, Horiba N, Sato R, Nakamura H. Factors affecting successful prognosis of root canal treatment. *J Endod* 1987: **13**: 239–242.

31. Åkerblom A, Hasselgren G. The prognosis for endodontic treatment of obliterated root canals. *J Endod* 1988: **14**: 565–567.

32. Molven O, Halse A. Success rates for gutta-percha and Kloroperka N-Ø root fillings made by undergraduate students: radiographic findings after 10–17 years. *Int Endod J* 1988: **21**: 243–250.

33. Shah N. Nonsurgical management of periapical lesions: a prospective study. *Oral Surg Oral Med Oral Pathol* 1988: **66**: 365–371.

34. Eriksen HM, Ørstavik D, Kerekes K. Healing of apical periodontitis after endodontic treatment using three different root canal sealers. *Endod Dent Traumatol* 1988: **4**: 114–117.

35. Augsburger RA, Peters DD. Radiographic evaluation of extruded obturation materials. *J Endod* 1990: **16**: 492–497.

36. Sjögren U, Hägglund B, Sundqvist G, Wing K. Factors affecting the long-term results of endodontic treatment. *J Endod* 1990: **16**: 498–504.

37. Murphy WK, Kaugars GE, Collett WK, Dodds RN. Healing of periapical radiolucencies after nonsurgical endodontic therapy. *Oral Surg Oral Med Oral Pathol* 1991: **71**: 620–624.

38. Ørstavik D, Hörsted-Bindslev P. A comparison of endodontic treatment results at two dental schools. *Int Endod J* 1993: **26**: 348–354.

39. Smith CS, Setchell DJ, Harty FJ. Factors influencing the success of conventional root canal therapy – a five-year retrospective study. *Int Endod J* 1993: **26**: 321–333.

40. Friedman S, Löst C, Zarrabian M, Trope M. Evaluation of success and failure after endodontic therapy using glass ionomer cement sealer. *J Endod* 1995: **21**: 384–390.

41. Caliskan MK, Sen BH. Endodontic treatment of teeth with apical periodontitis using calcium hydroxide: a long-term study. *Endod Dent Traumatol* 1996: **12**: 215–221.

42. Ørstavik D. Time-course and risk analyses of the development and healing of chronic apical periodontitis in man. *Int Endod J* 1996: **29**: 150–155.

43. Sjögren U, Figdor D, Persson S, Sundqvist G. Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis. *Int Endod J* 1997: **30**: 297–306.

44. Trope M, Delano O, Ørstavik D. Endodontic treatment of teeth with apical periodontitis: Single vs. multivist treatment. *J Endod* 1999: **25**: 345–350.

45. Weiger R, Rosendahl R, Löst C. Influence of calcium hudroxide intracanal dressings on the prognosis of teeth with endodontically induced periapical lesions. *Int Endod J* 2000: **33**: 219–226.

46. Chugal NM, Clive JM, Spangberg LSW. A prognostic model for assessment of the outcome of endodontic treatment: Effect of biologic and diagnostic variables. *Oral Surg Oral Med Oral Pathol* 2001: **91**: 342–352.

47. Abitbol S. Outcome of non-surgical endodontic treatment. MSc Dissertation. Toronto': University of Toronto, 2001.

48. Peak JD, Hayes SJ, Bryant ST, Dummer PMH. The outcome of root canal treatment. A retrospective study within the armed forces (Royal Air Force). *Br Dent J* 2001: **190**: 140–144.

49. Pettiette MT, Delano EO, Trope M. Evaluation of success rate of endodontic treatment performed by students with stainless-steel K-files and nickel-titanium hand files. *J Endod* 2001: **27**: 124–127.

50. Heling I, Bialla-Shenkman S, Turetzky A, Horwitz J. The

outcome of teeth with periapical periodontitis treated with nonsurgical endodontic treatment: a computerized morphometric study. *Quintessence Int*, 2001: **32**: 397–400.

51. Cheung GSP. Survival of first-time non-surgical root canal treatment performed in a dental teaching hospital. *Oral Surg Oral Med Oral Pathol* 2002; in press.

52. Peters LB, Wesselink PR. Periapical healing of endodontically treated teeth in one and two visits obturated in the presence or absence of detectable microorganisms. *Int Endod J* 2002: **35**: 660–667.

53. Fletcher RH, Fletcher SW, Wagner EH. *Clinical epidemiology: the essentials*, 3rd edn. Baltimore: Williams & Wilkins, 1996.

54. Ingle JI, Beveridge EE, Glick DH, Weichman JA. Modern endodontic therapy. In: Ingle JI, Bakland LK, eds. *Endodontics*, 4th edn. Baltimore: Williams & Wilkins, 1994: 27–53.

55. Ørstavik D, Kerekes K, Eriksen HM. Clinical performance of three endodontic sealers. *Endod Dent Traumatol* 1987: **3**: 178–186.

56. Byström A, Sundqvist G. Bacteriologic evaluation of the efficacy of mechanical root canal instrumentation in endodontic therapy. *Scand J Dent Res* 1981: **89**: 321–328.

57. Byström A, Sundqvist G. Bacteriologic evaluation of the effect of 0.5 percent sodium hypochlorite in endodontic therapy. *Oral Surg Oral Med Oral Pathol* 1983: **55**: 307–312.

58. Byström A, Sundqvist G. The antibacterial action of sodium hypochlorite and EDTA in 60 cases of endodontic therapy. *Int Endod J* 1985: **18**: 35–40.

59. Byström A, Claeson R, Sundqvist G. The antibacterial effect of camphorated paramono chlorphenol, camphorated phenol and calcium hydroxide. *Endod Dent Traumatol* 1985: **1**: 170–175.

60. Dalton BC, Ørstavik D, Phillips C, Pettiette M, Trope M. Bacterial reduction with nickel-titanium rotary instrumentation. *J Endod* 1998: **24**: 763–767.

61. Shuping GB, Ørstavik D, Sigurdsson A, Trope M. Reduction of intracanal bacteria using nickel-titanium rotary instrumentation and various medications. *J Endod* 2000: **26**: 751–755.

62. Messer HH, Chen R-S. The duration of effectiveness of root canal medicaments. *J Endod* 1984: **10**: 240–245.

63. Tronstad L, Yang Z-P, Trope M, Barnett F, Hammond BF. Controlled release of medicaments in endodontic therapy. *Endod Dent Traumatol* 1985: **1**: 130–134.

64. Fager FK, Messer HH. Systemic distribution of camphorated monochlorophenol from cotton pellets sealed in pulp chambers. *J Endod* 1986: **12**: 225–230.

65. Brynolf L. Histological and roentgenological study of periapical region of human upper incisors. *Odontol Revy* 1967: **18**: Suppl. 11.

66. Goldman M, Pearson AH, Darzenta N. Endodontic success -Who's reading the radiograph?. *Oral Surg Oral Med Oral Pathol* 1972: **33**: 432–437.

67. Goldman M, Pearson AH, Darzenta N. Reliability of radiographic interpretation. *Oral Surg Oral Med Oral Pathol* 1974: **38**: 287–293.

68. Reit C, Hollander L. Radiographic evaluation of endodontic therapy and the influence of observer variation. *Scand J Dent Res* 1983: **91**: 205–212.

69. Zakariasen KL, Scott DA, Jensen JR. Endodontic recall radiographs: how reliable is our interpretation of endodontic success or failure and what factors affect our reliability?. *Oral Surg Oral Med Oral Pathol* 1984: **57**: 343–347.

70. Eckerbom M, Andersson J-E, Magnusson T. Interobserver variation in radiographic examination of endodontic variables. *Endod Dent Traumatol* 1986: **2**: 243–246.

71. Reit C. Decision strategies in endodontics. on the design of a recall program. *Endod Dent Traumatol* 1987: **3**: 233–239.

72. Boucher Y, Matossian L, Rilliard F, Machtou P. Radiographic evaluation of the prevalence and technical quality of root canal treatment in a French subpopulation. *Int Endod J* 2002: **35**: 229–238.

73. Bender IB, Seltzer S, Soltanoff W. Endodontic success − a reappraisal of criteria. *Oral Surg Oral Med Oral Pathol* 1966: **22**: 780–802.

74. Ørstavik D, Kerekes K, Eriksen HM. The periapical index: a scoring system for radiographic assessment of apical periodontitis. *Endod Dent Traumatol* 1986: **2**: 20–34.

75. Dugas NN, Lawrence HP, Teplitsky MJ, Pharoah MJ, Friedman S. Periapical health and treatment quality assessment of root-filled teeth in two Canadian populations. *Int Endod J* 2002: in press.

76. Lin LM, Pascon EA, Skribner J, et al. Clinical, radiographic, and histologic study of endodontic treatment failures. *Oral Surg Oral Med Oral Pathol* 1991: **11**: 603–611.

77. Smith DE, Zarb GA. Criteria for success of osseointegrated endosseous implants. *J Prosthet Dent* 1989: **62**: 567–572.

78. Creugers NHJ, Kreulen CM, Snoek PA, de Kanter RJAM. A systematic review of single-tooth restorations supported by implants. *J Dent* 2000: **28**: 209–217.

79. Taintor JF, Ingle JI, Fahid A. Retreatment versus further treatment. *Clin Prev Dent* 1983: **5**: 8–14.

80. Ørstavik D, Pitt Ford TR. Apical periodontitis: Microbial infection and host responses. In: Ørstavik D, Pitt Ford TR, eds. *Essential endodontology: Prevention and treatment of apical periodontitis.* Oxford: Blackwell Science, 1998.

81. Caplan DJ, Weintraub JA. Factors related to loss of root canal filled teeth. *J Public Health Dent* 1997: **57**: 31–39.

82. Caplan DJ, Kolker J, Rivera EM, Walton RE. Relationship between number of proximal contacts and survival of root canal treated teeth. *Int Endod J* 2002: **35**: 193–199.

83. Anderson JD. Need for evidence-based practice in prosthodontics. *J Prosthet Dent* 2000: **83**: 58–65.

84. Oxman AD, ed. *Section VI. Preparing and Maintaining Systematic Reviews: The Cochrane Collaboration Handbook.* Oxford: Cochrane Collaboration, 1994.

85. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical Epidemiology: a basic science of clinical medicine*, 2nd edn. Boston: Little, Brown, 1991.

86. Green SB, Byar DP. Using observational data from registries to compare treatments. the fallacy of omnimetrics. *Stat Med* 1984: **3**: 361–373.

87. Benson K, Hartz AJ. A comparison of observational studies and randomized, controlled trials. *N Engl J Med* 2000: **342**: 1878–1886.

88. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *N Engl J Med* 2000: **342**: 1887–1892.

89. Barton S. Editorial. Which clinical studies provide the best evidence? *Br Med J* 2000: **321**: 255–256.

90. Department of Clinical Epidemiology and Biostatistics McMaster University Health Science Centre. How to read clinical journals. III. To learn the clinical course and prognosis of disease. *Can Med Assoc J* 1981: **124**: 869–872.

91. Bader JD, Shugars DA. Variation, treatment outcomes and practice guidelines in dental practice. *J Dent Ed*, 1995: **59**: 61–95.

92. Friedman S, Komorowski R, Maillet W, Klimaite R, Nguyen HQ, Torneck CD. Resistance of coronally induced bacterial ingress by an experimental glass ionomer cement root canal sealer *in vivo*. *J Endod* 2000: **26**: 1–5.

93. Cvek M. Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-percha. A retrospective clinical study. *Endod Dent Traumatol* 1992: **8**: 45–55.

94. Penick EC. Periapical repair by dense fibrous connective tissue following conservative endodontic therapy. *Oral Surg Oral Med Oral Pathol* 1961: **14**: 239–242.

95. Selden HS. Periradicular scars: a sometime diagnostic conundrum. *J Endod* 1999: **25**: 829–830.

96. Nair PNR, Sjögren U, Figdor D, Sundqvist G. Persistent periapical radiolucencies of root-filled human teeth, failed endodontic treatments, and periapical scars. *Oral Surg Oral Med Oral Pathol* 1999: **87**: 617–627.

97. Friedman S. Considerations and concepts of case selection in the management of post-treatment endodontic disease (treatment failure). *Endod Topics* 2002: **1**: 54–78.

98. Nair PNR, Sjögren U, Krey G, Sundqvist G. Therapy-resistant foreign body giant cell granuloma at the periapex of a root-filled human tooth. *J Endod* 1990: **16**: 589–595.

99. Nair PNR, Sjögren U, Schumacher E, Sundqvist G. Radicular cyst affecting a root-filled human tooth: a long-term post-treatment follow-up. *Int Endod J* 1993: **26**: 225–233.

100. Siqueira JF. Aetiology of root canal treatment failure: why well-treated teeth can fail. *Int Endod J* 2001: **34**: 1–10.

101. Fukushima H, Yamamoto K, Hirohata K, Sagawa H, Leung K-P, Walker CB. Localization and identification of root canal bacteria in clinically asymptomatic periapical pathosis. *J Endod* 1990: **16**: 534–538.

102. Baumgartner JC, Falkler WA. Bacteria in the apical 5 mm of infected root canals. *J Endod* 1991: **17**: 380–383.

103. Lin LM, Skribner JE, Gaengler P. Factors associated with endodontic treatment failures. *J Endod* 1992: **12**: 625–627.

104. Sundqvist G, Figdor D, Persson S, Sjögren U. Microbiologic analysis of teeth with failed endodontic treatment and the outcome of conservative retreatment. *Oral Surg Oral Med Oral Pathol* 1998: **85**: 86–93.

105. Molander A, Reit C, Dahlén G, Kvist T. Microbiological status of root filled teeth with apical periodontitis. *Int Endod J* 1998: **31**: 1–7.

106. Peciuliene V, Balciuniene I, Eriksen HM, Haapasalo M. Isolation of *Enterococcus faecalis* in previously root-filled canals in a Lithuanian population. *J Endod* 2000: **26**: 593–595.

107. Peciuliene V, Reynaud AH, Balciuniene I, Haapasalo M. Isolation of yeasts and enteric bacteria in root-filled teeth with chronic apical periodontitis. *Int Endod J* 2001: **34**: 429–434.

108. Hancock HH, Sigurdson A, Trope M, Moiseiwitsch J. Bacteria isolated after unsuccessful endodontic treatment in a North American population. *Oral Surg Oral Med Oral Pathol* 2001: **91**: 579–586.

109. Sundqvist G, Reuterwing C-O. Isolation of *Actinomyces israelii* from periapical lesion. *J Endod* 1980: **6**: 602–606.

110. Nair PRN, Schroeder JH. Periapical actinomycosis. *J Endod* 1984: **10**: 567–570.

111. Happonen R-P, Soderling E, Viander M, Linko-Kettunen L, Pelliniemi LJ. Immunocytochemical demonstration of *Actinomyces* species and *Arachnia propionica* in periapical infections. *J Oral Pathol* 1985: **14**: 405–413.

112. Happonen R-P. Periapical actinomycosis. A follow-up study of 16 surgically treated cases. *Endod Dent Traumatol* 1986: **2**: 205–209.

113. Haapasalo M, Ranta K, Ranta H. Mixed anaerobic periapical infection with sinus tract. *Endod Dent Traumatol* 1987: **3**: 83–85.

114. O'Grady JF, Reade PC. Periapical actinomycosis involving *Actinomyces israeli*. *J Endod* 1988: **14**: 147–149.

115. Sjögren U, Happonen R-P, Kahnberg KE, Sundqvist G. Survival of *Arachnia propionica* in periapical tissue. *Int Endod J* 1988: **21**: 277–282.

116. Sakellariou PL. Periapical actinomycosis: report of a case and review of the literature. *Endod Dent Traumatol* 1996: **12**: 151–154.

117. Gatti JJ, Dobeck JM, Smith C, White RR, Socransky SS, Skobe Z. Bacteria of asymptomatic periradicular endodontic lesions identified by DNA–DNA hybridization. *Endod Dent Traumatol* 2000: **16**: 197–204.

118. Sunde PT, Olsen I, Lind PO, Tronstad L. Extraradicular infection: a methodological study. *Endod Dent Traumatol* 2000: **16**: 84–90.

119. Sunde PT, Tronstad L, Eribe ER, Lind PO, Olsen I. Assessment of periradicular microbiota by DNA–DNA hybridization. *Endod Dent Traumatol* 2000: **16**: 191–196.

120. Pitt Ford TR. The effects on the periapical tissues of bacterial contamination of the filled root canal. *Int Endod J* 1982: **15**: 16–22.

121. Nair PNR. Light and electron microscopic studies of root canal flora and periapical lesions. *J Endod* 1987: **13**: 29–39.

122. Tronstad L, Barnett F, Cervone F. Periapical bacterial plaque in teeth refractory to endodontic treatment. *Endod Dent Traumatol* 1990: **6**: 73–77.

123. Tronstad L, Barnett F, Riso K, Slots J. Extraradicular endodontic infections. *Endod Dent Traumatol* 1987: **3**: 86–90.

124. Tronstad L, Kreshtool D, Barnett I. Microbiological monitoring and results of treatment of extraradicular endodontic infection. *Endod Dent Traumatol* 1990: **6**: 129–136.

125. Siqueira JF, Lopes HP. Bacteria on the apical root surfaces of untreated teeth with periradicular lesions: a scanning electron microscopic study. *Int Endod J* 2001: **34**: 216–220.

126. Yusuf H. The significance of the presence of foreign material periapically as a cause of failure of root treatment. *Oral Surg Oral Med Oral Pathol* 1982: **54**: 566–574.

127. Ørstavik D, Kerekes K, Molven O. Effects of extensive apical reaming and calcium hydroxide dressing on bacterial infection during treatment of apical periodontitis: a pilot study. *Int Endod J* 1991: **24**: 1–7.

128. Peters LB, Wesselink PR, Buys JF, van Winkelhoff AJ. Viable bacteria in root dentinal tubules of teeth with apical periodontitis. *J Endod* 2001: **27**: 76–81.

129. Gutierrez JH, Jofre A, Villena F. Scanning electron microscope study on the action of endodontic irrigants on bacteria invading the dentinal tubules. *Oral Surg Oral Med Oral Pathol* 1990: **69**: 491–501.

130. Sen BH, Piskin B, Demirci T. Observation of bacteria and fungi in infected root canals and dentinal tubules by SEM. *Endod Dent Traumatol* 1995: **11**: 6–9.

131. Love RM. Regional variation in root dentinal tubule infection by *Streptococcus gordonii*. *J Endod*, in press.

132. Oguntebi BR. Dentine tubule infection and endodontic therapy implications. *Int Endod J* 1996: **27**: 218–222.

133. Yared GM, Bou Dagher FE. Influence of apical enlargement on bacterial infection during treatment of apical periodontitis. *J Endod* 1994: **20**: 535–537.

134. Card S, Trope M, Sigurdsson A, Ørstavik D. The effectiveness of increased apical enlargement in reducing intracanal bacteria. *J Endod* 2002: in press.

135. Sirén E, Haapasalo M, Ranta K, Salmi P, Kerosuo E. Microbiological findings and clinical treatment procedures in endodontic cases selected for microbiological investigation. *Int Endod J* 1997: **30**: 91–95.

136. Vire DE. Failure of endodontically treated teeth: Classification and evaluation. *J Endod* 1991: **17**: 338–342.

137. Swanson K, Madison S. An evaluation of coronal microleakage in endodontically treated teeth. Part I. Time periods. *J Endod* 1987: **13**: 56–59.

138. Madison S, Swanson K, Chiles SA. An evaluation of coronal microleakage in endodontically treated teeth. Part II. Sealer types. *J Endod* 1987: **13**: 109–112.

139. Madison S, Wilcox LR. An evaluation of coronal microleakage in endodontically treated teeth. Part III. *In vivo* study. *J Endod* 1988: **14**: 455–458.

140. Torabinejad M, Ung B, Kettering JD. *In vitro* bacterial penetration of coronally unsealed endodontically treated teeth. *J Endod* 1990: **16**: 566–569.

141. Beckham BM, Anderson RW, Morris CF. An evaluation of three materials as barriers to coronal microleakage in endodontically treated teeth. *J Endod* 1993: **19**: 388–391.

142. Kvist T, Rydin E, Reit C. The relative frequency of periapical lesions in teeth with root canal-retained posts. *J Endod* 1989: **15**: 578–580.

143. Kvinnsland I, Oswald RJ, Halse A, Grønningsaeter AG. A clinical and roentgenological study of 55 cases of root perforation. *Int Endod J* 1989: **22**: 75–84.

144. Peters LB, van Winkelhoff AJ, Buys JF, Wesselink PR. Effects of intrumentation, irrigation and dressing with calcium hydroxide on infection in pulpless teeth with periapical bone lesions. *Int Endod J* 2002: **35**: 13–21.

145. Kerekes K, Tronstad L. Morphometric observations on the root canals of human anterior teeth. *J Endod* 1977: **3**: 24–29.

146. Kerekes K, Tronstad L. Morphometric observations on the root canals of human premolars. *J Endod* 1977: **3**: 74–79.

147. Kerekes K, Tronstad L. Morphometric observations on the root canals of human molars. *J Endod* 1977: **3**: 114–118.