Prognosis of initial endodontic therapy

SHIMON FRIEDMAN

‘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-
significant 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

<table>
<thead>
<tr>
<th>Appraisal categories</th>
<th>Outcome (%)</th>
<th>Cases observed</th>
<th>Follow-up (years)</th>
</tr>
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<tbody>
<tr>
<td>Cohort</td>
<td>Exposure</td>
<td>Assessment</td>
<td>Analysis</td>
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<tr>
<td>Healed</td>
<td>Healing</td>
<td>Functional*</td>
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<table>
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<th>Study</th>
<th>Cases observed</th>
<th>Follow-up (years)</th>
<th>Cohort</th>
<th>Exposure</th>
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<td>y</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>80</td>
<td></td>
<td></td>
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<tr>
<td>Graham &amp; Hansson 1961</td>
<td>105*</td>
<td>4–5</td>
<td>y</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>81*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seltzer et al. 1963</td>
<td>1223*</td>
<td>0.5</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>76</td>
<td></td>
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<tr>
<td>Bender et al. 1964</td>
<td>410*</td>
<td>2</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>77</td>
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<td>Grossman et al. 1964</td>
<td>98*</td>
<td>1–5</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
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<td>147*</td>
<td>4–5</td>
<td>y</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>73*</td>
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<td>n</td>
<td>n</td>
<td>86</td>
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<td>1</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>81</td>
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<td>n</td>
<td>n</td>
<td>n</td>
<td>91</td>
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<td>1–5</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>53</td>
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<td>83*</td>
<td>1–6</td>
<td>n</td>
<td>y</td>
<td>n</td>
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<td>n</td>
<td>n</td>
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<td>y</td>
<td>y</td>
<td>n</td>
<td>y</td>
<td>90*</td>
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<td>112*</td>
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<td>n</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>91*</td>
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<tr>
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<td>124*</td>
<td>1–9</td>
<td>n</td>
<td>n</td>
<td>n</td>
<td>y</td>
<td>59</td>
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<td>n</td>
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<td>n</td>
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<td>n</td>
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<td>n</td>
<td>n</td>
<td>n</td>
<td>y</td>
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<td>199*</td>
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<td>y</td>
<td>y</td>
<td>n</td>
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<td>52*</td>
<td>2–3</td>
<td>n</td>
<td>y</td>
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<td>n</td>
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<td>16*</td>
<td>2–12</td>
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Table 1. Continued

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<th>Appraisal categories</th>
<th>Outcome (%)</th>
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<td>n</td>
<td>y</td>
<td>y</td>
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<td>50*</td>
<td>0.3–2</td>
<td>y</td>
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<tr>
<td>Sjögren et al. 1990</td>
<td>204*, c</td>
<td>8–10</td>
<td>y</td>
<td>y</td>
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<tr>
<td>Murphy et al. 1991</td>
<td>89</td>
<td>0.3–2</td>
<td>n</td>
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<td>Ørstavik &amp; Hörsted-Bindslev 1993</td>
<td>133*</td>
<td>4</td>
<td>n</td>
<td>y</td>
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<td>Smith et al. 1993</td>
<td>481*</td>
<td>2–5</td>
<td>y</td>
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<td>Friedman et al. 1995</td>
<td>113*</td>
<td>0.5–1.5</td>
<td>y</td>
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<td>172</td>
<td>2–5</td>
<td>y</td>
<td>n</td>
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<td>Ørstavik 1996</td>
<td>126*, c</td>
<td>4</td>
<td>n</td>
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<td>53</td>
<td>≤5</td>
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<td>Trope et al. 1999</td>
<td>76</td>
<td>1</td>
<td>n</td>
<td>y</td>
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<td>Reiber et al. 2000</td>
<td>67</td>
<td>1–5</td>
<td>y</td>
<td>y</td>
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<td>177*, c</td>
<td>4</td>
<td>n</td>
<td>y</td>
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<td>y</td>
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<td>319</td>
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<td>n</td>
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<td>Cheung 2002</td>
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<td>n</td>
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<td>38</td>
<td>1–4.5</td>
<td>y</td>
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</table>

*Asymptomatic, without or with residual radiolucency (reduced or unchanged in size).
\*Data extracted from larger study material that includes also teeth without apical periodontitis.
\*Repeated material.
\*Roots considered as unit of evaluation, rather than teeth.
\*Recalculated after exclusion of cases classified as ‘uncertain’.
\*Cases with procedural errors excluded.
\*Cases with prepared but unfilled canals excluded.
\*All canals obliterated to some extent.
\*Teeth treated in two sessions without intracanal medication excluded.
\*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, asepsis 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 kloropcrka 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
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
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 evalu-ative process (55, 68, 70).

**Follow-up period**

Healing of apical periodontitis is a dynamic process, and sufficient time is required to evaluate its pro-gression 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 occurred 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.

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**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-
Prognosis of initial endodontic therapy

.. (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 periphery (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% complete 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.](image)

![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.](image)
‘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).
observational 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-
Friedman 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 radioluency 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 & Wesseling (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 microbial. Foreign materials and true cysts have been shown to cause apical periodontitis-like pathology 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 propionic*, 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...
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).
Friedman

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 mesiobuccal root is associated with apical periodontitis while the distobuccal 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).

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.

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-
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, 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Follow-up (years)</th>
<th>One session</th>
<th>Two sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>healed</td>
<td>n</td>
</tr>
<tr>
<td>Sjögren et al. 1990</td>
<td>8–10</td>
<td>204 86%</td>
<td>–</td>
</tr>
<tr>
<td>Sjögren et al. 1997</td>
<td>≤5</td>
<td>–</td>
<td>53 83%</td>
</tr>
<tr>
<td>Trope et al. 1999</td>
<td>1</td>
<td>22* 64%</td>
<td>19* 74%</td>
</tr>
<tr>
<td>Weiger et al. 2000</td>
<td>1–5</td>
<td>36 83%</td>
<td>31 71%</td>
</tr>
<tr>
<td>Abitbol 2001</td>
<td>4–6</td>
<td>12 58%</td>
<td>60 76%</td>
</tr>
<tr>
<td>Peters &amp; Wesselink 2002</td>
<td>1–4.5</td>
<td>21 81%</td>
<td>12 71%</td>
</tr>
</tbody>
</table>

*aOnly 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, definitive, 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
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’.

**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 Kereked & 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

50. Heling I, Biella Shenkman S, Turetsky A, Horwitz J. The


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.
128. Peters LB, Wesselink PR, Buys JF, van Winkelhoff AJ. Vi-
able bacteria in root dentinal tubules of teeth with apical
129. Gutierrez JH, Jofre A, Villena F. Scanning electron micro-
scope study on the action of endodontic irrigants on bac-
teria invading the dentinal tubules. *Oral Surg Oral Med
130. Sen BH, Piskin B, Demirci T. Observation of bacteria and
fungi in infected root canals and dentinal tubules by SEM.
131. Love RM. Regional variation in root dentinal tubule infec-
tion by *Streptococcus gordonii*. *J Endod*, in press.
132. Oguntebi BR. Dentine tubule infection and endodontic
133. Yared GM, Bou Dagher FE. Influence of apical enlarge-
ment on bacterial infection during treatment of apical peri-
134. Card S, Trope M, Sigurdsson A, Ørstavik D. The effective-
ness of increased apical enlargement in reducing intracanal
135. Sirén E, Haapasalo M, Ranta K, Salmi P, Kerosuo E. Microbiological findings and clinical treatment procedures in endodontic cases selected for microbiological investiga-
136. Vire DE. Failure of endodontically treated teeth: Classifi-
137. Swanson K, Madison S. An evaluation of coronal micro-
leakage in endodontically treated teeth. Part I. Time
138. Madison S, Swanson K, Chiles SA. An evaluation of co-
ronal microleakage in endodontically treated teeth. Part II.
139. Madison S, Wilcox LR. An evaluation of coronal micro-
leakage in endodontically treated teeth. Part III. *In vitro
140. Torabinejad M, Ung B, Kettering JD. *In vitro* bacterial
penetration of coronally unsealed endodontically treated
142. Kvist T, Rydin E, Reit C. The relative frequency of peri-
143. Kvinnland I, Oswald RJ, Halse A, Gronningsaeter AG.
144. Peters LB, van Winkelhoff AJ, Buys JF, Wesselink PR. Ef-
fects of instrumentation, irrigation and dressing with cal-
cium hydroxide on infection in pulpless teeth with peri-
145. Kerekes K, Tronstad L. Morphometric observations on the
29.
146. Kerekes K, Tronstad L. Morphometric observations on the
147. Kerekes K, Tronstad L. Morphometric observations on the
118.