Rüdiger Osswald, ruediger.osswald@t-online.de, www.tarzahn.de
Christian Deppe, deppedent1@online.de

The problem of endodontitis and managing it through conservative dentistry

Abstract:

Endodontitis is an infectious disease in a manageable anatomical environment that has been fully described for a century. Nair et al. in their prospective clinical study published in 2005 suggested that the problem of endodontic infection management could no longer be overlooked. The failure of the endodontic treatment protocol currently considered the gold standard has been subsequently confirmed in several reports. An overview of the evolution and results of endodontic treatment over the last 100 years has ramifications for endodontic research, education, and practice. Important changes in the endodontic treatment protocol are discussed.

I. Definition of endodontitis

We describe "endodontitis" as an endodontic infectious disease, i.e. inflammatory changes in the pulp tissues, periapical and periodontal tissue, and adjacent bone in its different stages and clinical manifestations. The concept "endodontitis" makes it possible to comprehend the diseases of the dental pulp tissue and its environment as an entity expressing different conditions of the same underlying disease. The concept makes this object of scientific investigation (endodontology) and practical application (endodontics) accessible as an entity.

II. Otto Walkhoff – founder of medical endodontology

The etiology and pathogenesis of endodontitis as a bacterial infectious disease and its indication-oriented treatment were fully described at the start of the 20th century by the German dentist Otto Walkhoff [46]. Walkhoff also took the first radiograph of human teeth and is still honoured today by his medical colleagues for his work in the development of radium therapy. His research work was predominantly shaped by his opposition to the doctrine of focal infection that arrived in Europe from the U.S. at the start of the 20th century. This was responsible for the loss of countless saveable teeth. In opposition, Walkhoff published his clinically and scientifically supported "System of medical treatment of severe diseases of the dental pulp and periodontium" [46] in 1928. His polemic paper "The problem of dental focal infection and combating it through conservative dentistry" published in 1931 [48], contributed significantly to the rejection of focal theory.

As a result of current publications that have brought to light the deficiencies of endodontic infection control [12, 24, 29, 36, 51, 52], the concept of "focal infection" has again unfortunately regained popularity [35]. Even implantologists are justifying the extraction of root canal-treated teeth, pointing to the persistence of chronic periapical infection following endodontic treatment [51].

III. Pathogenesis, anatomical environment and results of therapy

Endodontitis normally manifests itself as an acute, irreversible pulpitis. Without dental intervention, an intradental abscess forms over the intermediate stages of the partial gangrene after putrid decay of the pulp. Involvement of the periapical tissue does not occur just at this final stage. The entire process, however, can be clinically asymptomatic and only become manifest radiographically as an incidental finding of apical lucency or clinically as a submucosal abscess or by fistulisation after exacerbation. In the final stage of complete gangrene, all areas of the canal system and tubules, as well as the periapex, periapical bone, and periodontal space are bacterially contaminated. To clarify their relative importance, Otto Walkhoff in 1929 described the tubules as "motorways on which the bacteria deploy over four of the lanes" [46]. In 83% of cases, periapical infection with anaerobic bacteria can be detected. As a result of the untreated or unsuccessfully treated infection, granulomas or cysts form in the periapical bone as an immunological defence reaction. Among others, Schlesinger [31] as far back as 1938 demonstrated histologically the bacterial colonisation of granulomas and documented successful decontamination using the treatment method described by Walkhoff. In 2005, Tronstad et al. [45] used molecular biological evidence to show that granulomas can be colonised with biofilm-forming bacteria. This is not surprising, since there is no anatomical structure between the root tip and bone such as a lymph node that can prevent the invasion of the bone by bacteria from the infected dental root [26].

The complexity of the endodontic cavity system with few primary and countless collateral and auxiliary canals, niches and blind pouches, cross-connections, and an apical delta has been known since the publication of the impressive images of the Swiss anatomist Walter Hess at the start of the 20th century. Walkhoff [46] annotated these tables with the words: "Anyone who views what is represented in these images as unusual, insignificant and therefore as an anomaly to be neglected in treatment, and adapts and evaluates his treatment method accordingly, really cannot be helped." With this sentence, he underscores the impossibility of adequate mechanical decontamination of the complex cavity system and refers to mechanical preparation as a mere aide to the essential disinfection with potent chemotherapeutic agents. Almost 100 years later, only a maximum 50% of the endodontic cavity system is even accessible by mechanical cleaning, and of these areas only 65% can be mechanically cleaned during tooth preparation. In all, two-thirds of the canal and tubule system is left mechanically untouched even when applying state-of-the-art preparation techniques [30].

Although at the start of the 20th century mechanical preparation of the main canals was substantially limited due to the inadequate quality of the inflexible and easily broken instruments in use, the treatment outcomes of some scientists were not inferior to those of modern endodontics. In 1951, Castagnola [5] published a study of 1000 teeth treated using the Walkhoff method at the University of Zurich (Switzerland). He reported a healing rate of approx. 70% for radiographically manifest apical osteitis. It should be noted that at the time only radiographically complete bone density healing was considered a treatment success, while frequently today even a decline is treated statistically as success. Therefore, it cannot ruled out that apical osteitis was more successfully treated a half century ago than today. In their meta-analysis of endodontic studies, Kojima et al.[20] reported on comparable results in 2004.

In 1950, Engel [8] published a study comparing radiographical and histological findings of eighteen teeth with apical osteitis treated by the Walkhoff method. He resected them 5 years after their radiographically demonstrated healing in terms of bone density and examined the

sections histologically. In seventeen cases, the histological finding matched the radiographic finding and was better in one case. Engel confirmed that the sealer containing potent disinfectants that Walkhoff had developed and used and resorbed outside and in part inside the root canal had been replaced by nothing other than the body's own sterile tissue. In several cases, Engel even showed complete closure of the apical opening through newly formed root cement.

Endodontic infection control – problems, historical and medical data

After World War II, the concentration of endodontic research moved from the German-speaking countries to Scandinavia and the U.S. This corresponded with a renunciation of Walkhoff's primarily medical approach to endodontic infection control. His protocol consisted in careful mechanical preparation, long-term chemical disinfection with a potent disinfectant, and finally obturation with a disinfectant sealer. Walkhoff's complete description of indication-oriented treatment was subsequently displaced more and more in Germany also by the mechanical approach that dominated in America, which finds its expression in an aide memoire still often quoted today: "It is not important what one puts into a root canal, only what one takes out."

As a result, a treatment protocol caught on which gained international recognition as the so-called gold standard. It is characterised by the highly sophisticated preparation of the mechanically accessible main canals under half-hourly alternating irrigation with up to 5.5% sodium hypochlorite and up to 17% EDTA. Then, an obturation with neutral sealers is carried out technically in the same sitting. In complicated cases, a one- to three-week temporary filling with calcium hydroxide for long-term infection is recommended. The treatment protocol also requires that the treated tooth be fully sealed against bacteria after each sitting irrespective of the initial findings. The intradental abscess is treated differently from the "ubi pus, ibi evacua" medical dogma universally valid since Hippocrates [26].

David Figdor [10] was the first – in 2002 – to point out the unsatisfactory progress in healing apical osteitis over the last 50 years. He calculated the economic impact for the U.S. alone in the "billions of dollars". He saw the reason for this in neglect in eliminating the pathogens responsible for the endodontic infection.

In previous years, numerous studies had shown a wide range of bacteria and fungi in the root canals of infected teeth, depending on the clinical findings [7, 14]. These included the facultative, bio-film forming anaerobe Enterococcus faecalis that has been shown to survive even the most hostile conditions [11]. It also showed marked resistance against CHX, MTA, NaOCl and ozone gas, and full resistance against Ca(OH)2 [9, 27, 29]. Even at the start of the last century Walkhoff and Hess [49] had discarded Ca(OH)2 as being too mild an antiseptic to adequately control endodontic infection.

Enterococcus faecalis was cultured in 70% of root canal-treated teeth with manifest apical osteitis and was detected by molecular biological testing in a comparable percentage of gangrenous teeth. This germ is therefore an ideal model for measuring success in the control of endodontic infection. In 2002, Tronstadt et al.[45] reported evidence of biofilm-forming bacteria in an apical granuloma and showed that the spectrum of germs in deeply infected periodontal pockets was identical to that in gangrenous teeth. Haapasalo et al. [16] report in their review of endodontics in 2005 that neither increasing the concentration of NaOCl from 1% to 5.5% during the alternating irrigation procedure, nor its heating or ultrasonic activation,

nor the temporary insertion of current standard disinfectants, nor the use of modern preparation and obturation techniques have led to a measurable increase in performance when treating endodontitis.

In 2006, Gesi et al. [12] described the treatment of 256 undoubtedly vital pulpitic teeth without radiographically verifiable apical osteitis according to the internationally recognised protocol. The root canals of half of the teeth were definitively filled in the first sitting. The remaining half received an inlay of Ca(OH)2 for a minimum of one week before obturation. The results for both groups did not differ significantly. In about 7% of the cases, a radiographically diagnosable granuloma developed within 1 to 3 years irrespective of protocol. The authors concluded from their study that the study suggests that one sitting was adequate for endodontic treatment of acute pulpitis. Osswald interpreted the result differently than the authors and felt the study showed that the treatment protocol did not prove appropriate for the indication and thus needed modification. Walkhoff [46] had already reported that partial gangrene in acute pulpitis can never be diagnosed clinically but only histologically.

Marending et al. [22] determined in a prospective clinical study that one in three of the most important parameters for predicting healing of apical osteitis was the quality of the individual immune response of the particular patient. However, they did not draw the obvious conclusion – the necessity of modifying the treatment protocol [26].

It can therefore be stated that by the start of the new millennium the lack of endodontic infection control could no longer be overlooked. There is no doubt that international consensus about this has more recently emerged and that patient long-term treatment with suitable disinfectants must follow. However, there is also agreement that the search for such disinfectants internationally has not been to date successful [7, 13, 16, 18, 50].

V. Chlorphenol as an infection control agent

Parachlorphenol was introduced to dentistry by Otto Walkhoff. The "original Walkhoff ChKM solution" (Haupt-Dental, Würzburg, Germany; hereafter ChKM-W) when patiently applied is sufficiently potent to decontaminate all infected areas as completely as possible [5, 8, 23, 31]. ChKM-W also has so few side effects that it can be applied to all infected areas without risk. ChKM-W is the only disinfectant in Germany to receive authorisation also for disinfecting apical granulomas.

A special technical procedure is used to produce ChKM-W. The addition of the disinfectant camphor as a solvent up to the saturation point results in a stable solution at room temperature. The caustic effect of the parachlorphenol in the solution is fully offset without losing bactericidity. Weakly water-soluble menthol also acts as a disinfectant and has an anaesthetizing and astringent effect. ChKM-W contains no other solvent, and in particular no alcohol. Alcohol makes chlorphenol solutions volatile and negates tissue tolerance. Therefore, the pharmacology of the components, their ratios, and their preparation is important. In ChKM-W, the individual components are not combined chemically but physically only. The very loose chlorphenol-camphor-menthol compound breaks up upon entry of even the smallest volume of secretion. Menthol and camphor precipitate into fine crystals and form a long-term deposit. Parachlorphenol dissolves and in its steady state forms a non-caustic, but still bactericidal 1.3% carbol solution. The same concentration always materialises irrespective of the volume of secretion that enters [23]. Therefore, ChKM-W cannot cause

necrosis of healthy tissue in contrast to concentrated NaOCl, which breaks down not only dead but also vital tissue and – just as in the case of EDTA – dentin [2]. The concentration is too small in any case. Furthermore, ChKM is capable of creep. If one fills a root canal, it can be detected within 24 hours on the root surface [6]. In its gas form, it is able to penetrate the tubuli and medullary canals [46], reach the periapex, and thereby disinfect any bacterially contaminated tissues and surfaces.

Various products are offered under the "ChKM" name and all contain chlorphenol, camphor, and menthol. Of course, one can mix parachlorphenol and camphor in various ratios and add alcohol as a solvent. In each case, one obtains parachlorphenol-camphor solutions (CMCP). If one adds menthol to the solution, even ChKM is produced. In no case, however, does one obtain Prof. Walkhoff's original ChKM solution by simply mixing the components. Its particular achievement was a parachlorphenol-camphor-menthol solution fully saturated with camphor that contains no additional solvent and in particular no alcohol [23].

Unfortunately, ChKM-W has come into question because it has been mistakenly equated with a chlorphenol-camphor solution, which was studied by Spångberg [37] and labelled by him as too toxic for use on humans. The most effective controllable agent among starting materials of disinfectants for use on humans is actually parachlorphenol. Its drawback is that it just as caustic as concentrated sodium hypochlorite. If one reads Spänberg's article closely, it shows that he had studied the effect of an unsaturated solution with a lot of (inexpensive) chlorphenol, little (expensive) camphor, and with alcohol as a solvent. All unsaturated preparations had already been discarded as unsuitable by Walkhoff 50 years previously. Nonetheless, this simple "camphorated parachlorphenol" has also proven to be superior in all studies to all disinfectants introduced since. It kills Enterococcus faecalis completely well deep into the tubuli and is even used by some researchers as a reference preparation when testing the effectiveness of the disinfectants studied by them [13, 17, 25, 32, 40, 43, 44].

The reports about the severe, sometimes irreversible side effects of NaOCl are numerous [19]. As a result, its use in concentrated form with an open foramen apicale is contraindicated in Germany [21, 39]. In contrast, there is not a single similar report about ChKM-W in the world literature. The original solution according to Walkhoff is only very weakly protein precipitative, non-teratogenic, and non-carcinogenic. The only thing objectionable in the use of ChKM-W is that – like NaOC – it does not smell or taste good. Poor smell and taste, however, simply cannot be accepted by the dental practitioner as an argument for withholding a drug from the patient when confronted with its therapeutic potency and absence of side effects [26].

South American scientists have studied camphorated parachlorphenol mixed with Ca(OH)2. They have been able to create a significant improvement in its disinfectant efficacy against Enterococcus faecalis in particular [13, 32, 33]. The mixture was deemed necessary to reduce the caustic effect and cytotoxicity of the parachlorphenol solutions used. Mixing CMCP with Ca(OH)2 into a paste naturally obstructs the pharmacodynamics and pharmacokinetics of the CMCP solution substantially. ChKM-W is the only non-caustic, fully saturated solution that can be used in its pure form without creating undesirable side effects.

VI. "Biocompatible" disinfectants

German scientists basically rejected [4, 5, 37] the use of ChKM as a disinfecting long-term inlay due to its mistakenly judged excessive cytotoxicity. This position was justified with the

demand that only biocompatible disinfectants should be used on humans. They overlooked the fact that the concepts "disinfectant" and "biocompatible" are themselves contradictory. Bacteria are cells and part of our biological system. If they cause infectious diseases, they are aggressors from a medical perspective that must then be annihilated. If the agents used for this purpose are not cytotoxic, they are unable to fulfil their purpose. Therefore by definition, disinfectants are not an issue. In this context, it should be remembered that Ca(OH)2 and hypochlorite are also obviously cytotoxic [1], since otherwise they would not be able to kill bacteria. However, since the purpose of its use is to kill bacterial cells, Ca(OH)2 is evidently not cytotoxic enough [13].

It is a matter for scientific discussion whether a medicine should be used in humans. The decision on suitability and use depends on the type and extent of the side effects, including their reversibility and the question of whether potential side effects stand in a justifiable relationship to achieving the therapeutic goal. Consideration of these factors on the basis of observations and valid data is the hallmark of the authorisation process for a medicine by the national regulatory authorities.

VII. Infection control: Problems and requirements

For more than 100 years, the consensus has been that only approx. 50% of the endodontic cavity system is even accessible by means of mechanical disinfection. As a result of the continued development of preparation techniques in recent decades, mechanical cleaning of accessible areas has since increased to 65%. When the bacterially contaminated cavity system is looked at in its entirety, the rate of mechanical cleaning is only a little more than 30%, even with maximum technical expenditure. The potentially infected periapex and frequently bacterially contaminated granuloma are not even taken into account [26].

According to currently accepted doctrine, over-instrumentation absolutely has to stop in order to prevent bacterially contaminated debris from reaching beyond the apex. Despite every effort, this cannot be ensured by any known preparation technique [16]. Since concentrated NaOCl is contraindicated beyond the apex, one makes every technical effort to protect the apical foramen from enlarging during mechanical preparation. The ability of the disinfectant to access important areas of bacterial contamination is therefore made difficult. On close examination, treatment is stopped before decontamination of all potentially infected tissues and surfaces is complete [26]. Complete healing of the infection is left to the individual immune response and its variations in quality [22]. Against this background and in view of the long-term use of disinfectants that have little or no effect on substantial, endodontitis-relevant pathogens, it is no wonder that the healing rate of endodontic infectious disease has remained static for decades [10].

In contrast to sterilisation, disinfection does not entail annihilation of microbes but rather their reduction as far as possible. Walkhoff knew about resistance to treatment by endodontitis-relevant pathogens and therefore tirelessly admonished "to preferably overestimate rather than underestimate the refractoriness of the responsible agents for one's own benefit and that of the patient." He viewed it as absolutely necessary that an indication-oriented sealer contain lasting, potent disinfectants. These make it difficult for any surviving bacteria to multiply and spread after careful disinfectant pre-treatment.

In regard to sealers too, modern endodontics has recently distanced itself from the medical-infectiological approach to treating septic conditions in humans. Filling pastes that contain potent disinfectants were rejected due to their underlying cytotoxicity in favour of ever more technically sophisticated obturation techniques and a neutral sealer. The use of filling pastes with potent disinfectants has even been labelled recently as obsolete. However, scientific documentation of performance improvement through so-called modern trend-setting obturation procedures has not emerged [16]. Behind these modern procedures is an idea that one can and must enclose surviving bacteria in the cavity system [46] as in a mausoleum in order to prevent a contamination of the root canals wrongly interpreted as secondary to coronal leakage. In 1931, Walkhoff [43] wrote about the use of neutral sealers that at the time were described as an "American method":

> "No residual pulp, however, which still contains living micro-organisms after pre-treatment, is ever made aseptic by covering it with a purely technical agent. It then remains as a direct source of infection for the periodontium. This all the more if the residual pulp is continuously attached to medullary and vascular canals, which exist in the dentin and enamel of many teeth, particularly near the root apex. Each of these canals can induce severe sequelae through a persistent infection at its opening into the periodontium. In such cases, reinfection is much less at issue, rather the persistence of an already present and unresolved infection of the residual tissue in the main and any accessory canals."

In addition, Walkhoff called for easy removability of the inserted filling material if revision treatment should be required [48]. If due to endodontic failure ("posttreatment disease") the initial lack of disinfection has to be corrected by revision, the removal of neutral materials introduced with modern obturation procedures proves to be extremely difficult, even occasionally impossible – and not only for the general dentist. The success rate of revision treatments in healing manifest osteitis is also a modest 60% despite the recommended "intelligent case selection" [34].

VIII. Trend-setting study by Nair et al.

In a prospective clinical study, Nair et al. [24] treated eighteen apical bacterially infected lower molars according to the recognised gold standard. They filled the root canals definitively at the first sitting. They then immediately resected the apexes of the mesial roots in the same sitting and examined their endodontic cavity system by a molecular biology method. In 90% of the cases, they verified the existence of surviving bio-film forming bacteria and explained that only systematic errors in their examination had kept the verification rate below 100%. They found these pathogens in main canals and particularly in accessory canals, collateral canals, connection canals, blind pouches, and niches.

With this study, modern endodontics has arrived in 2005 where Walkhoff already stood in 1929 at the latest, at least in regard to the description of the causes of the deficiencies in endodontic infection control. In his polemic paper "The problem of dental focal infection and combating it through conservative dentistry" [48], he wrote about the bacteria involved and the relationship between endodontic sepsis and anatomy:

> "These bacteria are very much underestimated in their behaviour, their resilience, and their location in very much underappreciated hiding places

> even in the treatment of a simple gangrenous pulp. In their current design and when used only for a few days, few inlays are able to destroy bacteria. This effect can be achieved only by sufficiently powerful action on the micro-organisms that lasts for weeks and months!”

As a result of the study by Nair, international endodontic science has had to admit the failure of its gold standard treatment protocol [41, 51, 52]. Particularly striking among the range of scientific reflections is the editorial from Spångberg [36] published in the September 2006 issue of the journal "Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology" under the title "Infatuated by Enterococcus". Spångberg appears disappointed to have researched for more than 30 years in vain and calls on the honourable Robert Koch as a witness that Enterococcus faecalis may not absolutely have to be killed since Koch's postulates for clear evidence of microbes in endodontitis are not fulfilled. He calls upon science to increase its efforts to finally track down the previously unknown germ solely responsible for endodontitis. He also calls upon science to identify and verify additional germs that survive the use of known ineffective disinfectants. It would undoubtedly be more effective to call for research on more effective disinfectants that reliably kill already known pathogens, or to use known, effective, indication-oriented medicines. This editorial is not devoid of a certain tragic twist, since in the very same journal that Spångberg published his article in 1973 [37] described above, the very medicine that fully and quickly eliminates Enterococcus faecalis from deep into the tubuli [17] was wrongfully called into question.

Conclusions

Our conclusions favouring modification of the currently recognised protocol and our description of a possibly more successful protocol for treating endodontitis are almost inescapable. We must take advantage of the mechanical and technical means currently available to us today, but exalting them as an end in themselves should be discontinued. Instead, we must recall our medical roots and the universally valid medical principles for treating bacterial infectious diseases. Mechanical preparation is still the servant of disinfection today as it was 100 years ago.

On the basis of this insight, we turn to the patient use of potent, cytotoxic disinfectants with a low side effect profile before making a definitive closure – which should not be made very difficult to remove again. The tooth ultimately offers nearly ideal anatomical conditions for the required patient long-term use of such chemotherapeutic agents. The sealers applied must contain a long-acting disinfectant to make it difficult for any surviving pathogens to spread and multiply. The Endomethasone N (Septodont, Niederkassel) that we use contains dijodothymol, for example. In contrast to other sealers, Endomethasone N works well against Enterococcus faecalis [3].

We should point out for the sake of comparison that tuberculosis – also a disease difficult to heal medically – is not treated with less effective medicines over a very short period of time, but instead with effective therapeutic agents over a very long period of time.

In addition, we must ensure that through our mechanical procedures we open up all potentially infected areas to make them accessible to applied chemotherapeutic agents rather than devote our efforts to sealing these areas off from them [26]. The goal of any medical

intervention is ultimately to sustainably support the immune system of the individual patient – which is qualitatively different in each case – in its efforts to heal itself.

Munich, Germany, September 2005

LITERATURE:

1. Alacam T, Omurlu H, Ozkul A, Gorgul G, Misirligil A: Cytotoxicity versus antibacterial activity of some antiseptics in vitro. J Nihon Univ Sch Dent 35, 22-27 (1993)
2. *Barbosa SV, Safavi KE, Spangberg SW*: Influence of sodium hypochlorite on the permeability and structure of cervical human dentine. Int Endod J 27, 309-312 (1994)
3. Bodrumlu E, Semiz M: Antibacterial activity of a new endodontic sealer against Enterococcus faecalis. J Can Dent Assoc 72, 637-637c (2006)
4. Byström A, Claesson R, Sundquist G: The antibacterial effect of camphorated paramonochlorphenol, camphorated phenol and calcium hydroxide in the treatment of infected root canals. Endod Dent Traumatol 1, 170-175 (1985)
5. Castagnola L: Die Behandlung infizierter Pulpen und Wurzelkanäle und ihre Folgeerscheinungen. Helmut Haase-Verlag, Heidelberg 1951
6. Chang Y, Tai KW, Chou LS, Chou MY: Effects of camphorated parachlorphenol on human periodontal ligament cells In vitro. J Endodont 25, 779-781 (1999)
7. Chavez De Paz LE, Dahlen G, Molander A, Moller A, Bergenholtz G: Bacteria recovered from teeth with apical periodontitis after antimicrobial endodontic treatment. Int Endod J 36, 500-508 (2003)
8. Engel H: Die Behandlung infizierter Wurzelkanäle und Granulome nach der Methode von Walkhoff. Vergleichende rö-histologische Untersuchungen. Schweiz Monatsschr Zahnmed 11 (1950)
9. Estrela C, Estrela CR, Decurcio DA, Hollanda AC, Silva JA: Antimicrobial efficacy of ozonated water, gaseous ozone, sodium hypochlorite and chlorhexidine in infected human root canals. Int Endod J 40, 85-93 (2007)
10. *Figdor D: Apical periodontitis:* A very prevalent problem. Oral Surg Oral Med Oral Pathol 94, 651-652 (2002)
11. Figdor D, Davies JK, Sundqvist G: Starvation survival, growth and recovery of Enterococcus faecalis in human serum. Oral Microbiol Immunol 18, 234-239 (2003)
12. Gesi A, Hakeberg M, Warfvinge J, Bergenholtz G: Incidence of periapical lesions and clinical symptoms after pulpectomy – a clinical and radiographic evaluation of 1- versus 2-session treatment. Oral Surg Oral Med Oral Pathol 101, 379-388 (2006)
13. Gomes B, Ferraz C, Garrido F, Rosalen P, Zaia A, Teixeira F, de Souza-Filho F: Microbial susceptibility to calcium hydroxide pastes and their vehicles. J Endod 28, 758-761 (2002)
14. Gomes B, Pinheiro ET, Gade-Neto CR, Sousa EL., Ferraz CC, Zaia AA, Teixeira FB, Souza-Filho FJ: Microbiological examination of infected dental root canals. Oral Microbiol Immunol 19(2), 71-76 (2004)
15. Haapasalo M, Endal U, Zandi H, Coil JM: Eradication of endodontic infection by instrumentation and irrigation solutions. Endodontic Topics 10, 77-102 (2005)
16. Haapasalo M, Orstavik D: In vitro infection and disinfection of dentinal tubules. J Dent Res 66, 1375-1379 (1987)
17. Haapasalo M, Endal U: Control and elimination of endodontic infection. Endodontie Journal 4, 10 (2003)
18. Hülsmann M, Denden JM: Iatrogene Zwischenfälle bei der Wurzelkanalspülung - Literaturübersicht und Falldarstellung. Endodontie 3, 191-206 (1997)
19. Hülsmann M, Schäfer E: "Good clinical practice": Die Wurzelbehandlung. Stellungnahme der DGZ/DGZMK. Dtsch Zahnärztl Z 60, 418-423 (2005)
20. Kojima K, Inamoto I: Success rate of endodontic treatment of teeth with vital and nonvital pulps. A metaanalysis. Oral Surg Oral Med Oral Pathol 97, 95-99 (2004)
21. *LegeArtis:* Beipackzettel zu Histolith. 2006
22. Marending M, Peters OA, Zehnder M: Factors affecting the outcome of orthograde root canal therapy in a general dentistry hospital practice. Oral Surg Oral Med Oral Pathol 99, 119-124 (2005)

23. Nair P N, Henry S, Cano V,Vera J: Microbial status of apical root canal system of human mandibular first molars with primary apical periodontitis after ‘‘one-visit’’ endodontic treatment. Oral Surg Oral Med Oral Pathol 99, 231-252 (2005)
24. Orstavik D, Haapasalo M: Disinfection by endodontic irrigants and dressings of experimentally infected dentinal tubules. Endod Dent Traumatol 6, 142-149 (1990)
25. Osswald R: Die indikationsgerechte Behandlung der Endodontitis. Niedersächsisches Zahnärzteblatt 10, 14-20 (2006)
26. Portenier I, Waltimo T, Orstavik D, Haapasalo M: Killing of Enterococcus faecalis by MTAD and chlorhexidine digluconate with or without cetrimide in the presence or absence of dentine powder or BSA. J Endod 32, 138-141 (2006)
27. Ribeiro DA, Marques ME, Salvadori DM: Lack of genotoxicity of formocresol, paramonochlorophenol and calcium hydroxide on mammalian cells by comet assay. J Endod 308, 593-596 (2004)
28. Sathorn C, Parashos P, Messer H: Antibacterial efficacy of calcium hydroxide intracanal dressing: a systematic review and meta-analysis. Int Endod J 10, 2-10 (2007)
29. Schäfer, E.: Praxisletter. Dtsch Zahnärztl Z 3, 137-138 (2007)
30. Siqueira JF, Lopez HP: Kalziumhydroxid als antimikrobielle Einlage in der Endodontie - Wirkungsmechanismen, Vorteile und Grenzen. Endodontie 11, 333-347 (2002)
31. Sjogren U, Figdor D, Persson S, Sundqvist G: Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis. Int Endod J 30, 297 (1997)
32. Spångberg L: Infatuated by Enterococci. Oral Surg Oral Med Oral Pathol 102, 577-578 (2006)
33. Spångberg L., Engström B, Langeland K: Toxicity and antimicrobial effect of endodontic antiseptics in vitro. Oral Surg 36, 856-871 (1973)
34. Speiko: Beipackzettel zu Hypochlorid-Speiko. (2006)
35. Sukawat C, Srisuwan T: A comparison of the antimicrobial efficacy of three calcium hydroxide formulations on human dentin infected with Enterococcus faecalis. J Endodont 28, 102-104 (2002)
36. Sum C, Neo J, Kishen A: What we leave behind in root canals after endodontic treatment: some issues and concerns. Aust Endod J 31, 94-100 (2005)
37. Sundqvist G: Användningen av Chlumskyslösning inom tandvården. Tandläkartidningen 91(13), 51-53 (1999)
38. Tanriverdi F, Esener T, Erganis O, Belli S: An in vitro test model for investigation of disinfection of dentinal tubules infected with Enterococcus faecalis. Braz Dent J 8, 67-72 (1997)
39. Tchaou WS, Turng BF, Minah GE, Coll JA: Inhibition of pure cultures of oral bacteria by root canal filling materials. Pediatr Dent 18, 444-449 (1996)
40. Tronstad L., Sunde PT: The evolving new understanding of endodontic infections. Endod Topics 6, 57-77 (2003)
41. Walkhoff O: Mein System der medikamentösen Behandlung schwerer Erkrankungen der Zahnpulpa und des Periodontiums. Verlag von Hermann Meuser, Berlin 1928
42. Walkhoff O: Erläuterungen zu den heutigen Behandlungsprinzipien infizierter Zahnwurzeln. Zahnärztl Rundsch 38, 485-493 (1929)
43. Walkhoff O: Das Problem der dentalen Fokalinfektion und ihrer Bekämpfung durch die konservierende Zahnheilkunde. Verlag von Gustav Fischer, Jena 1931
44. Walkhoff O, Hess W: Lehrbuch der konservierenden Zahnheilkunde. Johann Ambrosius Barth Verlag, Leipzig 1954
45. Waltimo T, Trope M, Haapasalo M, Orstavik D: Clinical efficacy of treatment procedures in endodontic infection control and one year follow-up of periapical healing. J Endodont 31, 863-866 (2005)
46. Webber J: Now is the time to raise standards. Endod Pract 9(2), 3 (2006)
47. Wu MK, Dummer PM, Wesselink PR*:* Consequences of and strategies to deal with residual post-treatment root canal infection. Int Endod J 39, 343-356 (2006)