Endodontic Topics 2002, 2, 10–23
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ENDODONTIC TOPICS 2002
1601-1538

Dentin and pulp reactions to caries and operative treatment: biological variables affecting treatment outcome

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An important issue prior to restorative or endodontic treatment of carious teeth is the assessment of the different conditions of each individual case. This relates to the static, anatomical considerations of the location of the caries lesion, as well as the dynamic activity and extent of the carious process. Moreover, the restorative treatment may be carried out for prosthetic or cosmetic purposes and this may involve the cutting of sound and unaffected dentin. These aspects are more or less outlined in old textbooks going back to the principles described by Black (1). However, each factor and its relative importance have changed over the years. The major focus has been on improving the technical aspects of cavity design and the choice of restorative material, as well as examining the clinical procedures involved. Less attention has been paid to the pathology of caries in relation to restorative treatment and the different types of lesion progression.

Rapidly progressing lesions and slowly progressing lesions have seldom been related to different treatment strategies or guidelines in relation to excavation (2). In addition, the absence of a diagnostic device for estimating the degree and severity of pulp inflammation might also explain why an overall consensus is still lacking in relation to the operative or endodontic treatment of deep carious lesions. The deep lesion approach may be quite radical and invasive, and leaving intentionally carious tissue behind has not been recommended (3), but conservative procedures have also been advocated, such as the indirect pulp capping procedure (4, 5), as well as stepwise excavation procedures (6–9). With this background updated, pathological and anatomical aspects are presented that should guide the treatment of caries, including the deep lesion. Tooth selection criteria are presented for treatment of the deep lesion, including data on long-term prognosis.

Non-cavitated caries pathology and clinical implications

Initial pulp-dentinal reactions

The etiology of pulpal inflammation subjacent to caries is bacteria. It has been known for decades that the pulp can be inflamed subjacent to lesions in enamel only (10), as well as in relation to a deep dentin caries (11). Traditionally, the clinical focus of pulp reactions to caries has been centered on late stages of lesion progression. Consequently, it has most often been related to when and how the pulp tissue should be treated or removed. Less attention has been related to a systematic description of the nature of the pulp reactions in stages of different lesion progression prior to clinical pulp exposure. The following description of the earliest pulp-dentin reaction to caries is based on clinically well-defined lesions (12) and on the use of computerized histomorphometric analyses of thin undemineralized tooth sections (13, 14).

Even before alterations in the dentin have occurred,

a reduction of the odontoblast-predentin region can be observed as the very first cellular changes subjacent active progressing enamel lesions. Particularly, the size of the odontoblast cells has decreased as compared to unaffected odontoblasts of similar location and age. Moreover, the sub-odontoblastic region is less pronounced, as pulpal cells have proliferated into the cell-free zone. Dentin hypermineralization occurs concomitantly with cellular alterations along the odontoblast predentin region (Fig. 1) as the demineralized enamel is approaching the amelo-dentinal junction (12, 15). This dentin hypermineralization may be compared with a localized and accelerating process of dentinal sclerosis normally occurring as a physiological aging phenomenon. It is, therefore, not unaffected dentin that is initially demineralized in relation to caries, but the intratubular environment has an altered and increased mineral content. As soon as the demineralized enamel is in contact with the amelo-dentinal junction, demineralization of the dentin is initiated and reprecipitation of dissolved apatite (16) may take place in the mineral profile along the dentinal tubules described as whitlockite crystals (17). The interface between the advancing front of dentin demineralization and the early appearance of hypermineralization is established through pH-depending gradients that change constantly within the cariogenic environment (18), irrespective of the presence of vital cells, and cannot specifically be compared with sclerotic dentin.

Although the process of demineralization affects both the intertubular dentin and the intratubular environment (19), the advancing front of demineralization follows the direction of the dentinal tubules, this being the primary route for dissolution of the hard dentinal tissue (20). Consequently, the zone of dentin demineralization subjacent to non-cavitated lesions narrows as it progresses toward the pulp (Figs 2a, b). Notably, the sequence of initial dentin demineralization takes place without the presence of bacteria in

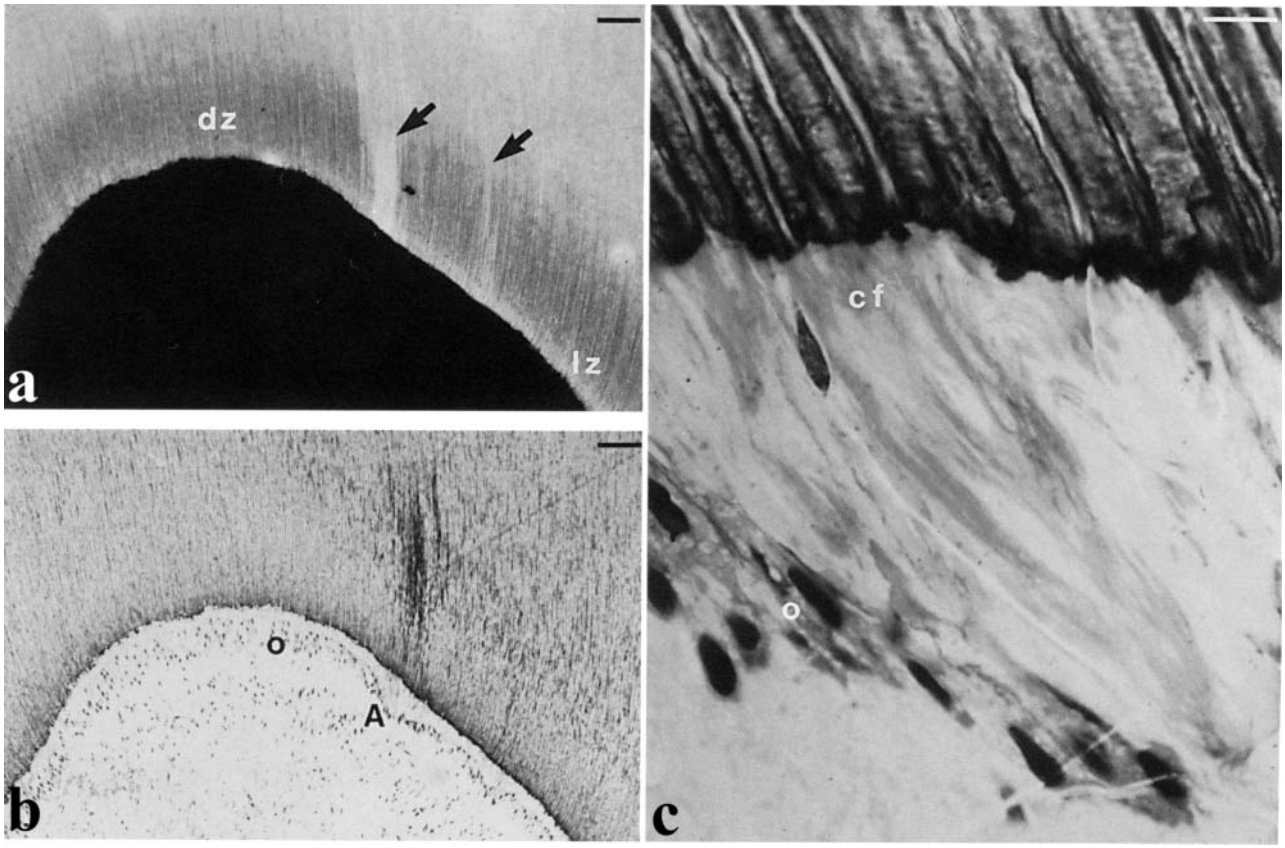

Fig. 1. Microradiographic (a) and light microscopic (b, c) evidence of hypermineralized dentin (arrows) in relation to enamel lesion approaching the amelo-dentinal junction. The affected area A is detailed in c. dz: dark sone, lz: light zone, o: odontoblast cells, cf: collagen fibers. Scales: 25 (m (a, b). Scale: 10 (m (c). From Bjørndal et al. (12). Reprinted with permission from Karger, Basel.

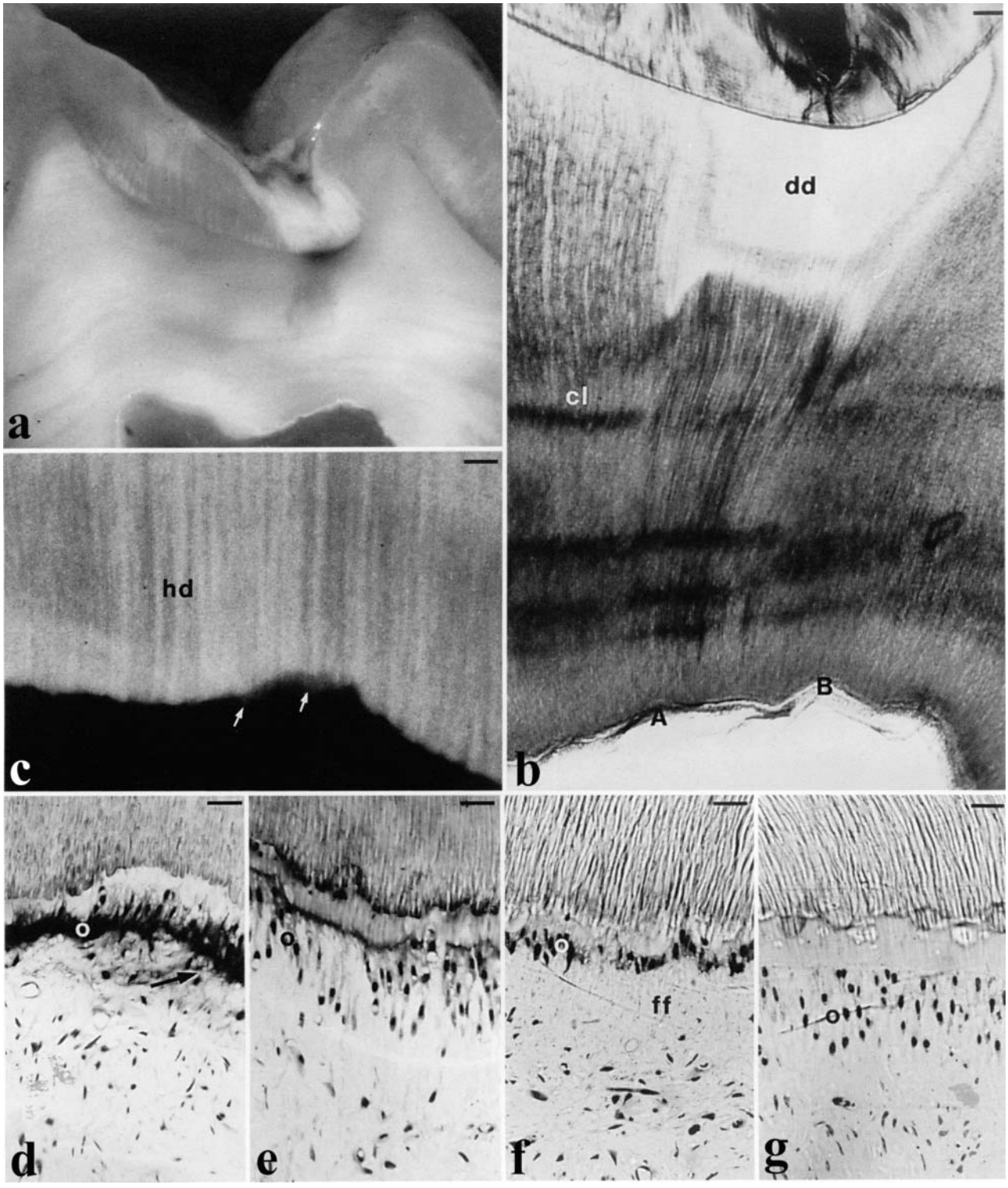

Fig. 2. Overview of an active lesion reaching the amelo-dentinal junction before (a) and after (b) thin section preparation. No lateral spread of dentin demineralization (dd), but follows the hypermineralized dentinal tubules (hd, c). A denotes lesion site from b detailed microradiographically and lightmicroscopically (arrows) in c and d. B denotes control area from b detailed in e. Lesion and control sites from a slow-progressing lesion are shown in f and d. cl: Owenπs contour lines. o: Odontoblast cells. ff: fine fibrils. Scale: 250 (m (b). Scales: 10 (m (c-g). From Bjørndal et al. (12). Reprinted with permission from Karger, Basel.

the dentin (21). The individual bacteria are still far too large to penetrate the demineralized rod and inter-rod enamel (Fig. 3). However, when the enamel layer crumbles, bacterial invasion of the demineralized enamel occurs (Fig. 4).

The color and consistency of the demineralized dentin in active progressing lesions is yellowish light-brown and is decreased in hardness in comparison to unaffected dentin, whereas arrested lesions appear darker and possess a less pronounced softening of the dentin. The pulpal response-taking place subjacent to enamel lesions with different lesion activity also discloses different cellular reaction patterns in the sub-odontoblastic region (12). A clear cellular proliferation is noted within the cell-free zone under that of actively progressing lesions (Fig. 2d, e), changes that might include the early onset of neurogenic inflammatory reactions. A similar cellular proliferation is not evident in arrested enamel lesions (Figs 2f, g). In active lesions the odontoblast cells are significantly smaller (compared to a control) than arrested lesions, and the presence of reactionary dentin formation, defined as tertiary dentin laid down by primary odontoblast cells (22), can be observed (Fig. 5). No formation of tertiary dentin is noted in slowly progressing or arrested lesions, because the stimuli needed for the tertiary dentinogenesis to take place are not present.

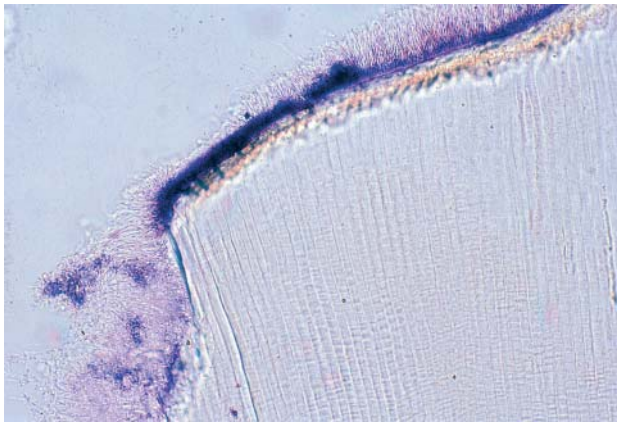

Fig. 3. Detail of enamel lesion covered with cariogenic plaque. Note the enamel rods are clearly visible in the 15 (m thin undemineralized tooth section. No bacteria are penetrating the rod and interod structure. Original magnification ×50.

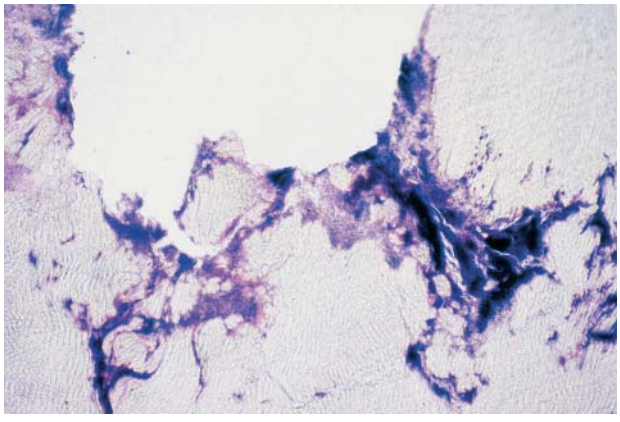

Fig. 4. Detail of an active enamel lesion, where the enamel layer has crumbled. Note a more wide spread appearance of bacteria. Original magnification ×25.

Taken together, it is not the initial dentin reactions *per se* that are the clinical key problem in the non-cavitated caries pathology which determines further progression. If the transmission of the cariogenic stimuli across the enamel layer is stopped, signs of arrested remission are apparent throughout the pulp-dentin organ, reflecting the reversible nature of the pulpal response. This information should be taken into account when deciding when or if the first operative intervention should be performed.

Caries and the amelo-dentinal junction

It has been commonly held that early spread of the dentin involvement by caries takes place even in non-cavitated stages of lesion progress, hereby undermining sound unaffected enamel (23). However, several recent studies have shown (24–26) that the demineralized dentin is strictly related to the contact area of the demineralized enamel (Figs 2a, b). The clinical implications are important, because early arrest of dentin caries is not necessarily related to an operative treatment approach, as the dentinal reactions at this stage are not developing as an isolated phenomenon, but are still determined by the superficial cariogenic plaque covering the outer enamel lesion. As indicated in the previous paragraph, the total enamel-dentin lesion complex can still be arrested by non-operative means, provided the transmission of bacterial products passing the enamel layer is stopped. On this basis, excavation procedures, such as the partial tunnel preparation (27) designed for a retrograde removal of the small dentin involvement, concomitantly saving the outer approximal enamel wall, does not seem to be justified as the first choice of treatment.

Dentin exposed caries pathology

Several factors are important when further describing the rapidly progressing caries lesion:

- clinical exposure of dentin;
- invasion and infection of the dentin by micro-organisms;
- an increasing number of cells recruited for the immune surveillance, eventually leading to inflammatory reactions;
- the undermining of enamel by demineralization of infected dentin along the amelo-dentinal junction.

'Closed' and 'open cariogenic ecosystems

It is not the clinical exposure of the dentin in itself that is crucial in relation to ongoing lesion progress, but the specific location of the exposure. A simple comparison between an occlusal dentinal exposure and a buccal cavitation outlines some relevant differences in relation to the state of lesion activity. The two locations have different growth conditions for developing and protecting the cariogenic plaque (Fig. 6). As defined by Edwardsson (28), a much more closed ecosystem develops in both approximal as well

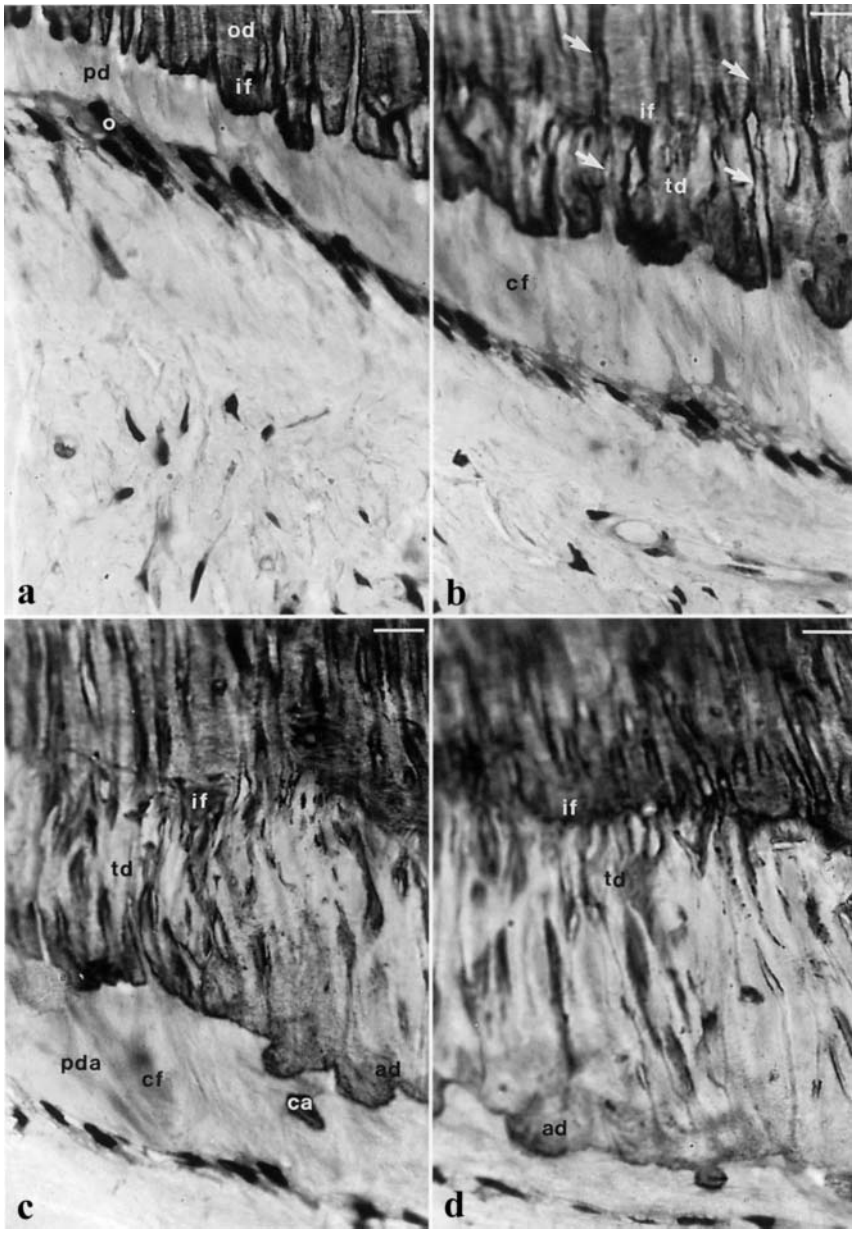

Fig. 5. Details of reactionary dentinogenesis developed subjacent an enamel lesion. The interface between orthodentin and tertiary dentin is noted and with primary dentinal tubules (arrows) passing through the lateral and youngest site (a, b). In the central and more advanced part of the lesion sites the frequence of dentinal tubules is decreased with signs of atubular hardtissue formation (c, d). Scales: 10 (m. From Bjørndal et al. (12). Reprinted with permission from Karger, Basel.

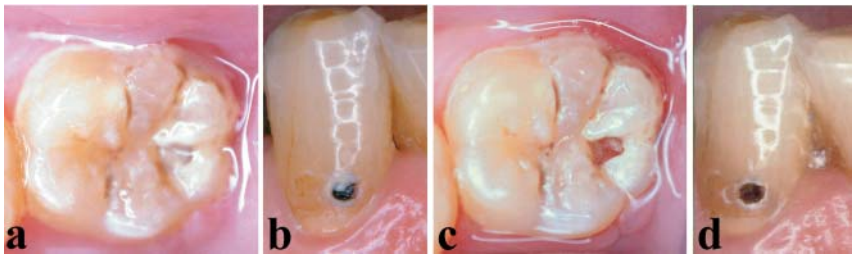

Fig. 6. Mandibular molar with a progressing dentinal exposed lesion covered by plaque (a). A mandibular canine with a buccal lesion with surface plaque partly covering the dark brownish discolored demineralized dentin (b). The occlusal cavity is clearly exposed after removing the cariogenic plaque showing light-brownish discoloration of the demineralized dentin (c). The enamel margins at the buccal lesion constitutes a plaque protecing factor, however to a much lesser extent than noted in a. After plaque removal a white and dull appearance of the thin enamel margins is noted reflecting a peripheral lesion progress (d).

as occlusal dentinal exposed lesions, whereas smooth surface located lesions from the very beginning are placed an open environment. Therefore, the slow-progressing nature of caries at these sites can be explained as a less pronounced protection of the plaque covering the surface.

In untreated cases, a stage of so-called mixed lesion activity may develop where the undermined enamel breaks down (Figs 7a, b) and a temporary conversion of the ecosystem occurs (Fig. 7c). These differences at the clinical level can also be observed microbiologically (29). A very homogenous microflora is apparent in the deep closed lesion environment containing several different subspecies of lactobacilli, whereas a much more heterogeneous microflora can be detected as the dentin exposure increases and becomes more open with various signs of proximal surface destruction (29). Even though the pattern of untreated deep lesions could involve a decrease in lesion activity (Fig. 8a), it will only be temporary because in the peripheral parts in the cariogenic process continues (Fig. 8b), and finally the crown will break off, leaving remnants of roots behind (Fig. 8c).

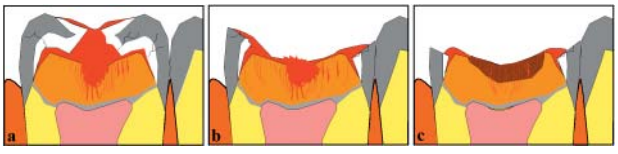

Fig. 7. Diagrams showing the temporary conversion of the cariogenic ecosystem during untreated lesion progress. A closed lesion environment develops in relation to an occlusal lesion (a). Eventually the white demineralized and undermined enamel breaks due to mechanical stress, changing the environment into an open ecosystem (b). Consequently, a stage of mixed lesion activity develops. In the occlusal part classical signs of slow lesion progress is noted in terms of a darker appearance of the demineralized dentin, whereas at the margins optimal growth conditions for the plaque is apparent and active lesion progress continues (c). Red zones indicate plaque.

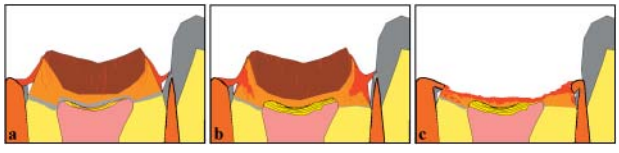

Fig. 8. The pattern of untreated deep lesions may involve a decrease in lesion activity (a), but it might be temporary as the enamel margins will obtain protection for the cariogenic process (b). Eventually the entire crown breaks leaving remnants of roots behind (c). Red zones indicate plaque.

In exposing dentin lesions, discoloration of the demineralized dentin is particularly evident (Fig. 6). It is related to the organic component of dentin, and involves an interaction between dentin proteins and small aldehydes produced by the bacteria; this is also described as the Maillard reaction (30). The clinical changes to the demineralized dentin that occur during slow lesion progression, where it becomes darker and increases in consistency (Figs 6b, d), may also be related to an increased influx of external stain, as well as to the overall results of an acidogenic environment converting into neutral pH-values, whereby reprecipitation of dissolve mineral is introduced. In addition, the modification of amino acids in dentin collagen during the caries process may lead to increased resistance against new proteolytic reactions (31).

The immune response

The inflammatory cell infiltrate situated in relation to progressive stages of caries involves various immunocompetent cells, and the proportions of B- and T-lymphocytes have shown to increase to the depth of penetration of the caries lesion (32). The onset of the immune response is linked to antigen-expressing cells already present in the unaffected pulp (33), e.g. T-lymphocytes, macrophages, and pulp dentritic cells close to the odontoblast layer (34). In experimental animal studies in rats, Ia-antigen-expressing cells, as well as antigen-expressing cells associated with macrophages, are observed during superficial caries (35). Also for human caries, immunological data has been presented that relates to caries, in particular to the presence of HLA-DR antigen-expressing cells (36). Dendritic-like cells have been reported along the impaired odontoblast layer in rapidly progressing lesions with enamel cavitation just reaching the dentin (37). However, more precise well-defined information is needed concerning the immune response to the influx of bacterial antigens in clinical caries lesions.

Tertiary dentinogenesis and caries

The histopathological features of tertiary dentin formation correlate in part to the degree of clinical cavitation. In young, rapidly progressive lesions with enamel cavitation extending into the dentin, the odontoblast cells may already be absent (38). Thus, lesions that turn into stages of clinical dentin exposure within a short period of time, may never show evidence of reactionary dentinogenesis, simply because the extensive transmission of bacterial stimuli has caused early odontoblast cell necrosis. Consequently, any extra hard tissue formation that may be formed, is without the presence and activity of the primary odontoblast cells, and has been defined as fibrodentine (38) or interface dentin (16). Tertiary dentin produced by the primary odontoblast could be interpreted as a local, physiological growth of orthodentin, whereas atubular types of hard tissue formation (Fig. 9) should be regarded as repair processes following the complex interplay of inflammatory reactions. In principle, this assumption is supported by experimental animal data following cavity preparation procedures. No immune competent cells are observed when formation of hard tissue has occurred (41). The various qualities of tertiary dentin can be related to the type of stimuli. In very slowly progressing dentinal lesions (Fig. 10a) dentin tertiary resembles orthodentin (Figs 10b, c), but notably also with evidence of new secondary odontoblast-like cells mixed in-between (Figs 10d, e). In lesions with such converted activity (Figs 11a, b) the formation of a new dentin matrix is laid down on top of the fibrodentin (Fig. 11c–f) and has been termed reparative dentinogenesis (40).

In untreated caries lesions, the correlation between the type of tertiary dentinogenesis and the present state of the pulp is presumably as close as it can get.

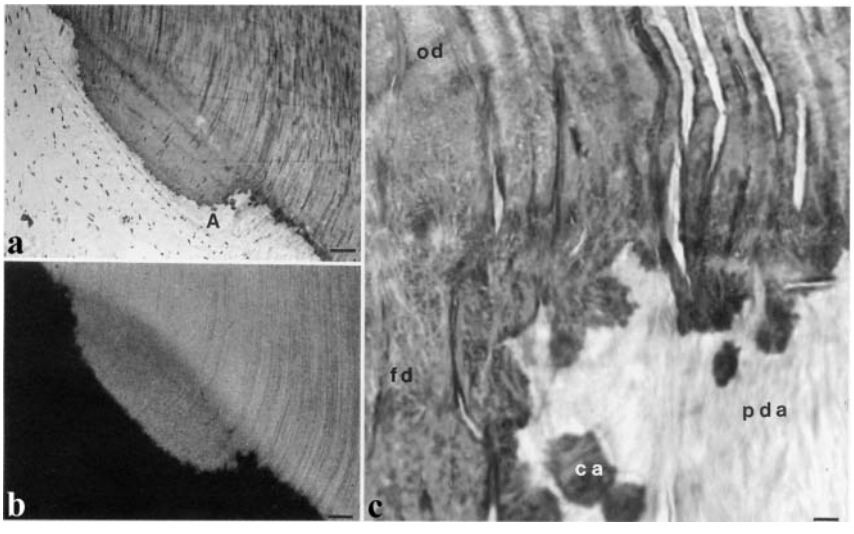

Fig. 9. Lightmicroscopic (a, c) and microradiographic (b) details of atubular fibrodentinogenesis subjacent an active and closed lesion environment. Detail of A shows the interface between orthodentin (od) and fibrodentin (fd). ca: calcospherit. pda: predentin area. Scales: 25 (m (a, c). Scale: 5 (m (b). From Bjørndal and Darvann (52). Reprinted with permission from Karger, Basel.

However, it is important to be aware that the presence of tertiary dentin only reflects past repair processes of the pulp (Fig. 12).

Clinical implications

The formation of hypermineralized dentin in relation to caries explains the result obtained from permeability studies (43) that show an overall decrease in permeability under carious dentin in comparison to unaffected dentin. Consequently, whenever dentin is cut in relation to the design of the final preparation and not related to the removal of carious tissue, the clinician exposes dentinal tissue with a much higher degree of permeability and runs the risk of introducing potential post-operative symptoms. In caries lesions at different stages of progression, the difference in permeability between unaffected dentin and carious dentin would be most pronounced in cases with slow progressing lesions, as more well-defined zones of hypermineralization are noted subjacent to these lesions (25, 44). Correspondingly, in very rapidly progressing lesions, the permeability will be high. The clinical implications of incorporating data on permeability might be neglected following optimal clinical procedures, although post-operative symptoms are frequently reported following the placement of restorations (43). The effects of peripheral excavation may be most pronounced in treatment of the deep lesion, where the borderline between completed peripheral excavation and removal of sound unaffected dentin is sharp, and provides an example where over-excavation might occur quite frequently. Therefore, over-excavation of dentin in the surrounding and unaffected areas of the excavated infected and demineralized dentin is to be avoided. This concept is also supported by bacterial data indicating low levels of cultivable flora in discolored and hard dentin along the amelo-dentinal junction during caries excavation (44).

The deep caries lesion dilemma

At present, it is not possible by objective means to assess the state of pulpal inflammation, i.e. whether it is reversible or irreversible. Current evidence concerning the progression of pulpal inflammation follows the classical interpretation of such data, and it is assumed that an increase in the severity of the pulpal inflammation is noted as the untreated carious lesion

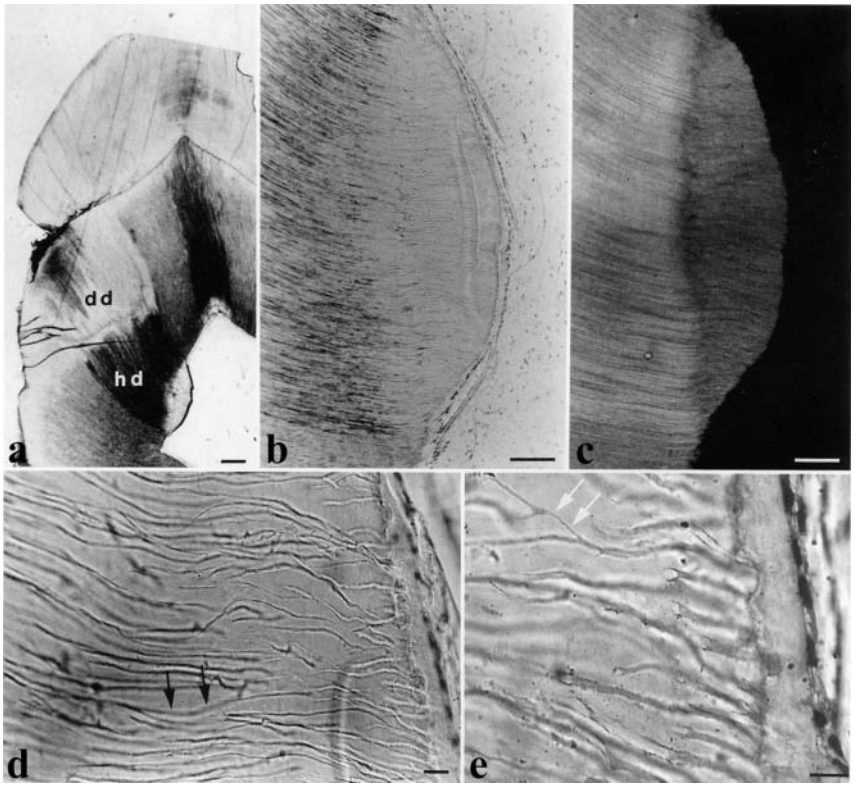

Fig. 10. A slow progressing dentinal exposed lesion with a marked hypermineralized zone (hd) subjacent the dentin demineralization (dd, a). Reactionary dentin (b, c) is noted but also with new secondary odontoblast-like cells mixed in between (d, e) old primary (black arrows) and new dentinal tubules (white arrows). Scale: 250 (m (a). Scales: 100 (m (b, c). Scales: 10 (m (d, e). From Bjørndal and Darvann (52). Reprinted with permission from Karger, Basel.

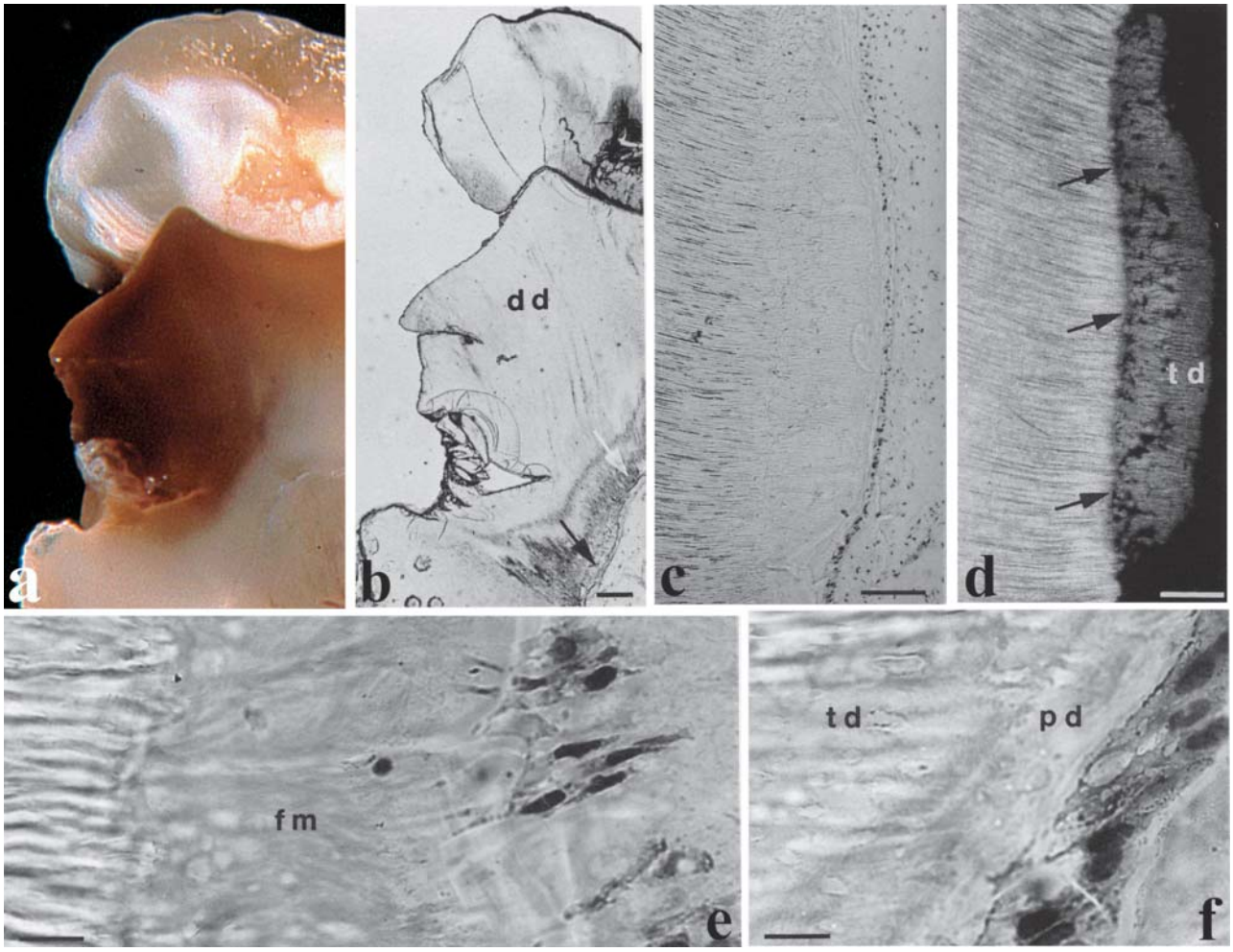

Fig. 11. A lesion with a change of the cariogenic ecosystem, due to a total enamel breakdown. The demineralized dentin (dd) is dark brownish (a) and no surface plaque is noted (b). Lightmicroscopic and microradiographic overviews of the reparative dentinogenesis are noted in c and d. New tubular dentin (td) has been laid down on fibrodentin (arrows). Details of the peripheral fibroblast-like cells in contact with fibrodentinal matrix (fm, e) and in the central part an odontoblast-predentin-like region is associated with tubular dentin (td) f. Scale: 250 (m (b). Scales: 100 (m (c, d). Scales: 10 (m (e, f). From Bjørndal and Darvann (52). Reprinted with permission from Karger, Basel.

progresses towards the pulp (11). However, there is no simple answer to what happens when a successfully non-invasive pulp treatment, producing pulpal repair, can no longer be performed. In this context, the treatment of a deep secondary caries lesion, defined as caries developing in relation to a restoration, provides a good example of a case where there may be a historical reason for the pulpal conditions. What was the reason of the first restoration made, including the state of the caries lesion? How was the operative procedure performed? The pulpal tissue accumulates the various types of injuries, and it may end up being impossible to predict the actual degree of inflammation, the sequence of repair, or the healing capacities of the pulp. As long as we do not have non-invasive tools to assess the pathological condition of the pulp or the severity of the pulpal inflammation, the discussion of the reversible or irreversible development of pulpitis will still be controversial in relation to the treatment of the vital, non-symptomatic deep lesion. On this basis, the only alternative is to depend on the results from indirect clinical examinations methods (45) from the following three areas:

- patient description of subjective symptoms;
- pulp sensibility testing;
- radiographic examinations. In addition to apical lesions, includes pulp stones, obliteration, etc., all of which contribute to a pulpal diagnosis.

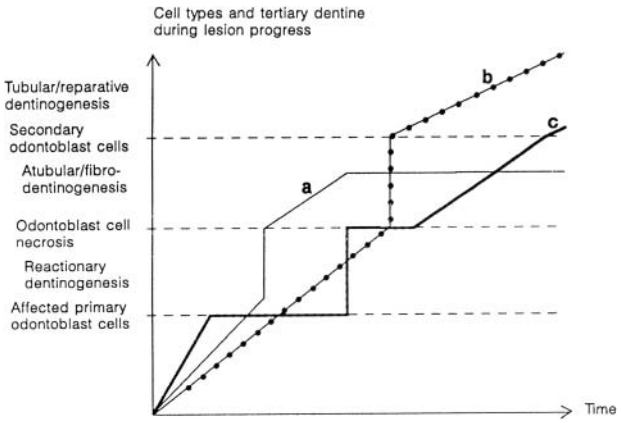

Fig. 12. The diagram shows types of cells and the corresponding tertiary dentin related to a time scale. a: An active cavitated lesion progress. b: A slow progressing environment. c: A lesion with a mixed lesion activity changing from a rapid progress toward a more open a slow-progressing environment. From Bjørndal and Darvann (52). Reprinted with permission from Karger, Basel.

Different treatment concepts of the deep caries lesions

Different methods have been advanced for preventing exposure and damage to the pulp. The first is the indirect pulp-capping procedure employed particularly in the primary dentition (46) as well as in mixed dentitions (4, 5). The second method is the two-stage excavation procedure (47, 48) or stepwise excavation (6); more recently, this has also been applied in permanent teeth (8). The main difference is that the indirect pulp-capping procedure almost completely removes the affected dentin, leaving a thin layer of residual demineralized dentin and re-entry is not made, (i.e. it is a one-step procedure) (Fig. 13), while the stepwise excavation involves re-entry at varying intervals (Fig. 14).

A new approach has been proposed for the treatment of deep lesions (Fig. 15). Here, the observation that a change of caries activity takes place in untreated caries lesions, is taken in support of a less invasive stepwise excavation procedure (9). The focus of this particular treatment is not towards complete caries excavation, but towards changing the environment from one of rapidly progressing caries into a chronic or arrested place. The clinical consequence of this approach is that relatively larger amounts of carious dentin are left behind during the first excavation. Moreover, the final excavation is performed on carious dentin that would show the classical clinical signs of arrested caries, being more brownish and of a harder consistency. The final excavation becomes easier as excavation in harder and darker carious dentin is more controllable than in soft demineralized dentin (Fig. 15). The general procedure is illustrated in Fig. 17 a–d.

The effectiveness of the stepwise excavation procedure for the management of deep carious lesions has been documented (Fig. 16), and long-term recalls

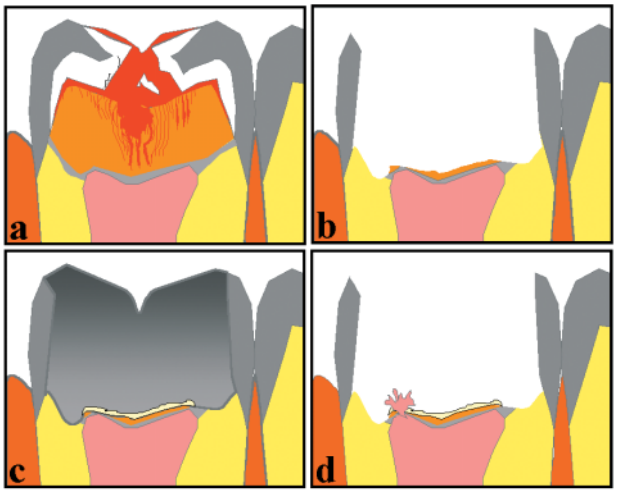

Fig. 13. Diagrams showing the indirect capping procedure. A deep lesion before treatment (a). After excavation to the residual level (b) the permanent restoration is made at once (c). Iatrogenic pulp exposures might be a potential risk (d). Red zones indicate plaque.

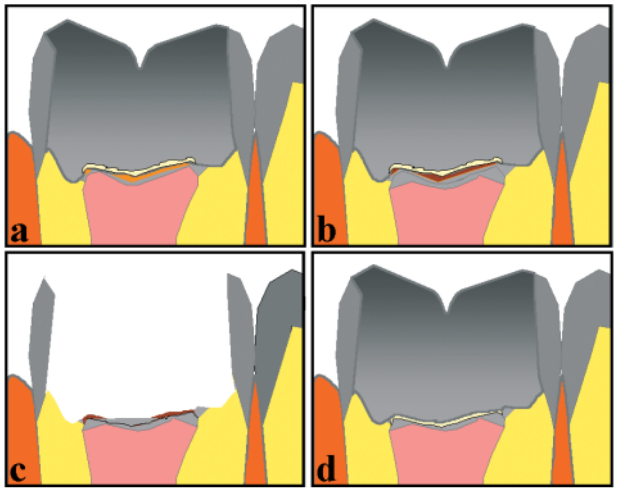

Fig. 14. Diagrams showing the stepwise excavation procedure. After excavation to the residual level calcium hydroxide containing base material and a provisional restoration is made (a). After a treatment interval of a varying length (b) reentry is made (c) and the permanent restoration is made (d).

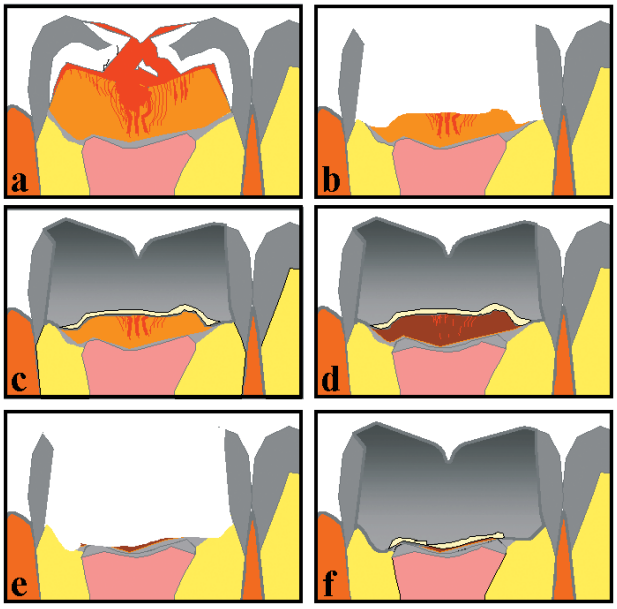

Fig. 15. Diagrams showing the less invasive stepwise excavation procedure. A closed lesion environment before and after first excavation (a, b) followed by a calcium hydroxide containing base material and a provisional restoration. During the treatment interval the retained demineralized dentin has clinically changed into signs of slow lesion progress, evidenced by a darker demineralized dentin (c, d). After final excavation (e) the permanent restoration is made (f). Red zones indicate plaque.

($3\frac{1}{2}$–$4\frac{1}{2}$ years) have shown a high success rate (92%) for teeth treated by this approach (49). Although the total group of failed cases was less than 10%, in half of these cases, insufficient temporary and permanent restorations were noted, underlining the importance of performing a high-quality temporary as well as permanent seal. Control examinations are mandatory because of the possibility of asymptomatic development of irreversible pulp degeneration over time. Five percent of the cases treated by the general practitioners in the above study had pulpal complications during the final excavation. In contrast, the traditional step-by-step approach (6, 8) presents a higher proportion of pulp complications during the final treatment (~15%).

Case selection is primarily of deep lesions considered likely to result in pulp exposure if treated in one visit by complete excavation. The dentinal lesion typically involves more than 75% of the entire dentin thickness evaluated by radiographs (Fig. 17a). There should be no history of subjective pretreatment symptoms, such as spontaneous pain or provoked pulpal pain, and the pulp should test vital; furthermore, pretreatment radiographs should exclude apical pathosis. Whereas the peripheral cavity preparation must reach sound tissues, in the deepest part of the lesion a central excavation is performed removing the only outermost necrotic and infected demineralized dentin (Fig. 17b). The remaining lesion is lined with a calcium hydroxide or zinc oxide-eugenol cement. Decide which provisional restorative material (amalgam, glass ionomers or composites) that will be used, related to the length of the treatment interval, ranging between 6 and 8 months. The altered dentinal changes gained during the treatment interval (Figs. 17b, c) may consequently lead to a less invasive final excavation (Fig. 17d).

Concluding remarks

The concepts behind and the treatment principles of the deep caries lesion are an area of debate and constant change. The difficulties in assessing the true clinical state of the pulp-dentition organ in this situation make a precise diagnosis difficult, and the choice of treat-

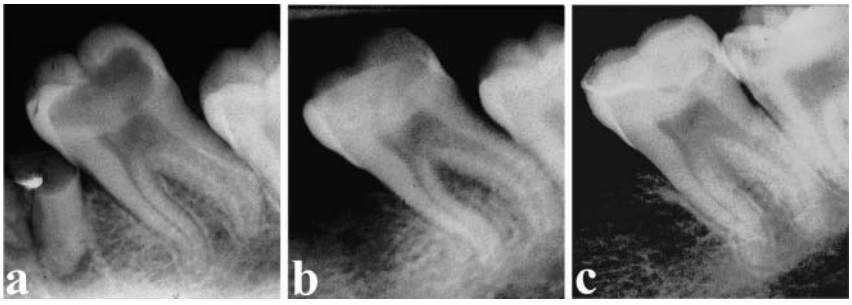

Fig. 16. Mandibular molar with a deep occlusal lesion. Remnants of neighbouring roots indicate a very high caries activity (a). One-year after treatment, pulp vitality was confirmed, and control radiograph shows no apical radiolucency (b). Four-year control confirms the vitality of the pulp as well as absence of apical radiolucency. Complete arrest of caries activity has not been achieved; a new proximal lesion has progressed in the third molar. From Bjørndal (50).

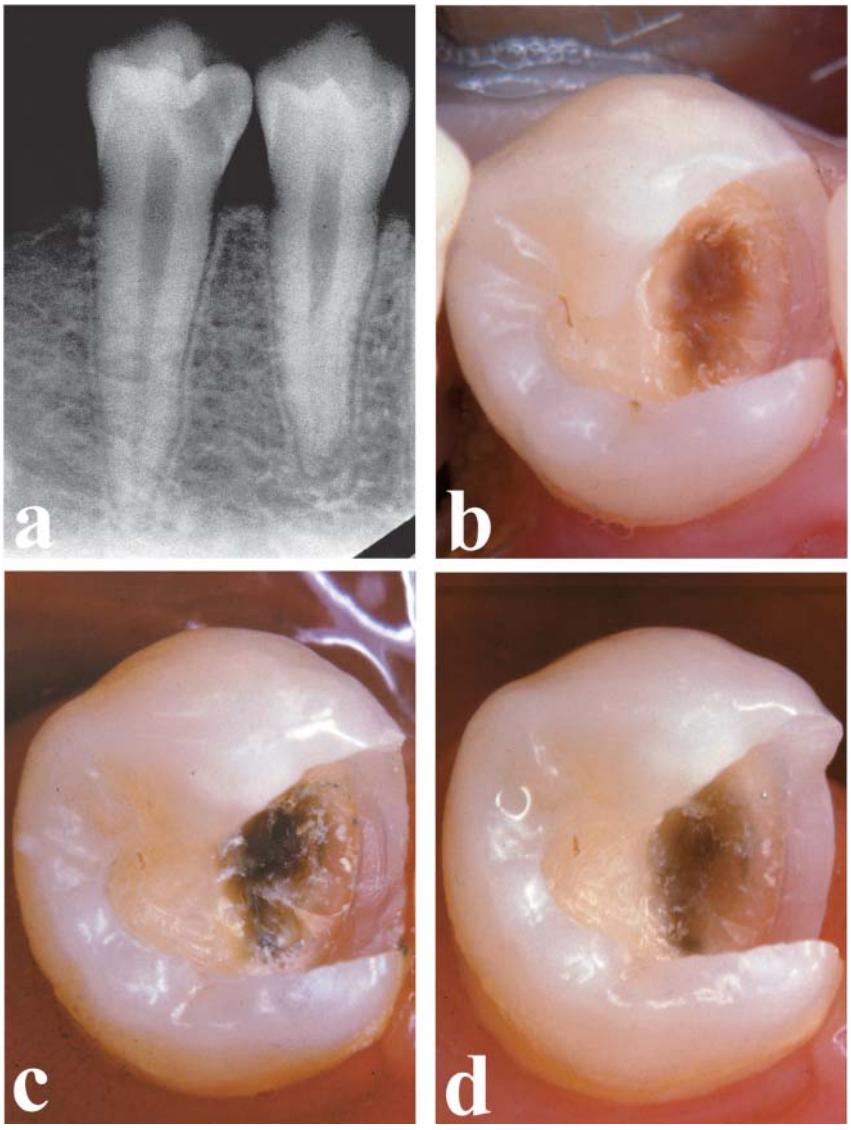

Fig. 17. Radiograph of a mandibular premolar with a deep lesion. No evidence of apical pathosis (a). A stepwise excavation is decided and an overview of the cavity following first excavation is observed (b). After a six months treatment interval and removal of base material and provisional filling (amalgam) the retained carious dentin shows signs of a slow-progressing lesion (c). The premolar with final excavation completed and final restoration can be performed (d). From Bjørndal (53). Reprinted with permission from Operative Dentistry.

ment is similarly complicated. This overview has focused on the histopathological changes that occur in dentin and pulp during caries progression. These changes represent the variable background against which the endodontic procedures of caries excavation, pulp capping or pulpotomy are performed. A thorough knowledge of the histopathology of deep dentinal caries is, therefore, a prerequisite for studies on treatment outcome following such procedures, which are highlighted in other articles in this issue.

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