Endodontic Topics

Endodontic Topics 2009, 16, 27–63

ENDODONTIC TOPICS 2009
1601-1538

Complications during root canal irrigation

MICHAEL HÜLSMANN, TINA RÖDIG & SABINE NORDMEYER

Although endodontic irrigants are generally considered to be safe, severe complications can occur during or as a consequence of root canal irrigation. However, no data on the incidence of irrigation incidents could be found. In the following paper, a review is presented on the possible incidents that may occur during root canal irrigation with different irrigation solutions, the sequelae, as well as prevention and therapy of such intra- and post-operative problems.

Received 25 April 2008; accepted 7 August 2008.

Introduction

Root canal irrigation plays an important role in the debridement and disinfection of the root canal system and is an integral part of root canal preparation procedures. The most frequently used irrigants in contemporary endodontic treatment concepts are sodium hypochlorite, hydrogen peroxide, the combined use of both, chlorhexidine (CHX), citric acid, iodine-potassium-iodide, alcohol, and EDTA solutions (1, 2). More recently, several new solutions such as bioglass, MTAD, deionized water, and some more have been advocated for disinfection. Hydrogen peroxide has been used in concentrations of 3–5%, and sodium hypochlorite in concentrations of 0.5–5.25% (2, 3). In a questionnaire study among Swiss general dental practitioners ($n = 2091$), 75% used hydrogen peroxide, 74.2% used sodium hypochlorite, 14.6% alcohol, 11.7% ringer's solution or saline, and 14.6% other irrigants (4). Among the latter were EDTA (5.7%) and CHX (3.2%).

The endodontic literature on irrigation incidents mainly comprises case reports on major incidents. No definition of the term 'irrigation incident' has been proposed so far and systematic data on the frequency of such incidents are missing entirely. It may be supposed that irrigation incidents occur not infrequently, especially minor incidents, without the necessity for immediate intervention due to minimal exposure of vital tissue to irrigants.

Irrigants

Sodium hypochlorite

Sodium hypochlorite is an alkaline irrigant with a pH of approximately 11–12. It oxidates and hydrolyzes proteins and causes hemolysis of red blood cells (5). It has been demonstrated to be an effective agent against a broad spectrum of bacteria and to dissolve vital as well as necrotic tissue (6). The benefits of the good tissue-dissolving and disinfecting capabilities of sodium hypochlorite, due to the release of chloramine, have been demonstrated in several investigations (6–14). The concentration of the irrigant is still a matter of debate and remains controversial; many authors recommend a 5.25% concentration of sodium hypochlorite (3) while others prefer a lower concentration of 3% or even 0.5% (15, 16). It is recommended to use higher volumes of low-concentrated NaOCl (i.e. 0.5–1%) instead of highly concentrated solutions (5.25%) (17).

However, it has also been shown that sodium hypochlorite has toxic effects on vital tissues, resulting in hemolysis, skin ulceration, and necrosis (5). Several studies have reported on increased tissue-dissolving capacity when the temperature of the solution is increased (18–22). Sodium hypochlorite is corrosive to metals and might exert some damage to preparation instruments and rubber dam clamps (23).

Hydrogen peroxide

Hydrogen peroxide has been used as an endodontic irrigant for a long period of time, mainly in concentrations ranging between 3% and 5% (3, 24, 25). It is active against bacteria, viruses, and yeasts. Hydroxy-free radicals ($^{\bullet}OH$) destroy proteins and DNA. The tissue-dissolving capacity of hydrogen peroxide is clearly lower than that of sodium hypochlorite. When used in combination with sodium hypochlorite, bubbling will occur as a result of evaporating oxygen (26). Although no longer recommended as a routine irrigant, its use is still not uncommon in some countries.

EDTA

Chelating agents were introduced into endodontics in 1957 by Nygaard-Østby as an aid for the preparation of narrow and calcified root canals. A liquid solution of EDTA was thought to chemically soften the root canal dentine and dissolve the smear layer as well as to increase dentine permeability. Massilamoni et al. (27) reported that a 15% sodium-EDTA solution had toxic effects *in vitro*. Complete prevention of cell growth was detected after *in vitro* use of EDTA-T (28). Additionally, 15% solutions of EDTA and EDTAC at pH 7.3 have the potential to cause severe irritation (29). These authors found that 15% and 17% EDTA solutions and 2.25% NaOCl solutions produce severe cytotoxic effects, while 1% solutions of both agents evoked only moderate reactions. Comparing the cytotoxicity of three irrigants, EDTA provoked more cytotoxic effects than oxidative potential water or NaOCl (30). EDTA is used intravenously in medicine for chelation therapy in patients with cardiovascular disease. EDTA can be regarded as a safe irrigant when used adequately and carefully; no reports on adverse effects during clinical use have been published so far.

Citric acid

The use of citric acid in concentrations between 1% and 50% has been suggested for the removal of the smear layer instead of EDTA. Biocompatibility is reasonably good and no reports on negative side-effects or incidents during its use in endodontics have been published. A 10–25% citric acid solution showed good biocompatibility with no reduction in cell viability (28, 31–33).

CHX

CHX, a synthetic cationic bis-guanide and one of the most frequently used disinfectants, is used as gluconate salt and shows good antibacterial, antifungal, and antiviral properties. Its pH is 5–8. In low concentrations, it acts bacteriostatically; in high concentrations, bactericidally. CHX has no capability to dissolve vital or necrotic tissue (34). In laboratory experiments, it has been demonstrated that CHX is highly cytotoxic to human periodontal ligament (PDL) cells and human fibroblasts via inhibition of protein synthesis (35, 36). The clinical relevance of these findings has yet to be proven.

Iodine-potassium-iodide

Iodine-potassium-iodide has been proposed and used as an endodontic disinfectant due to its excellent antibacterial properties and low cytotoxicity (15, 37, 38). It is used as a solution of 2% iodine in 4% potassium-iodide and may act as a severe allergen and also stain dentine (26).

Alcohol

Alcohol (95%) may be used to dry a root canal before obturation in order to reduce surface tension and facilitate adhesion of the obturation material to dentine and penetration of sealer into dentinal tubules (39, 40).

MTAD

MTAD is a solution composed of citric acid, doxycycline, and Tween 80, a detergent. It has been introduced by Torabinejad et al. (41) and is marketed as Biopure (Dentsply, Tulsa, OK, USA). In combination with 1.3% NaOCl, it has been shown to be helpful in the removal of the smear layer and to have antimicrobial efficacy. The cytotoxicity of MTAD *in vitro* has been shown to be lower than eugenol, 3% hydrogen peroxide, calcium hydroxide, 5.25% NaOCl, CHX, and EDTA (42). In combination with 1.3% NaOCl, it shows tissue-dissolving activity (26). Some concern has been expressed on the tetracycline concentration, which might favor tetracycline resistance of intracanal bacteria (1, 26).

Incidents and problems due to root canal irrigation

Several mishaps during root canal irrigation have been described in the dental literature. These range from damage to the patient's clothing, splashing the irrigant into the patient's or operator's eye, injection through the apical foramen, air emphysema, and allergic reactions to the irrigant, to inadvertent use of an irrigant as an anesthetic solution. In discussing the nature of such incidents and defining a preventive strategy as well as therapy in these cases, physical, mechanical, and anatomical aspects of such problems should be considered.

Irrigation hydrodynamics, irrigation pressure, and tissue pressure

Efficacy of root canal irrigation in terms of debris removal and eradication of bacteria depends on several factors: penetration depth of the needle, diameter of the root canal, inner and outer diameter of the needle, irrigation pressure, viscosity of the irrigant, velocity of the irrigant at the needle tip, and type and orientation of the bevel of the needle (43). Basically, the flow of an irrigant through a needle is described by the Hagen–Poiseuille law:

$$F = \frac{\pi r^4 \Delta p}{8 \mu l}$$

where l is the length of needle, μ is the coefficient of viscosity, F is the volume of fluid flowing per unit time, Δp is the pressure difference across the needle, and r is the radius of needle.

It has to be considered that the size (and length) of the irrigation needle – in relation to root canal dimensions – is of utmost importance for the effectiveness of irrigation and at the same time for the irrigation pressure (43, 44), as indicated by the fourth power of the radius. The effect of irrigation, i.e. exchange of irrigant, is limited to a distance of approximately 1 mm beyond the tip of the needle (45, 46). Abou-Rass & Piccinino (47) and Druttman & Stock (48) stressed the need to place the needle tip as far apically as possible and achieved better results with a 30-gauge needle when compared with 23-gauge tips. Ram (44) demonstrated the influence of root canal diameter on the effectiveness of irrigation. Following instrumentation to size 25, a radiopaque material could not be flushed out sufficiently from the apical part of the root canals with a 25-gauge needle, while preparation to size 40 allowed complete removal in eight out of 10 canals and preparation to size 60 achieved complete removal in five of five canals. Especially for roots with higher degrees of curvature, increased apical enlargement seems to be necessary to achieve adequate delivery of the irrigant (49).

The external diameter is of relevance for the depth of introduction into the root canal and for rigidity of the tip, which is important for irrigation of curved canals. The internal diameter determines the necessary pressure for moving the syringe plunger and the velocity with which the irrigant is extruded. Narrow needles need more pressure onto the plunger and extrude the irrigant with higher velocity than large needle sizes, which otherwise extrude larger amounts of irrigants but cannot be introduced as deep. Moser & Heuer (50) measured the pressure necessary for activation of the plunger in different sizes and types of irrigation needles and found the lowest pressure for irrigation with larger needle sizes (23–24 gauge) compared with smaller sizes (24–30 gauge). However, larger needles with greater distance to the apex are less efficient than smaller needles with increased penetration depth (43). Common injection needles have an external diameter of 0.40 mm (27 gauge), but special irrigation tips with external diameters of 0.30 mm (30 gauge) are available as well (Table 1). Boutsioukis et al. (51) also reported an increased average and maximum irrigation pressure with decreasing internal needle diameter sizes. Intrabarrel pressure for finer needles in their study rose up to 400–550 kPa. With smaller diameters, sodium chlorite crystals have demonstrated a tendency to block the lumen of the needle, consequently requiring an increased pressure (6, 50). To improve safety of irrigation and prevent apical extrusion of the irrigant, some of these needles release the solution via lateral openings and have a closed, safe-ended tip.

The Stropko Flexi-Tip (30 gauge) needle is fabricated out of nickel–titanium (NiTi) to improve penetration into curved root canals and has been reported to exceed ISO limits for dimensions (52). It has been shown that although standardized by ISO

Table 1. Sizes and manufacturers of needles used for root canal irrigation

Manufacturer	Product	Gauge	Outer diameter in mm
Dentsply	Max-I-Probe	21–30	0.3; 0.4; 0.5; 0.6; 0.7; 0.8
Ultradent, South Jordan, UT, USA	NaviTip	29, 30	0.3; 0.33
	NaviTip FX Tip (brush-covered needle)	30	0.3
	Capillary Tip	25, 28	0.35; 0.5
	Endo-Eze Tip/Deliver Eze	18, 19, 20, 22, 30, 31	0.25; 0.3; 0.7; 0.9; 1.06; 1.25
	Endo-Eze Irrigator Tip/Deliver Eze Spülkanüle	27	0.4
KerrHawe, Bioggio, Switzerland	NaviTip	21–30	
Hager & Werken, Duisburg, Germany	Miraject Endotec	21–25	
Vista Dental Products	Stropko Flexi-Tip (NiTi)	30	
KerrHawe	KerrHawe irrigation probe		
Transcoject, Neumünster, Germany	Spülkanülen Endo	23, 25, 27, 30	0.3; 0.4; 0.5; 0.6

specifications 9626:1991 and 962:1991/Amd 1.2001, the internal and external diameters of irrigation needles show considerable deviations (52).

Salzgeber & Brilliant (53), in a study on 19 roots with vital pulps and 19 roots with necrotic pulps, investigated the hydrodynamics of irrigation. They used a radiopaque solution comparable to sodium hypochlorite in terms of viscosity, surface tension, and specific gravity, with a 23-gauge irrigation needle following enlargement to sizes 30, 35, and 45, respectively. Extrusion of the radiopaque irrigant into the periradicular tissue, verified by radiographs, occurred in only two teeth with vital pulps following preparation to size 45, which was attributed to obvious mistakes in length determination. Extrusion already occurred in three teeth with necrotic pulps after preparation to size 35. The solution was distributed over random portions of the rarefied areas, suggesting a higher risk for apical extrusion in teeth/roots with necrotic pulps. Mohorn et al. (54) measured a negative pressure below atmospheric pressure at some time in the periapical tissues of mongrel dogs following vital pulp extirpation, but could not obtain constant results over the complete period of measurement. However, it is well known that inflammation results in increased tissue pressure, which in endodontics might be expected in cases of apical periodontitis. Nevertheless, in cases of a vital as well as necrotic pulp, the pressure at the periapex cannot be reliably determined or prognosticated and a certain risk of apical extrusion due to negative tissue pressure should be considered in any case. There seems to be no reliable barrier beyond the apical foramen preventing extrusion of irrigant.

Pathways for extrusion of irrigants

The main pathways for extrusion of irrigants are the apical foramen and iatrogenic perforations. The diameter of lateral or furcational canals seems to be small enough to exert sufficient resistance to irrigant flow and prevent extrusion of a relevant amount of an irrigant (Fig. 1a–c), although no evidence exists for this assumption.

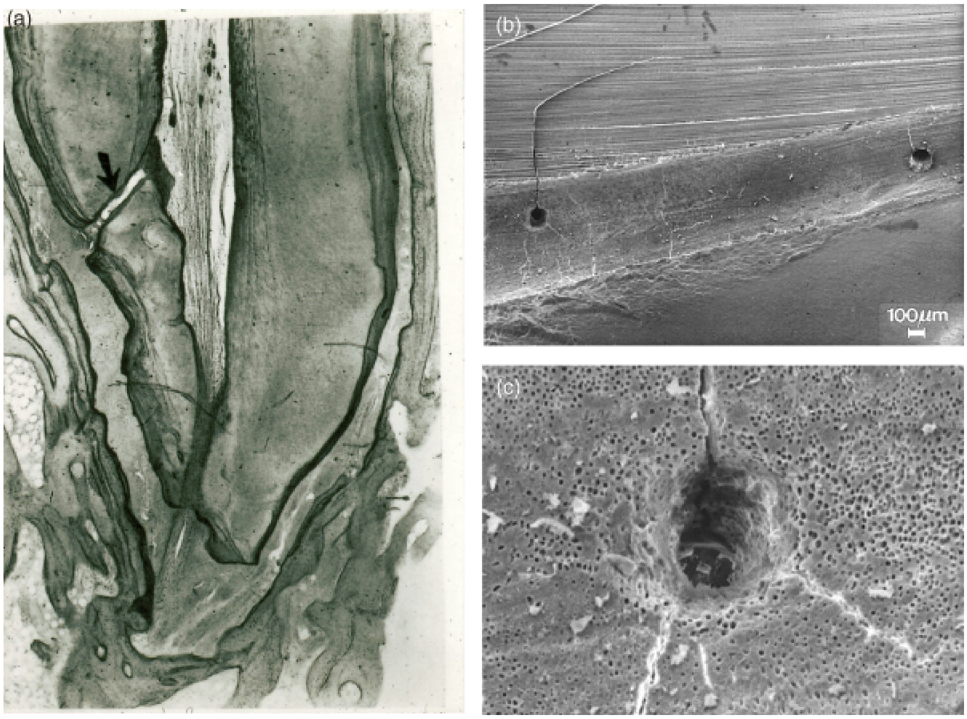

Fig. 1. (a) Longitudinal section of a root showing a large lateral canal in the apical third of the root. (b) SEM view of a large lateral canal. (c) Magnification of (b) showing a large lateral canal. It seems questionable whether critical amounts of irrigant may be extruded through such lateral canals. Courtesy of C. Kockapan.

Perforating resorptive defects of the root could also present portals of exit (POE) for an irrigant and be a cause for concern in the treatment of traumatized teeth, but no such case has been reported in the literature.

Lateral canals or branches represent POE of the root canal system and it has been demonstrated that frequently the size of these canals and branches allows extrusion of root filling materials (mainly sealer) when obturation is performed using thermoplastic filing techniques. Nevertheless, only a minority of these lateral canals is obturated (55). Lateral canals have also been shown to be bacterial pathways in cases of lateral lesions of endodontic origin or in combined endo-perio lesions (56). Miyashita et al. (57) investigated the internal anatomy of mandibular incisors and reported that the majority of accessory canals or lateral branches (81%) were smaller than or equal to an instrument size 15 and none exceeded size 30. In maxillary central incisors, the same group described the size of the majority of lateral canals (80%) to be size 10 or less; only 3% were larger than size 40 (58). This is supported by a study by Venturi et al. (59) demonstrating that only a minority of these canals exceeds an internal diameter size of 150 μm. To estimate the risk of extrusion of a liquid via any lateral canal, the length of the canal also must be taken into consideration. It seems unlikely that a lateral irrigation pressure high enough to press an irrigant through narrow (and more or less long) tubes such as lateral canals may occur. The situation during irrigation is not comparable to that during thermoplastic obturation: in the latter preparation, form and obturation instruments are selected intentionally to create hydraulic pressure in a vertical and a lateral direction. Nevertheless, extrusion of minor amounts of irrigant vial lateral (or furcational) canals cannot be excluded completely, although no clinical case has thus far been reported.

Apical extrusion during root canal preparation

Apical extrusion of material (including dentine chips, tissue remnants, and irrigant) caused by movement of instruments in an apical direction, instruments acting as a plunger, or by irrigation should be expected during any endodontic treatment. The only way to prevent such extrusion would be a non-desirable iatrogenic blockage of the apical foramen. Finally, endodontic treatment will always be a balance between blockage and some degree of extrusion of debris including irrigant. The amount of extruded material as measured in several different *in vitro* experiments varies considerably and has been shown to depend on the preparation technique. Fairbourn et al. (60) described the lowest amount of extrusion for a sonic preparation technique followed by a cervical flaring technique, ultrasonic technique, and conventional preparation. In resin blocks, step-back preparation produced more extrusion than crown-down-pressureless instrumentation, but no technique could completely prevent apical extrusion (61). The mean amounts of extruded debris varied between 0.12 mg (sonic instrumentation) and 0.30 mg (conventional technique) and were not significantly different. Martin & Cunningham (62) detected less extrusion for an ultrasonic preparation technique (0.22 mg) than for a manual preparation (0.53 mg). When protruding instruments beyond the foramen, ultrasonic preparation produced 0.87 mg and hand preparation 1.39 mg of extruded debris. McKendry (63) found significantly less debris following balanced-force preparation (mean 0.24 mg) compared with ultrasonic (0.42 mg) or step-back preparation (0.45 mg). Myers & Montgomery (64) found more extruded debris following preparation to the apical foramen (mean: 0.78–1.58 mg), whereas preparation 1 mm short of the foramen resulted in less extrusion (mean: 0.22 mg) but in frequent apical plugging. Comparing eight manual preparation techniques, AlOmari & Dummer (65) measured 0.47–0.72 mg extruded debris. In a study by Tanalp et al. (66) comparing three rotary NiTi systems, ProTaper pushed more debris (1.5 mg) through the foramen than ProFile (0.56 mg) or HERO Shapers (0.94 mg). According to Ferraz et al. (67) rotary preparation using NiTi instruments produced less extruded debris than manual instrumentation (hybrid technique: 0.46 mg, balanced-force: 0.25 mg, Quantec 2000: 0.188 mg, ProFile .04: 0.177 mg, Pow-R: 0.18 mg). Beeson et al. (68) compared conventional filing to rotary preparation using ProFile .04 instruments to the foramen and 1 mm short. When instrumenting to the foramen they measured 1.6 mg extruded debris for manual preparation and 0.47 mg for ProFile and when staying 1 mm short of the foramen, 0.35 mg for manual, and 0.03 mg for rotary preparation. Zarrabi et al. (69) reported 0.2–0.5 mg extruded material for FlexMaster, Race, and ProFile rotary preparation but 2.1 mg for manual instrumentation. The amount of extruded irrigant was significantly higher when filing was undertaken to the foramen. In most of the cited studies (60, 63, 64) debris was dried and desiccated before measurements so that the weight of the extruded irrigant was not included in the data; nevertheless the extrusion of large amounts of irrigant was noted.

Apical extrusion of irrigant

Although there are several studies on the amount of apically extruded debris during root canal preparation (Table 2), there are few data on the amount of apically extruded irrigant.

In an *in vitro* study in 153 extracted single root teeth, the apical extrusion of irrigant was evaluated. The root canals were prepared using the balanced-force technique, keeping the foramen patent by the use of a size 10 file and irrigated with 2.5% sodium hypochlorite. In one group, the needle was inserted to maximum depth and withdrawn 1 mm (deep irrigation group); in the second group, only the pulp chamber was flooded with the irrigant, which was transported into the root canal during instrumentation (reservoir group). The volume of apically extruded irrigant was measured using emission spectrophotometry calculating the concentration of sodium present in the extruded and collected debris. It was demonstrated that the amount of extruded irrigant was significantly larger in the deep irrigation group than for the reservoir group. It may be interesting to know that the absolute mean volumes of extruded irrigant were 1.68 mL (group I), and 0.98 mL (group II), respectively (70), but it should be noticed that no periapical tissue pressure was simulated, so that the results cannot be directly extrapolated to the clinical situation.

In a study by Ferraz et al. (67), the amount of extruded irrigant was determined following rotary preparation using NiTi instruments. The results were hybrid technique: 0.55 mL, balanced-force: 0.32 mL, Quantec 2000: 0.20 mL, ProFile .04: 0.45 mL, Pow-R: 0.26 mL. Hinrichs et al. (71) found a positive correlation between the amount of extruded debris and the amount of extruded irrigant. Foramen size in that study did not affect the amount of extruded material. The mean values for extruded debris ranged from 1.1 to 1.5 mg; the amount of collected irrigant ranged

Table 2. Amounts of extruded debris and irrigant as reported in experimental *in vitro* studies

Authors	References	Year	Techniques/ instruments	Working length	Mean extrusion Debris	Irrigant	Apical plug+H26
Martin & Cunningham	(62)	1982	Manual	1 mm short	0.53 mg	Desiccated	
				Protruding	1.39 mg		
			Ultrasonics	1 mm short	0.22 mg		
				Protruding	0.87 mg		
Fairbourn et al.	(60)	1987	Sonic	1 mm short	0.12 mg	Desiccated	
			Cervical flaring		0.18 mg		
			Ultrasonic		0.2 mg		
			Conventional filing		0.3 mg		
McKendry	(63)	1990	Balanced-force	1 mm short	0.25 mg	Desiccated	
			Endosonic		0.60 mg		
			Step-back filing		0.46 mg		
Myers and Montgomery	(64)	1991	Filing	1 mm short	0.22 mg	Desiccated	16 plugs
			Filing	To foramen	1.58 mg		3 plugs
			Canal Master	To foramen	0.78 mg		1 plug
Brown et al.	(70)	1995	Balanced-force	1 mm short			
			Deep irrigation			1.68 mL	
			Coronal irrigation			0.98 mL	
AlOmari & Dummer	(65)	1995	Standardized preparation	1 mm short	0.47 mg	Desiccated	1 blockage
			Step-back+reaming		0.48 mg		1 blockage
			Step-back+circumf. filing		0.72 mg		16 blockages
			Step-back+anticurv. filing		0.69 mg		19 blockages
			Double-flare		0.61 mg		11 blockages
			Stepdown		0.48 mg		2 blockages
			Crown-down pressureless		0.46 mg		1 blockage
			Balanced-force		0.38 mg		No blockage
Williams et al.	(75)	1995	Needle tip 2–3 mm from foramen		2.35 g	Desiccated	Primary teeth
			Needle tip 6–7 mm from foramen		1.76 g		

Table 2. Continued

Authors	References	Year	Techniques/ instruments	Working length	Mean extrusion Debris	Irrigant	Apical plug+H26
			Inverted needle 2–3 mm from foramen		1.63 g		
			Ultrasonic tip 2–3 mm from foramen		0.21 g		
			Ultrasonic tip 6–7 mm from foramen		0.08 g		
Beeson et al.	(68)	1998	Filing	To foramen	1.65 mg	0.35 mg	4 plugs
				1 mm short	0.35 mg	0.14 mg	15 plugs
			ProFile .04 series 29	To foramen	0.47 mg	0.59 mg	2 plugs
				1 mm short	0.03 mg	0.18 mg	9 plugs
Hinrichs et al.	(71)	1998	LightSpeed	0.5–1 mm short	1.5 mg	1.8 g	
			ProFile .04	Patency technique	1.1 mg	2.6 g	
			NT McXim		1.2 mg	3.0 g	
			Flex-R SS		1.2 mg	1.9 g	
Ferraz et al.	(67)	2001	Hybrid	1 mm short	0.47 mg	0.55 mL	
			Balanced-force		0.25 mg	0.32 mL	
			Quantec 2000		0.19 mg	0.20 mL	
			ProFile .04		0.18 mg	0.45 mL	
			Pow-R		0.19 mg	0.26 mL	
Lambrianidis et al.	(72)	2001	Conventional step-back	1 mm short		Desiccated	
			Constriction intact		0.40 g		
			Constriction en-larged		0.02 g		
Tanalp et al.	(66)	2006	ProTaper	1 mm short	1.53 mg	Desiccated	
			HERO shaper		0.94 mg		
			ProFile		0.56 mg		
Zarrabi et al.	(69)	2006	Step-back manual	0.5 mm short	2.1 mg	Desiccated	
			ProFile		0.3 mg		
			RaCe		0.2 mg		
			FlexMaster		0.5 mg		

from 1.8 to 3.0 g. In contrast, Myers & Montgomery (64) did not find such a correlation.

Beeson et al. (68) measured 0.35 mg extruded irrigant for manual preparation and 0.59 mg for Profile, respectively, when instrumenting to the foramen and 0.14 and 0.18 mg, respectively, when staying 1 mm short of the foramen. The amount of extruded irrigant was significantly higher when filing was undertaken to the foramen.

Lambrianidis et al. (72) reported that the amount of extruded debris (i.e. dentine shavings, tissue remnants, and irrigant) was significantly greater when the size of the apical constriction remained intact compared with enlargement of the foramen. Thirty-three human maxillary incisors were prepared and irrigated with 1% NaOCl and the amount of extruded material collected in a vial and measured. Following this the foramen was intentionally enlarged and a new constriction prepared using a step-back technique. Again the extruded material was measured; no distinction between debris and irrigant was made. No patency file was used with either technique. The authors assume the reason for this result to be an apical plug of dentine and tissue remnants created during the first phase of the study, which prevented apical extrusion following enlargement of the foramen. The results of that study obviously cannot be transferred to preparation using a patency concept with penetration of an instrument through the apical constriction. The results of the study also may be interpreted to mean that attention should be paid to the geometry of the (apical) part of the root canal as this geometry (taper, ledges, irregular narrowing) may influence the hydrodynamics of the irrigant. If apical extrusion of debris occurs during preparation of infected root canals, viable bacteria are also extruded (73).

Salzgeber & Brilliant (53) could demonstrate that vital tissue (and probably tissue remnants in lateral canals) prevented the apical extrusion of an irrigant whereas in cases of necrotic tissue the irrigant was extruded into the lesion.

The amount of extruded irrigant was higher when apical patency was larger (0.4 mm compared with 0.2 mm); no difference was found between manual and rotary preparation (74). In primary teeth with open apices, less extrusion of irrigant occurred with an endosonic unit than with hand irrigation (75).

Kustarci et al. (76) compared the amount of apically extruded debris and irrigant following the use of various manual and rotary instrumentation techniques *in vitro*. While no significant difference was detected for debris extrusion, the K3 NiTi instruments forced significantly less irrigant through the foramen than manual instrumentation. In general, engine-driven NiTi instruments produced less extrusion of debris and irrigant, although differences were not significant (76).

In a recent *in vitro* study it was shown that the amount of apically extruded irrigants during the use of Er:YAG and Er,Cr:YSGG pulsed lasers is higher than during the use of Max-I-Probe (Dentsply, Konstanz, Germany) irrigation needles and manual irrigation (77).

Summarizing, the cited studies demonstrate that apical extrusion of debris and irrigant should be expected during endodontic treatment, although the amount of extruded material may vary considerably.

Anatomical relations

Most frequently the anatomical structures surrounding the tooth and the root such as PDL, mandibulary and maxillary bone, maxillary sinus, and N. mandibularis are involved in complications during root canal irrigation, but in some cases even more distant structures such as intraoral soft tissues, throat, skin, eyes, or airways may be compromised inadvertently by irrigants.

Maxillary sinus

The close relationship of the maxillary sinus to the roots of maxillary teeth has been well documented in the dental literature (for a review of the aspects with contributions to endodontics, see Hauman et al. (78)). Inflammation and infection may spread from the root canal to the sinus (79) and a maxillary sinusitis not infrequently develops symptoms similar to an acute pulpitis. With regard to these anatomical and pathological relationships, Selden (80) created the term ‘endo-antral-syndrome.’

The maxillary sinus is a pneumatized cave that is lined by a respiratory mucosal membrane in close proximity to the root tips of the maxillary posterior teeth. In 50% of people, the floor of the sinus expands into the alveolar process of the maxilla. The root apices, mainly the second premolar and the first and second molar but sometimes even the first premolar and the canine, may extend into the sinus or be clearly separated from the sinus by bone. In elderly people, the bony lamella between root tips and sinus may become rather thin, or sometimes even non-existent, leaving only a thin sinus membrane. The exact anatomical relationship in many cases is difficult, if not impossible, to estimate from conventional radiographs (periapical or panoramic radiographs); modern computed tomographic (CT) scans or magnetic resonance imaging seem better suited for that purpose.

A CT investigation on the relationship between the apices of the maxillary posterior teeth and the sinus floor revealed that the mesio-buccal root of the first molar showed the shortest distance to the sinus (mean distance 0.83 mm), followed by the palatal root of the first molar (1.56 mm), the palatal root of the second molar (2.04 mm), and the disto-buccal root of the second molar (2.79 mm). The buccal root tip of the first premolar (6.18 mm) and the palatal root tip of the first premolar (7.05 mm) showed the largest distance (81). In a CT study, the floor of the maxillary sinus was observed most frequently at a level between the bifurcation and the apices of the first and second maxillary molar. In patients with infections, a mucosal thickening of the maxillary sinus was found in 88% of the cases (79).

Periapical pathosis may result in destruction of the bone between root tip and sinus floor (80, 82, 83). In a Hungarian Dental Clinic, Pataky et al. (84) conducted a radiographic survey of complications to the maxillary sinus through endodontic treatment on 427 upper molars and 1640 upper premolars that had been endodontically treated. In 29% of the cases (209 out of 2067 teeth), they detected sinus complications; in 34 cases, filling or chemical materials were identified as the origin.

Case reports

- Following inadvertent injection of 5.25% NaOCl via the palatal root canal of a maxillary first molar into the maxillary sinus, Ehrich et al. (85) reported that the patient only complained of a taste of sodium hypochlorite; no pain or signs of edema or hemorrhage were noted. The sinus was irrigated via the palatal root canal with 30 mL of sterile water and the patient was prescribed antibiotics. Except for a slight soreness of the tooth, the patient reported no symptoms the following day and 4 days later he was completely asymptomatic. The root canals were obturated 4 weeks later.
- Kavanagh & Taylor (86) presented a case of inadvertent injection of sodium hypochlorite into the maxillary sinus. Following irrigation of a maxillary second right premolar with approximately 5–10 mL of sodium hypochlorite with an unknown concentration, the patient experienced acute, severe facial pain and swelling and was immediately referred to the Dental Clinics. Occipito-mental radiographs demonstrated an air fluid level in the right maxillary sinus. The patient was administered antibiotics. As drainage through the root canal could not be obtained, the antrum was drained surgically under general anesthesia. Three weeks later most of the symptoms had resolved and only the premolar presented with localized discomfort; this led to the decision to extract the tooth. Further healing was uneventful and complete.

A survey on irrigation incidents involving the maxillary sinus is presented in Table 3.

Nerve injury

Apical extrusion of root canal filling materials may result in severe damage to the mandibular nerve such as temporary or permanent anesthesia, hypesthesia, paresthesia, or in rare cases a hyperesthesia (87). The highest risk of iatrogenic nerve damage exists during endodontic treatment of second mandibular molars. In a retrospective analysis of 24 cases of overfill of obturation materials in the second premolars and second molars, paresthesia of the lip occurred more frequently than in other posterior teeth (87).

Denio et al. (88) investigated the location of the inferior alveolar nerve in 22 human cadavers. The mean distance between the mandibular nerve and the root tips was 3.7 mm for the second mandibular molar, 6.9 mm for the mesial root of the first molar, and 4.7 mm for the second premolar. Littner et al. (89) radiographically investigated the relationship of the mandibular canal to the adjacent molar root apices in 46 mandibular skulls. The distance between the inferior alveolar nerve to the root tips increased from the third molar to the first molar. The shortest distance was 3.45 mm for the distal root of the second mandibular molar; the longest distance was 5.47 mm for the mesial roots of the first molars.

Table 3. Case reports from the endodontic literature reporting involvement of the maxillary sinus

Authors	References	Year	Irrigant	Tooth	Symptoms	Treatment	Duration of symptoms	Further treatment
Becking	(99)	1991	NaOCl	27	Pain, irritation behind and below eye, swelling	Analgesics	2 weeks	Not reported
Ehrich et al.	(85)	1993	NaOCl 5.25%	16	Asymptomatic	Antibiotics	4 days	RCT
				Palatal root canal		No further treatment necessary		
Kavanagh & Taylor	(86)	1998	NaOCl	15	Pain, swelling	Surgical drain of sinus, antibiotics	>30 days	Extraction

In a retrospective evaluation of iatrogenic injuries of the trigeminal nerve, Hillerup (90) listed 10 cases (2%) that were due to endodontic treatment among 449 such incidents. In all cases, the inferior alveolar nerve was affected; no details are presented on the direct cause of the injury. Although several reports have been published on nerve damage following over-extension of obturation material, overinstrumentation, periapical inflammation, endo-perio-lesions, or temporary medication (87, 91–94), no report on mandibular nerve damage by root canal irrigants could be found for the present review. In some cases, peripheral neurological symptoms have been reported after irrigation mishaps (95–98). Rowe (91) reported on one incidence with paresthesia of the lower lip after use of a liquid filling material containing parachlorphenol, camphor, and menthol in a second left mandibular bicuspid, but could not rule out that symptoms were due to overinstrumentation.

Becking (99) described two cases with temporary anesthesia and paresthesia of the mental nerve. Additionally, formocresol, applied with a cotton pellet, has caused paresthesia of the lower lip and chin. Paresthesia of the lower lip has also been reported by Hülsmann & Hahn (96) (Fig. 2a–c).

No explanation could be found in the literature regarding the difference in frequency of neurological complications due to overfilling of solid materials and liquids as used for irrigation. Although still speculative, the major reason should be the differing hydrodynamics between solids and liquids. Irrigation pressure may be smaller than compaction pressure; a liquid may distribute – even into a lateral direction – into the small structures of cancellous bone with the pressure rapidly decreasing whereas a solid substance with larger particle size more likely will be pressed with only slowly decreasing pressure straightforward toward the mandibular nerve canal.

Fig. 2. (a) Massive swelling of the lower lip and right cheek region after injection of sodium hypochlorite and hydrogen peroxide through a perforation in a mandibular right cuspid. (b) One week after the incident, an ulcer in the lower lip developed. The patient reported paresthesia of the right lower lip. (c) Four weeks later swelling has not resolved completely. One year after the injury, the patient still complaints of a slight hypesthesia of the lower lip.

Case reports

The above-mentioned case reports include:

- Paresthesia of the right side of the lower lip for more than 1 year following extrusion of sodium hypochlorite through a perforation in a mandibular right canine (96) (Fig. 2a–c).

- Paresthesia of the upper lip, the nasal floor, and the ala of the nose for 15 months following injection of 1–2 mL of 1% sodium hypochlorite through a mid-root perforation in a maxillary central incisor in a 44-year-old male patient (95). Further treatment of the tooth was performed surgically with a retrograde amalgam filling.
- Lip paresthesia and facial weakness over 6 months after endodontic treatment of a maxillary right lateral incisor with apical periodontitis and a draining sinus tract after irrigation with sodium hypochlorite of unknown concentration (98). Following the typical symptoms of sodium hypochlorite extrusion such as pain, swelling, and ecchymosis, an altered sensation in the distribution of the right infra-orbital nerve was reported as well as weakness of the buccal branch of the facial nerve with resulting functional problems. The right corner of the patient's mouth was pulled down as the lower lip muscles were not sufficiently opposed by the upper mouth musculature.
- During endodontic treatment of the second right maxillary premolar in a 44-year-old female patient, sodium hypochlorite of unknown volume and concentration was inadvertently pressed through the apical foramen. The patient experienced the typical symptoms but additionally loss of sensation in the right infra-orbital nerve and weakness of the buccal branch of the facial nerve were noted, which resulted in a dropping of the right corner of the patient's mouth. Facial weakness and paresthesia completely resolved after 3 months. Treatment of the last two cases included intravenous application of dexamethasone (8 mg thrice a day for 2 days) and amoxicilline (1.0 g thrice a day) and an oral analgesics (diclofenac, 50 mg thrice a day for 2 days) (98).
- Becking (99) presented two cases of damage of the mental nerve following apical extrusion of NaOCl with unknown concentration through a perforation in a lower left second molar and through the apical foramen in a mandibular left second premolar. In both cases, complete healing of anesthesia and paresthesia were reported after 1–2 months.

The authors of the latter cases presume that apical periodontitis with resulting bone destruction should be considered one important factor in the genesis of the described incidents. Additionally, increased irrigation pressure cannot be ruled out as a co-factor.

Injection of sodium hypochlorite beyond the apical foramen

According to Mehdipour et al. (100), 23 cases of NaOCl incidents have been reported in the dental literature, the majority on apical over-extrusion (95–99, 101–116). A survey of some of the published cases is presented in Table 4; clinical cases are documented in Figs. 3–5.

Inadvertent injection of sodium hypochlorite beyond the apical foramen may occur in teeth with wide apical foramina or when the apical constriction has been destroyed during root canal preparation or by resorption. Additionally, extreme pressure during irrigation or binding of the irrigation needle tip in the root canal with no release for the irrigant to leave the root canal coronally may result in contact of large volumes of the irrigant with the apical tissues. If this occurs, the excellent tissue-dissolving capability of sodium hypochlorite will lead to tissue necrosis. A similar situation may occur following iatrogenic perforation of the root, and in cases of horizontal root fracture or perforating resorption (116, 117) (Table 4) (Fig. 6).

It should be noted that in a preliminary study on beagle dogs, atypical apical lesions as a short-term response to endodontic instrumentation have been described. The lesions were related to the apical foramina and characterized by total cellular destruction. Although the exact etiology of these lesions could not be definitely determined, the authors presume these lesions to be a reaction to the 2.5% sodium hypochlorite (118) that had been used.

Several case reports have described the symptomatology of sodium hypochlorite when injected into the periapical and periradicular tissues. The main symptoms and treatment considerations in cases of periapical sodium hypochlorite injection are summarized in Table 5 (96, 119, 120).

Case reports

- After wedging the irrigation needle in the root canal, 5.25% sodium hypochlorite was forced beyond the apex of a maxillary right cuspid, which led to immediate strong reactions with extreme pain (101). Within a few seconds, the patient's cheek and upper lip showed signs of hematoma and ecchymosis inferior to the right zygoma and profuse hemorrhage from the root canal. Wet

Table 4. Case reports from the endodontic literature reporting apical or lateral extrusion of sodium hypochlorite into the periradicular tissues

Authors	References	Year	Irrigant	Tooth	Symptoms	Treatment	Duration of symptoms	Further treatment
Becker et al.	(101)	1974	NaOCl 5.25%	13	Pain, edema, hematoma, ecchymosis, hemorrhage	Cold compresses, antibiotics, analgesics	4 weeks	RCT
Grob	(121)	1984	NaOCl 3%	22	Pain, swelling, abscess	Analgesics, incision	Remaining hypesthesia >4 years	Not reported
Reeh & Messer	(95)	1989	NaOCl 1%	11 perforation	Pain, swelling, erythema, anesthesia of upper lip, draining, ulceration, hemorrhage	Antibiotics, rinsing	Remaining paresthesia over 15 months	RCT, apicectomy
Sabala & Powell	(104)	1989	NaOCl 5.25%	25	Swelling, pain, ecchymosis	Apical trephination, analgesics, antibiotics	9 days	RCT, apical surgery
Neaverth & Swindle	(103)	1990	NaOCl 2.5%	12 perforation	Pain, hemorrhage, swelling, edema, eccymosis	Analgesics, antibiotics	3 weeks	Extraction
Gatot et al.	(102)	1991	NaOCl 5.25%	11	Pain, edema, hematoma, tissue necrosis, ecchymosis anesthesia	Hydrocortisone i.v., antibiotics surgical debridement	2 weeks remaining paresthesia	Not reported
Becking	(99)	1991	NaOCl	37 perforation	Pain, swelling, necrosis, anesthesia of mental nerve	i.v. antibiotics (penicillin and metronidazole)	2 months	RCT
			NaOCl	35	Pain, swelling, necrosis, anesthesia of mental nerve	Antibiotics (penicillin and metronidazole)	>1 months	Not reported
Joffe	(111)	1991	NaOCl 5.25%	23	Pain, swelling, hemorrhage, ecchymosis	Antibiotics	5 weeks	RCT
Linn and Messer	(106)	1993	NaOCl 1%	13 perforation	Pain, facial swelling, lip ulceration, paresthesia	Antibiotics	3 months	RCT, perforation repair
Cymbler & Ardakani	(112)	1994	NaOCl 2%	21	Pain, swelling, paresthesia	Antibiotics	1 week	RCT
Tosti et al.	(113)	1996	NaOCl	24	Pain, swelling, hemorrhage, ecchymosis	Prednisolone, analgesics	1 month	Not reported

Table 4. Continued

Authors	References	Year	Irrigant	Tooth	Symptoms	Treatment	Duration of symptoms	Further treatment
			NaOCl	12	Pain, edema, swelling, ecchymosis	Systemic steroids, analgesics	3 weeks	Not reported
Hülsmann & Denden	(129)	1997	NaOCl 3%+H_2O_2	23	Pain, swelling, edema, ecchymosis, hemorrhage	Analgesics	1 week	RCT
Hülsmann & Hahn	(96)	2000	NaOCl 3% and H_2O_2 5%	43 perforation	Pain, swelling, ulceration, paresthesia		2 months, paresthesia >1 year	Extraction
Mehra et al.	(105)	2000	NaOCl	63	Pain, swelling, hematoma, ecchymosis, hemorrhage	Hospitalization, i.v. antibiotics, narcotics, surgical intervention	5 weeks	Extraction
Hales et al.	(120)	2001	NaOCl 5.25%	24	Pain, hemorrhage, swelling, ecchymosis	Analgesics, antibiotics	>12 months	RCT
Balto & Al-Nazhan	(114)	2002	NaOCl 1%	11	Swelling upper lip, pain, ecchymosis, hemmorrhage	Irrigation, incision, antibiotics	4 days	RCT
Gernhardt et al.	(115)	2004	NaOCl 5.25%	34 perforation, resorption?	Pain, swelling, ulceration hematoma	Antibiotics, analgesics	2 weeks	RCT
Witton and Brennan	(97)	2005	NaOCl	12	Pain, swelling, edema, ulceration, ecchymosis, paresthesia	Antibiotics, analgesics	4 weeks	Not reported
Witton et al.	(98)	2005	NaOCl	15	Pain, swelling, ecchymosis, paresthesia	Antibiotics, analgesics, stereocorticoids	3 months	Not reported
Bowden et al.	(110)	2006	NaOCl	37	Pain, swelling, ecchymosis, airway obstruction	i.v. antibiotics, hospitalization	1 month	Not reported
						i.v. stereocorticoids, surgical decompression		Not reported
Schwerin & Gerlach	(107)	2007	NaOCl 3%+ H_2O_2	11 perforation	Pain, swelling, hematoma, edema	Antibiotics	2 weeks	RCT, apicectomy

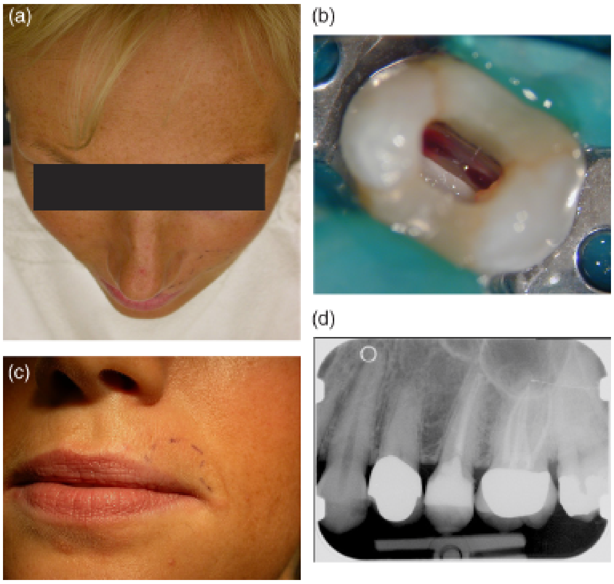

Fig. 3. (a) Apical extrusion of 5% NaOCl during irrigation of tooth 25 resulted in immediate pain and hemorrhage. Swelling of the upper lip and left cheek developed as well as paresthesia. (b) Profuse bleeding from the root canals. (c) Symptoms resolved after 4 weeks; only slight paresthesia in the dotted region remained. Root canal treatment could be completed. (d) Radiograph following obturation of tooth 25. Case courtesy of Dr. Hager.

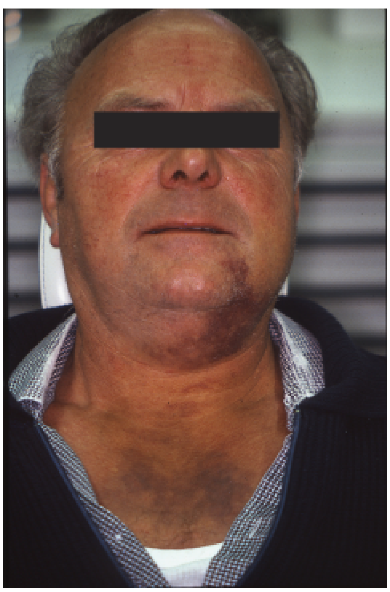

Fig. 4. Severe swelling and ecchymosis extending down to the patient's chest following apical extrusion of 5% sodium hypochlorite during root canal treatment of tooth 35. Case courtesy of Dr. Gehrig.

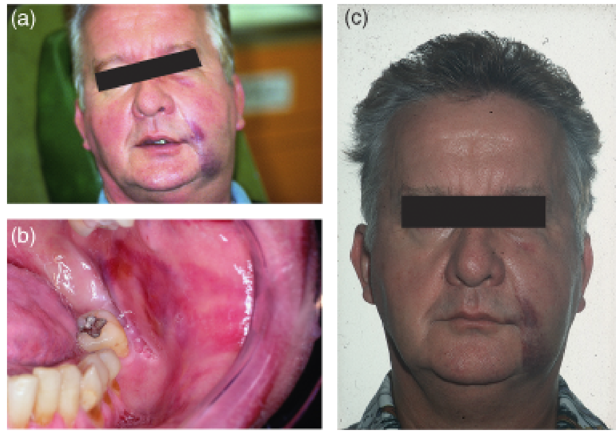

Fig. 5. (a) Swelling and extraoral ecchymosis following inadvertent extrusion of sodium hypochlorite (3%) through the apical foramen of a maxillary left cuspid. (b) Large intraoral ecchymosis extending to the left cheek. (c) Four weeks later, swelling and ecchymosis had resolved and root canal treatment could be completed.

Fig. 6. Extrusion of 2% NaOCl through a perforation in tooth 21 with resulting severe pain and edema of the upper lip. One week later swelling had resolved. Case courtesy of Dr. Versümer.

compresses continuously applied to the face relieved the pain and the burning sensation felt by the patient. The patient was prescribed antibiotics and analgesics, and the root canal was left open for drainage. Although the swelling increased during the next few hours, the pain diminished. The patient was advised to replace the cold compresses with hot compresses to stimulate local systemic circulation. One month after the incident, the

Table 5. Symptomatology and recommended therapy in cases of extrusion of NaOCl into the periradicular tissues (96,119,120)

Symptomatology
Immediate severe pain attack
Immediate edema of neighboring soft tissues
Possible extension of edema over the injured side of the face, upper lip, infra-orbital region
Profuse bleeding from the root canal
Profuse interstitial bleeding with hemorrhage of the skin and mucosa (ecchymosis)
Chlorine taste and irritation of the throat after injection into the maxillary sinus
Secondary infection possible
Reversible anesthesia or paresthesia possible
Therapy
Patient information on reason, kind, and severity of complication
Pain control: local anesthesia, analgesics
In severe cases: referral to a hospital
Extraoral cold compresses for reduction of swelling
After 1 day: warm compresses and frequent warm mouth rinses for stimulation of local systemic circulation
Daily recall for control of recovery
Antibiotics: not obligatory! Only in cases of high risk or evidence of secondary infection
Antihistamine: not obligatory!
Corticosteroids: discussed controversy
Further endodontic therapy with sterile saline or chlorhexidine as root canal irrigants in most cases possible

patient's face had returned to normal and root canal therapy could be completed.

- After iatrogenic perforation of the root canal of a lateral maxillary incisor, a 3% NaOCl solution was injected beyond the apex (121). The patient experienced 'heavy' spontaneous pain followed by a rapid swelling of the left cheek. Eight days later an abscess had developed, probably due to the spread of infected material from the root canal into the periapical tissue; this had to be treated surgically. Large amounts of pus and necrotic tissue were found. Four years later, the patient still reported hypesthesia and extreme sensitivity to cold temperatures.
- In a case presented by Neaverth & Swindle (103), extrusion of 2.5% NaOCl through a perforated maxillary incisor resulted in severe pain and swelling over the left side of the face extending from the infra-orbital rim to the upper lip.
- Reeh & Messer (95) reported on a case of injection of sodium hypochlorite (1%) through a mid-root perforation of a maxillary central incisor. The patient experienced the typical symptoms of immediate severe pain and swelling, followed by fistulation and erythema extending to the infra-orbital area. Paresthesia of the floor and ala of the patient's nose persisted for more than 15 months.
- In a case report presented by Sabala & Powell (104), 5.25% sodium hypochlorite was injected into the periapical tissues of a left maxillary second premolar. The patient experienced symptoms of sudden, severe pain and rapidly developing swelling, followed by ecchymosis of the skin. Root canal treatment was completed at the same appointment. To prevent secondary infection, antibiotics were prescribed and a surgical drainage performed. Nine days later the symptoms had resolved.
- Following injection of 5.25% NaOCl during endodontic treatment of a right maxillary central incisor, Gatot et al. (102) reported that the patient immediately experienced severe pain and marked edema developed extending from the lip to the right eye. The patient received hydrocortisone intravenously and penicillin. Thirty-six hours later there was a large ecchymosis under the right orbit and diffuse ecchymosis over the upper lip as well as epithelial necrosis. Surgical debridement with excision of a large amount of necrotic tissue had to be performed under general anesthesia. Healing took more than 2 weeks, leaving a scar on the right cheek and right infra-orbital nerve anesthesia.
- In a similar case, over-extrusion of NaOCl occurred during endodontic treatment of a primary maxillary canine in a 51-year-old woman. Following a sudden onset of severe pain, a heavy swelling of the left side of her face appeared including hematoma formation and heavy bilateral circumorbital ecchymatosis. Despite antibiotic treatment, the symptoms

increased and the patient had to be hospitalized. The hematoma was incised surgically and the necrotic tissue was removed. Five weeks later the symptoms had disappeared completely (105).

- Becking (99) presented three cases of sodium hypochlorite injection into the periapical soft tissues. In the first case, NaOCl of unknown concentration was extruded through the apical foramen of a mandibular left second molar with a perforation at the cemento-enamel junction, resulting in a progressive swelling of the left side of the mandible extending to the patient's neck. After 1 day, necrosis of the mucosa and anesthesia of the mental nerve was apparent. Under antibiotic and analgesic therapy, pain and swelling diminished after 5 days, paresthesia of the nerve resolved after 10 days, and healing of the mucosa took 2 months. In the second case, NaOCl of unknown concentration was injected into the periapical tissues of a left maxillary second molar causing irritation behind and below the patient's left eye and severe pain in the left cheek, eye, and temporal region. Additionally, the patient reported a chlorine taste and irritation of the throat. It was presumed that the irrigant had been pressed into the maxillary sinus. In this case, no antibiotics were given, only analgesics; the symptoms resolved completely within 2 weeks. In the third case, apical over-extrusion of NaOCl occurred during root canal preparation of a mandibular left second premolar, resulting in severe pain, swelling, and anesthesia of the mental nerve. Again, no antibiotics were initially prescribed. Four days later, necrosis and infection became evident and antibiotic therapy was initiated. Resolution of pain and swelling took 1 month; anesthesia turned into hyperesthesia, which slowly resolved.
- Linn & Messer (106) reported a case of injection of 1% NaOCl through a mid-root perforation of a maxillary canine. Severe pain and facial swelling involving lip and eyelid occurred as well as an increasing ulceration (diameter 12 mm) of the oral aspect of the lip.
- Schwerin & Gerlach (107) described a case of sodium hypochlorite extrusion through a perforation in a maxillary central incisor. Following initial severe pain, an immediate swelling of the patient's upper lip and cheeks accompanied by severe ecchymosis of the complete upper lip region appeared. The patient was prescribed antibiotics and advised to cool the swelling. Two weeks later, the swelling had completely resolved and the tooth was treated by apicectomy and surgical closure of the perforation.
- Sennhenn-Kirchner & Hülsmann (116) presented a case of extrusion of sodium hypochlorite through a buccal perforation in a maxillary incisor. As the patient had an anamnesis of several allergies, she was first referred to a physician, followed by hospitalization in a surgical hospital as an anaphylactic reaction to the local anesthetics or the irrigant were supposed. Following consultation of a neurologist and a dermatologist, finally a dentist and an oral surgeon were contacted. Six weeks after the incident, the patient still complained of slight ecchymosis and hypesthesia as well as an ulcer of the upper lip (Fig. 7a–d).

It should be noted that in the majority of published cases, root canal treatment could be completed without the need for surgical intervention such as apicectomy or extraction.

Injection of hydrogen peroxide beyond the apex

Incidents due to apical or lateral extrusion of hydrogen peroxide seem to appear less frequently as in the past due to the decreasing popularity of that solution for irrigation purposes. Nevertheless, a number of case reports can be found in the literature (Table 6). The symptomatology of such type of incident seems to be similar in most cases: sudden and severe pain, swelling and emphysema, and crepitus. It is recommended that analgesics and antibiotics be prescribed. In most cases, further intervention seems unnecessary and swelling will subside in a few days (Figs. 8 and 9). In severe cases hospitalization is necessary.

Case reports

- As a result of insufficient access and a lateral root perforation of a right maxillary central incisor, Bhat (108) reported that hydrogen peroxide of unknown concentration was injected into the soft tissues. As treatment was performed under local anesthesia, the patient experienced no pain but complained of the rapid development of upper lip swelling and some difficulty in breathing. The root canal was left open and the patient was prescribed

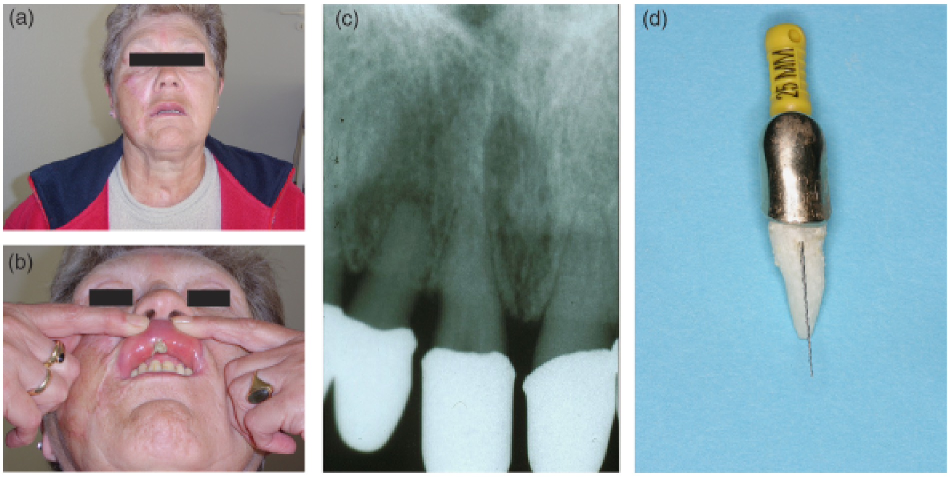

Fig. 7. (a) Swelling of the patient's lip following extrusion of sodium hypochlorite through a perforation of the root of the first right maxillary incisor. (b) Ulcer at the inner side of the upper lip 6 weeks after the incident. (c) Radiograph of the maxillary right first incisor. (d) The instrument extends through the buccal perforation of the root. Case courtesy of Dr. Sennhenn-Kirchner.

antibiotics and instructed to apply cold packs. The emphysema, caused by oxygen liberated from the hydrogen peroxide, subsided in 1 week and root canal treatment was completed.

- Walker (122) presented a case of inadvertent extrusion of 40% hydrogen peroxide through the root canal of a maxillary first molar. A sudden swelling appeared accompanied by mild pain. Examination of the swelling revealed a mildly tender swelling with crepitus. It is probable that a previous infection of the periapical area had provided a pathway for the hydrogen peroxide through the buccal bone to the buccal and facial soft tissues. Under antibiotic therapy, the symptoms resolved completely after a few days.
- After extrusion of hydrogen peroxide (10%) beyond the apical foramen of a right first maxillary premolar, Patterson & McLundie (123) reported the typical symptoms of sudden, severe pain accompanied by a rapid swelling and erythema in the region of the treated tooth. The tooth was immediately extracted by the general dental practitioner and the patient was prescribed antibiotics. Two days later the pain had resolved almost completely, but edema and erythema were still present. The patient was instructed to use warm mouthrinses for symptomatic relief and take further antibiotics. After 2 weeks, the patient had returned to normal.
- Essig et al. (124) described an injection of hydrogen peroxide through an iatrogenic root perforation in a right maxillary canine. The patient developed immediate swelling and increasing airway obstruction. A diagnosis was made by the dentist of an anaphylactic shock and corticosteroids and antihistaminica were administered. As no relief of symptoms appeared, the patient was referred to the surgical department of the dental clinic. The swelling resolved after 3 days and the root was apiceted.

Seidner (125), Pöllmann (126), Kaufman et al. (127), Kaufman (128), Hülsmann & Denden (129) (see Fig. 5) and Nahieli & Neder (130) presented similar cases of hydrogen peroxide injections into the periapical tissues with identical symptoms (Table 6).

Apical extrusion of EDTA

There is much discussion as to whether and to what degree inflammatory tissue reaction can be caused by chelating agents passing through the apical foramen. Nygaard-Østby (109) investigated the effect of a 15% EDTA solution (pH 7.3) on human periapical tissue as well as on pulpal tissue under clinical conditions in cases with vital and necrotic pulps. No periapical tissue damage could be detected after a period of action of up to 14 months even though EDTA was intentionally forced through the apical constriction using a file. The histological examination revealed normally regenerated alveolar bone and new functional PDL fibers. In addition, clinical studies showed that placement of EDTA for up to 28 days after pulpotomy fails to produce any pulpal tissue necrosis. In an investigation

Table 6. Case reports from the endodontic literature reporting extrusion of hydrogen peroxide into the periradicular tissues

Authors	References	Year	Irrigant	Tooth	Symptoms	Treatment	Duration of symptoms	Further treatment
Seidner	(125)	1938	H_2O_2	Maxillary molar with fistula	Swelling		2 days	Not reported
			H_2O_2	Mandibular molar with fistula	Swelling		Some days	Not reported
			H_2O_2	Maxillary canine with fistula	Swelling		> 4 days	Not reported
			(Note: these cases were treated by intentional irrigation of the, fistula)					
Bhat	(108)	1974	H_2O_2	11 perforation	Pain, swelling, difficulty in breathing	Antibiotics	1 week	Not reported
Walker	(122)	1975	H_2O_2 40%	16	Pain, swelling, crepitus, emphysema	Antibiotics	Some days	Not reported
Pöllmann	(126)	1980	H_2O_2 10%	46	Swelling	Hospitalization, antibiotics	4 days	RCT
Kaufmann	(128)	1981	H_2O_2	24	Pain, swelling, crepitus, hemorrhage	Incision		Not reported
Hirschmann & Walker	(188)	1983	H_2O_2	25	Tissue emphysema	Antibiotics	5 days	Extraction
Kaufman et al.	(127)	1984	H_2O_2 2%	35 or 45	Pain, swelling, crepitus	Incision	Immediate pain relief	Not reported
Patterson & McLundie	(123)	1989	H_2O_2 10% mixed with Milton solution	14	Pain, swelling, erythema	Antibiotics	2 weeks	Extraction
Nahlieli & Neder	(130)	1991	H_2O_2	48	Swelling, difficulties in breathing	Hospitalization, antibiotics	2 weeks	Extraction
Essig et al.	(124)	2007	H_2O_2	13 perforation	Swelling, difficulties in breathing, emphysema	Supervision	3 days	Apicectomy

Fig. 8. Swelling of the right cheek up to the infra-orbital region after inadvertent injection of hydrogen peroxide through the apical foramen of a right maxillary first premolar. On careful palpation, the swelling exhibited a crepitus, which is a typical symptom after air emphysema or soft tissue injection with hydrogen peroxide. Case courtesy of Dr. Schönbach.

Fig. 9. Severe swelling of the right side of the face following over-extrusion of hydrogen peroxide through a maxillary right canine. Case courtesy of Dr. Essig.

of the tissue reaction in rats after intramuscular implantation and injection of EDTA and EDTAC (15%), the latter caused much greater tissue irritation after implantation and after injection than 10% EDTA (131). No periapical tissue irritation or damage of any kind occurred in 200 clinical cases where EDTA was used as an irrigant. Acute exacerbation did not seem to occur more frequently than with other irrigants.

Extrusion of even a low concentration of EDTA solution through the apical constriction results not only in an irreversible decalcification of periapical bone but can also have consequences for neuroimmunological regulatory mechanisms (132). Segura et al. investigated the effect of EDTA and EGTA on the binding of vasoactive intestinal peptides (VIPs) to macrophages. VIPs act not only as vasoactive substances but also play an important role as neuropeptides in the communication between nerves and immune cells in the pulp and periapical tissue by modifying the macrophage function. EDTA inhibits VIP binding to macrophages even in lower concentrations than those used in endodontics (10%). EDTA can prevent the adhesion of macrophages to substrate; this is time and concentration dependent (133). EDTA concentrations measurable in the periapical tissues are capable of reducing binding by 50%. The degree to which VIP and substrate control of macrophage function affects the healing process is not clear. However, changes in macrophage activity can cause the inflammatory reaction to be more easily initiated, but reduced capacity of phagocytosis can result. In addition, it has been discovered that EDTA improves plasma extravasation and mediator action (133). In an investigation of the effects of dental etchants and chelators on nerve compound action potentials (134), RC-Prep and File-EZE were shown to reduce the compound action potentials after an application time of 160 min by 61.8% and 62.4%, respectively.

Apical extrusion of sulfuric acid

There is one single case report on the apical extrusion of a 20% solution of sulfuric acid used alternately with a solution of baking soda known as the Johnston–Callahan technique of root canal disinfection (135). Apical extrusion during endodontic treatment of a maxillary left central incisor resulted in pain, swelling, erythema, and facial discoloration, followed by development of a draining sinus tract and tissue and skin necrosis of the left ala of the patient's nose, which had to be removed surgically. The nose had to be reconstructed using plastic surgery.

Allergic reactions

- *Sodium hypochlorite:* Although few reports on allergy-like reactions to sodium hypochlorite have been published (136–139) (Table 7), real allergies to sodium hypochlorite are unlikely to occur as both sodium and chlorine are essential elements in

Table 7. Case reports from the endodontic literature reporting allergies or allergy-like reactions to NaOCl

Authors	References	Year	Irrigant	Tooth	Symptoms	Treatment	Further treatment
Kaufmann & Keila	(148)	1989	NaOCl		Pre-operative diagnosis	Solvidont for irrigation	RCT
Caliskan et al.	(149)	1994	NaOCl 1%		Pain, burning, swelling, eccymosis, hemorrhage, breathing problems	Emergency unit: systemic corticosteroids and antihistaminica, antibiotics, further irrigation with H_2O_2 and saline	RCT
Hülsmann & Denden	(129)	1997	NaOCl 3% +H_2O_2	23	Pain, swelling, edema, ecchymosis, hemorrhage	Analgesics	RCT
Dandakis et al.	(152)	2000	NaOCl		Pre-operative diagnosis	Isotonic saline, EDTA, calcium hydroxide	RCT
Al-Amri & Kreusch	(137)	2005	NaOCl	31 perforation	Pain, swelling, erythema, ecchymosis, emphysema, necrosis, allergic exanthema	Antibiotics, antihistaminica	Extraction
Crincoli et al.	(153)	2008	NaOCl	13	Pain, profuse bleeding, swelling, ecchymosis	Analgesics, antibiotics, antihistaminica, further irrigation with H_2O_2	RCT

the physiology of the human body. Nevertheless, hypersensitivity and contact dermatitis may occur in rare cases (136, 138, 139). In cases of hypersensitivity against sodium hypochlorite, CHX should not be used either due to the chlorine content and the use of an alternative irrigant with high antimicrobial efficacy such as iodine-potassium-iodide should be considered. Before use, an allergy against iodine must be ruled out. Further irrigants such as alcohol or tap water are less effective against microorganisms and do not dissolve vital or necrotic tissue. Calcium hydroxide should be used as a temporary medicament as it dissolves both vital and necrotic tissue (140, 141).

- *CHX*, although reported to be a relatively safe solution, may induce allergic reactions. The sensitization rate has been reported in several studies to be approximately 2% (142). One case of an anaphylactic shock after application of 0.6% CHX to intact skin, only showing signs of a rash following a minor accident, has been presented in the dermatological literature (143). Further allergic reactions such as anaphylaxis, contact dermatitis, and urticaria have been reported following direct contact to mucosal tissue or open wounds (142–147). No publication reporting on allergic reactions following root canal irrigation with CHX could be found.
- *Iodine-potassium-iodide:* Disinfectants containing iodine in concentrations up to 10% are frequently used for disinfection of wounds or operating fields due to its fast and good antibacterial effect. Although the allergenic and irritating potential of solutions containing iodine is well known (148, 149), there are no studies or case reports on allergenic reactions to iodine-potassium-iodide; nevertheless, the irrigant should not be used in patients with known or suspected allergies to iodine preparations, struma, or hyperthyreosis.

Case reports

- Kaufman & Keila (150) reported a case of hypersensitivity to sodium hypochlorite. As this reaction was detected before initiation of endodontic therapy, the patient was referred to an allergist. Following a skin patch test, the allergist diagnosed a hypersensitivity to household materials containing NaOCl and recommended not to use NaOCl during root canal treatment. Thus, the root canals were irrigated with Solvidont (DeTrey/ Dentsply, Konstanz, Germany) and the procedure was uneventful. In a second case (151), sodium hypochlorite (1%) was used for irrigation of a maxillary central incisor with a mid-root horizontal fracture. The patient immediately reported severe pain and a burning sensation; within a few seconds, the upper lip and cheek up to the infra-orbital area became swollen, accompanied by ecchymosis and profuse hemorrhage from the root canal. Pain diminished after a few minutes but the patient complained about problems in breathing and was referred to an emergency care unit. Systemic corticosteroid and antihistamine were administered intravenously and antibiotics were prescribed. Swelling dissolved after 3 days but a paresthesia on the left side of the face remained for 10 days. Further endodontic therapy was performed with hydrogen peroxide and sterile saline and was uneventful. A skin scratch test was performed some days after the incident and gave a very rapid positive allergic reaction including erythema and edema.

- Dandakis et al. (152) presented a case of a 12-year-old girl with a history of contact dermatitis and bronchial reactions to sodium hypochlorite (household bleach and indoor swimming pools). Pre-endodontic immunologic evaluation showed no serious symptoms and no immunological dysregulation. The authors described the patient's condition as 'non-allergic hypersensitivity.' Instead of sodium hypochlorite, isotonic saline was used as an irrigant and RC-prep as a chelator; calcium hydroxide was placed as an interappointment dressing and the root canal treatment was completed without further problems.
- Recently, Crincoli et al. (153) presented a case of adverse reactions following irrigation with sodium hypochlorite during endodontic treatment of a maxillary right canine in a female patient with a known history of adverse reactions to some household cleaners containing sodium hypochlorite. The symptoms included severe pain for 1 day, profuse bleeding, ecchymosis of the cheek and upper lip, and increasing swelling over 2 days. A skin patch test did not reveal the presence of a direct allergy to sodium hypochlorite. Following treatment with analgesics, antibiotics, and antihistaminica, the symptoms resolved within 2 weeks and root canal treatment could be continued without further problems. Hydrogen peroxide was used as the root canal irrigant.

Genetic damage

In a comprehensive review on possible induction of genetic damage by endodontic compounds, Ribeiro (154) reports two studies using Syrian hamster embryo in which EDTA, hydrogen peroxide, and sodium hypochlorite showed a positive genotoxicity *in vitro*. Summarizing several studies on DNA changes induced by CHX, contradictory results were found.

Inadvertent dental anesthesia with sodium hypochlorite

Four case reports have been presented in which the irrigation carpule containing sodium hypochlorite inadvertently was used for anesthesia (155–158) (Table 8). Owing to the excellent tissue-dissolving ability of sodium hypochlorite, severe tissue and bone necrosis may occur. Correct labelling of the carpules or the use of differently sized and colored tips are safe and easy techniques to prevent such incidents. As well, in the case of irrigation, rubber stops or similar markings for control of depth of introduction into the root canal should be placed, clearly distinguishing the carpule from an anesthetic one. The use of 5 mL carpules for irrigation and 2 mL carpules for anesthesia can be recommended.

Case reports

- An injection of 1.8 mL of 5.25% sodium hypochlorite for an inferior alveolar nerve block resulted in severe pain, immediate swelling, and trismus. The edema extended to the peritonsillar and pharyngeal area and led to difficulties in swallowing. The patient was administered fentanyl intravenously and was prescribed antibiotics and admitted to an intensive care unit. After 4 days, she was discharged from the hospital, but it took 2 weeks for the symptoms to resolve (155).
- In a 35-year-old woman, an unknown volume of 1% sodium hypochlorite inadvertently was injected into the lingual region of teeth 35–37 before application of the rubber dam. The patient

Table 8. Case reports on inadvertent anesthesia with NaOCl

Authors	References	Year	Irrigant	Tooth	Symptoms	Treatment	Duration of symptoms	Further treatment
Herrmann & Heicht	(155)	1979	NaOCl 5.25%	Mandibular molar	Severe pain, edema, trismus	i.v. analgesics, antibiotics	2 weeks	
			Mandibular block		Difficulty in swallowing	Hospitalization		
Gursoy et al.	(157)	2006	NaOCl 2.5%	Infiltration maxillary palatal mucosa	Pain, soft tissue and bone necrosis		2 weeks	
Hülsmann & Schäfer	(158)	2007	NaOCl 3%	Infiltration N. mentalis	Pain, swelling, hypesthesia, ecchymosis	Incision, antibiotics	2 months	
Pontes et al.	(156)	2008	NaOCl 1%	Lingual infiltration	Pain, soft tissue, and bone necrosis	Corticosteroids, antibiotics	2 months	RCT

reported immediate severe pain and the injection was stopped. Despite prescription of anti-inflammatory drugs and antibiotics, pain relief could not be achieved until 3 days later. Approximately 2 months later, the lingual mucosa of the affected teeth showed marked necrosis and bone sequestration, which had to be treated surgically. Endodontic treatment could then be completed without additional problems (156).

- For the treatment of two maxillary premolar teeth, a palatal injection of 2.5% NaOCl was inadvertently given. The patient reported immediate pain and swelling. Pain subsided after 2 h but in the following 2 weeks, necrosis of the palatal bone and soft tissues developed. The lesion could be treated conservatively and healed within 2 weeks (157).
- Hülsmann & Schäfer (158) presented a case in which anesthesia of the Nervus mentalis was administered with 3% sodium hypochlorite (Fig. 10). Besides pain and immediate swelling, a hypesthesia developed and the patient had to be referred to an oral surgeon. An incision was made and antibiotics and analgesics were prescribed. During the following hours, an intraoral ecchymosis appeared and extraoral swelling increased, both extending into the middle of the patient's chest. Symptoms decreased slowly during the following days but it took 4 weeks for swelling and hypesthesia to resolve completely.

Fig. 10. (a) Following inadvertent injection with sodium hypochlorite instead of an anesthetic solution into the mucosa of tooth 45, swelling, ecchymosis, and an intraoral hematoma and hypesthesia developed. (b) Intraoral view showing massive hematoma. (c) Ecchymosis is still present 2 weeks after the incident; pain and hypesthesia resolved 2 months later. The dotted region still painful to palpation. Case courtesy of Prof. E. Schäfer.

Damage to eyes and skin

Damage to the patient's eyes may occur when needle and syringe are not connected tightly and thus separate during irrigation. This may be facilitated by inadequate irrigation pressure. When using irrigation needles with a small diameter, it must be kept in mind that much more pressure is necessary to apply the same amount of the solution in the same time compared with tips with larger diameters. When using such small needles, blockage of the tips may occur by deposition of sodium chlorite crystals.

- *Sodium hypochlorite* in a 4% solution did not provoke severe alterations of the cornea after a short contact time (159). Pashley et al. (5) reported hyperemia and edema of the conjunctival tissue. A 0.25% solution provoked severe skin reactions (148).
  Contact with the patient's or operator's eyes has given rise to reports of immediate pain, profuse watering, intense burning, and erythema (160). Loss of epithelial cells in the outer layer of the cornea may occur. Immediate ocular irrigation with large amounts of tap water or sterile saline should be performed by the dentist and the patient referred to an ophthalmologist for further examination and treatment (161).
- *CHX* is used as a disinfectant for contact lenses and in concentrations of 0.1%, 1.0%, and 2.0% it has been shown to induce no alterations or abnormalities in rabbit eyes (162). Concentrations up to 2% do not cause visible or light-microscopical changes of the cornea (163). Only larger volumes of CHX may provoke corneal swelling (164), but even a 4% concentration was shown to be significantly less irritating to skin than 0.25% NaOCl (148).
- No reports on sequelae of eye contact of hydrogen peroxide, citric acid, or EDTA were found.

Skin injuries may occur following inadequate isolation, leakage of the rubber dam, or splashing of the irrigant. In order to prevent such mishaps, the patients' eyes may be protected with glasses; additionally, patients should be asked to close their eyes during irrigation. Luer lock syringes should preferably be used to avoid separation from the irrigation needles.

Treatment

The treatment of incidents of contact of the irrigant with the eye should be immediate irrigation of the eye with saline or tap water and referral to an ophthalmologist (119).

Case reports

- During root canal treatment of a 15-year-old patient, the irrigation needle was wedged in the root canal. The syringe, containing a 5.25% NaOCl solution, was not securely attached to the needle, separated and the irrigant was splashed into the patient's right eye. The patient immediately experienced sudden and severe pain, an intense burning sensation, profuse tearing, and erythematous swelling. Pain resolved slightly after 10 min of intense irrigation with tap water. Ophthalmological investigation revealed edema of the conjunctiva and superficial punctuate keratopathy. The patient was prescribed a combination of an antibiotic and steroidal ophthalmic solution and an α-receptor stimulant (sympathicomimetic) and H1-receptor antagonist (antihistamine) combination. Two days later the patient was asymptomatic.
- During root canal treatment of a maxillary left second premolar, a patient's complaints of burning sensations around the rubber dam following irrigation with 2.5% sodium hypochlorite were ignored. Exposure to the irrigant for approximately 2 h resulted in a massive skin rash and a chemical burn on her facial skin with scab formation. After 3 months, the symptoms had disappeared (165).

Ingestion of irrigants and airway obstruction

Although root canal treatment needs to be performed using a rubber dam, irrigant inadvertently may come into contact with the airway or be ingested. For sodium hypochlorite in high concentrations (5.25%), only minor adverse effects such as mucosal irritation are reported as a consequence of ingestion (166). It can cause major esophageal problems such as burns or edema only in cases of ingestion of larger amounts ($>10\,cm^3$ over a 5-min period); for a 2-min contact, a volume of $30\,cm^3$ was required (167). Liquid chlorine bleach in cat esophagus resulted in severe injury to the stomach and esophagus after 3 min (168).

Severe complications of sodium hypochlorite may occur when swelling of tissues results in obstruction of the airways. One case with such life-threatening obstruction has been reported recently (110).

To our knowledge, there have been no reports on the negative consequences of ingestion of CHX (169).

Exposure of airways to citric acid may provoke bronchoconstriction (170).

Case report

- During endodontic treatment of a mandibular second molar, extrusion of sodium hypochlorite resulted in immediate severe pain and swelling which progressively worsened. Eight hours later the swelling had already extended to the submandibular, submental, and sublingual areas and also provoked a marked elevation of the patient's tongue. Ecchymosis was present at the floor of the mouth, the soft palate, and the tongue. The patient, who was also showing trismus and paresthesia of the lingual and inferior dental nerves, was referred to an emergency unit. Despite intravenous antibiosis and intravenous administration of corticosteroids, his condition deteriorated to life-threatening status and surgical decompression was performed as well as awake naso-tracheal intubation. Three days later his situation had significantly improved and complete healing was reported 1 month later. The tooth was extracted (110).

Damage to clothing

Probably the most common incidents during root canal irrigation concern damage of the patient's clothing. As sodium hypochlorite is a common household bleaching agent, even small amounts may cause severe damage. When using an ultrasonic device for root canal irrigation, the aerosol may also cause damage. These mishaps should be prevented by proper protection of the patient's clothing. When using hand irrigation, one should ensure that the irrigation needle and syringe are securely attached and will not separate during transfer or irrigation in order to prevent leakage on clothing.

Air emphysema

Air emphysema is defined as the abnormal presence of air under pressure along or between facial plates (171). Many cases reports are available from the 1920s when drying of cavities with hand-held devices was replaced by drying with compressed air from the dental unit (129). The use of a high-speed handpiece in restorative dentistry or the use of compressed air during surgery have been reported as causes of subcutaneous emphysema as well (171). Battrum & Gutmann (171), in their exhaustive review of emphysema of endodontic origin, report 30 cases in the dental literature due to endodontic treatment; Shovelton (172) presented 11 cases. Heyman & Babayof (173) analyzed 75 case reports of emphysema during dental treatment published during the years 1960–1993; nine of those occurred during endodontic therapy and five were caused by hydrogen peroxide irrigation. More than 30% ($n = 36$) of 129 dental emphysema cases were identified as related to root canal treatment (174). Some of the reported cases are summarized in Table 9.

When low-pressure air (5 psi, 260 mmHg) was injected into a root canal with a Stropko air syringe, higher apical pressure was recorded when the needle was wedged into the root canal and when the apex was enlarged to size 30 or more (175). In a laboratory study, Eleazer & Eleazer (176) could measure significant pressures up to 26 mmHg using a low-pressure Stropko air syringe and up to 240 mmHg for a standard three-way syringe beyond the apex when root canals were dried with these devices. Periapical pressure increased with larger diameters (size 20–25) of the apical foramen.

During endodontic therapy, such incidents may occur when drying root canals with compressed air (Figs. 11 and 12) or when large amounts of hydrogen peroxide are injected beyond the apical foramen, releasing oxygen inside tissue compartments and causing edema by gas dissection. The spread of air is rapid and extensive, resulting in immediate edema that may cross the facial midline. A few cases of delayed-onset swelling have been reported (174). Swelling frequently is accompanied by a typical crepitus. Intensity of pain varies but in most cases seems to last for only a short duration. The majority of emphysema caused by endodontic therapy does not require any special treatment and mostly resolve in approximately 1 week due to resorption of the entrapped air (172). A review of the literature shows that the majority of cases have been treated with antibiotics and analgesics were also sometimes prescribed. Surgical intervention has been necessary in only a few cases with subsequent infection or obstruction of airways. In some cases, severe sequelae have been described such as respiratory problems, which may require hospitalization and surgical intervention. Reports on air emphysema during endodontic treatment have been published by Nehlsen (177), Berg (178), Müller-Stade (179), Salvas (180), Seidner (125), Langegger (181), Glahn (182), Magnin (183), Lloyd (184),

Table 9. Case reports from the endodontic literature reporting facial emphysema following drying the root canal using compressed air

Authors	References	Year	Irrigant	Tooth	Symptoms	Treatment	Duration of symptoms	Further treatment
Nehlsen	(177)	1927	Compressed air	22 perforation	Swelling, crepitus		2 weeks	Apicectomy, extraction
Berg	(178)	1928	Compressed air	13 and 14	Swelling		6 days	Apicectomy 13 and 14
			Compressed air	13	Swelling		2 days	Not reported
Müller-Stade	(179)	1931	Compressed air	12	Swelling, pain, crepitus, difficulties in swallowing	Analgesics	6 days	Not reported
Langegger	(181)	1950	Compressed air	13	Swelling extending to chest		5 days	RCT
Magnin	(183)	1958	Compressed air	21	Swelling extending to left eye, edema		Few days	RCT
Sikora	(191)	1966	Compressed air	12 perforation	Swelling	Decompression	1 week	Not reported
				11	Swelling	Observation	4 days	Apicectomy
Lloyd	(184)	1975	Compressed air	33	Swelling of neck and face, difficulties in swallowing, pneumomediastinum	Antibiotics, observation	5 days	Not reported
Arnold	(187)	1979	Compressed air	25	Crepitus, swelling down to the chest		10 days	RCT
Hirschmann & Walker	(188)	1983	Compressed air	23	Swelling	Antibiotics	3 days	Not reported
Kaufman et al.	(127)	1984	Compressed air	23 perforation	Swelling, crepitus	Antibiotics	5 days	Not reported
Falomo	(189)	1984	Compressed air	11	Swelling	Antibiotics	6 days	RCT
Wright et al.	(190)	1991	Compressed air	Primary incisor	Swelling of the lip, abscess	Antibiotics, surgical intervention, hospitalization	>4 weeks	Extraction
Pynn et al.	(117)	1992	NaOCl 5% (?) and compressed air	22 perforation	Swelling, crepitus	Antibiotics	6 weeks	Not reported

Fig. 11. Following drying of the root canal of tooth 15 with compressed air, the patient experienced severe pain and immediate swelling of the right side of his face. One day later the swelling is still present but the pain has resolved. A typical crepitus is present upon palpation. Swelling resolved within 1 week; paresthesia persisted some days longer. Root canal therapy could be completed without further problems. Case courtesy of Dr. Wettlin.

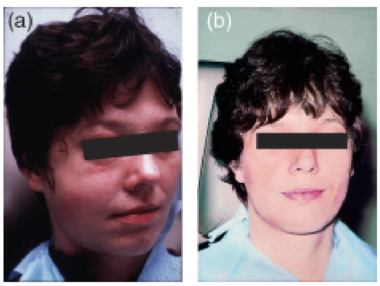

Fig. 12. (a) Massive swelling of the right side of the face after air emphysema during root canal treatment of a right maxillary first molar. (b) Patient's view after resolution of the symptoms 1 month later. Case courtesy of Prof. C. Löst.

Walker (122), Harnisch (185), Spaulding (186), Arnold (187), Hirschman & Walker (188), Hülsmann & Denden (129), Kaufman et al. (127), Falomo (189), Wright et al. (190), Sikora (191), and others.

In an animal study by Rickles & Joshi (192), the possibility that air emphysema during root canal therapy was the reason for the death of four out of seven dogs could not be completely excluded. One case has been described in which drying of the root canal might have been causative for lethal air emboly (130).

Prevention

The use of compressed air for drying the root canal should be avoided. If it is necessary to use air inside the root canal, the tip of the application device must not be wedged into the root canal.

There is no indication today for the use of hydrogen peroxide as an endodontic irrigant as more effective and safer irrigants are available.

Treatment

Emphysema is self-limiting in most cases and does not require any special therapy. Pain usually subsides in a rather short time. Swelling resolves in a few days and only in rare cases is accompanied by persistent pain. The prophylactic administration of a broad-spectrum antibiotic is recommended in all cases (174).

Case report

The case reports mostly present typical symptoms: immediate swelling ('ballooning') of tissues, lips or cheeks accompanied by a typical crepitus. Swelling may extend over the complete face, neck, and chest.

- During endodontic treatment of a right maxillary first bicuspid, hydrogen peroxide (3%) was inadvertently extruded beyond the apex. The patient felt a sudden sharp pain and immediate swelling of the right side of the face occurred. Profuse watering of the right eye and pressure in the right side of the cheek were also reported by the patient. The pain diminished after a few minutes and only a mild pressure in the cheek region was felt by the patient over the next 5 days. Palpation of the right cheek during this period produced the sign of crepitus. Healing occurred without any further medication and was uneventful (129).

Post-operative and inter-appointment pain

Post-operative pain may occur due to several reasons, one of these being apical extrusion of the irrigant. It cannot be clearly distinguished clinically whether post-operative discomfort is due to overinstrumentation, extrusion of infected debris, extrusion of the irrigant, or a combination of these factors, and nearly no valid and reliable data on this problem are available.

Harrison et al. (193) studied the incidence and degree of post-operative pain following different irrigation regimes: irrigation with 2.5% NaOCl, 5.25% NaOCl combined with 3% H_2O_2, or saline did not result in significant differences with respect to inter-appointment pain. In a second study, the same group evaluated incidence and severity of inter-appointment pain following two different irrigation and medication regimes (194). Irrigation was performed alternately with H_2O_2 (3%) and NaOCl (5.25%) and the teeth medicated with one of the following three solutions: camphorated parachlorophenol, formocresol, or sterile water. There was no difference in the frequency and degree of inter-appointment pain; 17.6% experienced slight pain and 5.7% needed some palliative treatment or analgesics.

In a randomized clinical trial involving 73 patients with different periradicular diagnoses, irrigation with 1.3% NaOCl followed by smear layer removal with a 5-min application of MTAD did not result in significantly different degrees of post-operative discomfort than an irrigation sequence of 5.25% NaOCl followed by 17% EDTA and a final rinse of 5 mL NaOCl (5.25%) (195). None of the patients experienced swelling, severe pain as assessed by means of a visual analogue scale or other post-operative sequelae necessitating removal from the study. Pain in both groups slightly increased during the 6 h post-operatively and significantly decreased during the succeeding time intervals.

Staining/discoloration

Clinical use of low concentrations of CHX may cause intraoral discoloration, mainly of soft tissues such as tongue and gingival, but staining of filling materials (silicate) and of dental hard tissues has also been reported (196). To our knowledge, discoloration of dentine and enamel following irrigation with 2% CHX has not been reported thus far.

The subsequent use of CHX and sodium hypochlorite as proposed for final irrigation of the root canal system has been demonstrated to result in discoloration of dentine (1, 197). This brownish flocculate will occur with different concentrations (NaOCl: 0.5–5%, CHX: 0.2–2%) and the combinations of the two solutions. The lowest concentration of NaOCl to induce such discoloration has been shown to be 0.19% (198). A spectrometric analysis revealed the presence of Ca, Fe, and Mg in the flocculate (196). Using X-ray photon spectroscopy and secondary ion mass spectrometry, Basrani et al. (198) identified the brownish precipitate to be para-chloroaniline (PCA, C_6H_4Cl). The authors recommend not using these irrigants in direct sequence as PCA has been reported to be both cytotoxic by formation of methemoglobin and carcinogenic in animal studies. PCA may compromise the final seal of the obturated root canal (197). Remaining NaOCl should be washed out with alcohol or EDTA before rinsing with CHX (198). When used in combination or separately, the interaction of CHX and calcium hydroxide is potentially genotoxic and tissue damage to the periapical tissues should be considered when used in higher concentrations and extruded through the apical foramen as generation of reactive oxygen species has been shown under laboratory conditions (199).

The sequential use of 1.3% NaOCl and MTAD (BioPure MTAD, Dentsply, Tulsa, OK, USA) as recommended by Torabinejad et al. (41) has been reported to result in a red-purple discoloration of the root and crown dentine. This phenomenon is related to a red-ox reaction similar to that being reported for photo-oxidation and red-purple staining of tetracycline, which is part of the MTAD solution. The process includes chelation of Ca ions (201). This reaction takes place only under light exposure and may be prevented by the use of ascorbic acid (201).

Iodine-potassium-iodide has also been reported to stain dentine (26).

Other side-effects of irrigants

Further sequelae and problems of irrigation procedures have also been reported. Corrosion of rubber dam clamps and endodontic instruments may occur as a result of long-time contact with sodium hypochlorite.

Mercury release from amalgam fillings: Rotstein et al. (202) investigated the release of mercury from amalgam fillings after 20-, 40-, or 60-min contact with several endodontic irrigants: 1% and 3% NaOCl, 10% EDTA in 1% or 3% NaOCl, EDTA distilled water, and phosphate buffer. Mercury release increased with increasing concentration of NaOCl; the addition of EDTA slightly reduced mercury release. The effect was time dependent with an onset after 10 min; after 40 min the release clearly decreased.

Air contamination: Lambrianidis (160) suggested paying attention to increased concentrations of chlorine in the environment of the dental office. A fine mist of chlorine may affect skin, eyes, and airways of the office personnel and the patient, especially when used with an ultrasonic unit.

Ultrasonic irrigation

Martin & Cunningham (62) and Fairbourn et al. (60) investigated the amount of extruded debris during *in vivo* preparation and found less extrusion for sonic and ultrasonic preparation techniques than for manual preparation with stainless-steel instruments (Table 1). It should be noted that no periapical tissue served as a natural barrier against apical extrusion in these studies so that the results regarding the amount of extruded material should not be transferred to the clinical situation.

Ultrasonic activation results in a fine fog of sodium hypochlorite that may affect the eyes and skin of the patient, the dentist, and the dental assistant. Therefore eyes should be protected with glasses.

New irrigation and disinfection techniques and devices

Other than conventional irrigation, additional techniques for disinfection of the endodontic cavity have been proposed and tested, including laser systems and gaseous ozone. Recently several new devices for endodontic irrigation and/or disinfection have been introduced, among which are the Quantec-E irrigation system, RinsEndo (Dürr-Dental, Bietigheim, Germany), EndoVac (Discus, Culver City, CA, USA), Vista irrigator (Vista Dental Products, Racine, WI, USA), a non-instrumenting technique (NIT), and similar systems. These new devices use pressure, vacuum, oscillation, and/or a combination with suction. For most of these devices and techniques, no data on the risk, frequency, and intensity of apical extrusion of the irrigant or the problems encountered with the use of pressure and negative pressure or oscillation are available.

Quantec-E irrigation system

The Quantec-E irrigation system is attached to an endodontic handpiece and allows continuous irrigation during rotary preparation, facilitating fast and permanent exchange of the irrigant and application of an increased volume of irrigant per time unit (203, 204). No reports on safety or on irrigation-related incidents of this device are available.

RinsEndo

RinsEndo represents an automated irrigation technique using combined irrigation and suction under hydrodynamic pressure. The irrigant (1–2% sodium hypochlorite) is agitated to an oscillation of approximately 1.6 Hz. Until now, only a few studies have been published on this device. Hauser et al. (205) mentioned that in *in vitro* studies, a higher risk of apical extrusion of the irrigant (80% of teeth) was evident compared with conventional irrigation using a syringe (13%). Also the penetration depth of a colored irrigant into the dentine was higher for the RinsEndo device used with a 0.45 mm diameter needle, demonstrating the efficacy of the oscillation in distribution of the irrigant. No further studies on that system have been published so far.

- One case of massive apical extrusion of sodium hypochlorite used with the RinsEndo device in tooth 13 has come to the attention of the author but has not yet been published (Fig. 13). The patient presented with severe ecchymosis descending to his chest.

EndoVac

EndoVac (*http://www.discusdental.com/endo*) is a combined irrigation–evacuation system. The irrigant is extruded from the system with pressure at the root canal orifice. The evacuator, a micro-cannule, extends to the apical region of the root canal; the dimensions of the needle are size 55 with a 2% taper. High-volume suction from the dental unit results in negative apical

Fig. 13. Severe swelling and ecchymosis of the face following apical extrusion of sodium hypochlorite. Case courtesy of Dr. Gerner.

pressure and thus passively sucks the irrigant from the orifice to the apical part of the root canal (206). Apical extrusion will probably be reduced as low pressure will appear apically.

A similar device has been presented by Fukumoto et al. (207). The irrigant is delivered by a needle (outer diameter 0.41 mm, inner diameter 0.19 mm) and a tubing pump (Masterflex, Cole Palmer Instruments, Vernon Hills, IL, USA) to the coronal or middle part of the root canal and aspired by a second needle (outer diameter 0.55 mm, inner diameter 0.30 mm), which is introduced to the apical part of the root canal. The aspiration pressure is -20 kPa. The irrigant is aspired from the coronal to the apical part of the root canal and there finally suctioned. This technique in an *in vitro* experiment on teeth with resected apices resulted in significantly less over-extrusion of irrigant than a conventional irrigation technique with the needle tip placed 2 mm before the apex. When the needle was placed 3 mm from the apex, the results did not significantly differ (208).

Safety irrigator

The Safety irrigator (Vista Dental Products) is an irrigation/evacuation system that delivers the irrigant via a thin needle containing a lateral opening with positive pressure to the apical part of the root canal and evacuates the solution via a large needle at the root canal orifice. No information on risks and safety are available thus far.

NIT

This technique, developed by Lussi and colleagues (209–211), uses a pump system producing a negative pressure (vacuum) down to approximately 3×10^4 Pa with microscopic and macroscopic bubbles inside the root canal system. A rapid rise of pressure up to 9×10^4 Pa causes collapse of the bubbles and hydrodynamic turbulence, allowing the irrigant to penetrate the root canal system. Attin et al. (212) reported on two (out of 22) cases of severe pain (despite anesthesia) during irrigation using the NIT such that treatment had to be stopped. In 14 of the remaining 20 cases, some blood was detected in the NIT adapter, demonstrating an inflow of blood from the periradicular tissues due to the negative pressure. *In vitro* no over-extrusion of NaOCl through the apical foramen was detected (213).

Ozone

Ozone has been proposed for endodontic disinfection (214, 215). The hazards of ozone when used in endodontics have not been investigated thus far. Care should be taken with regard to the patient's and the dentist's exposure to the gas.

Laser

Lasers are well known to exert several negative side-effects if not used properly and according to the manufacturers' guidelines (216, 217). Recently, it has been shown *in vitro* that some types of lasers (Er:YAG and Er,Cr:YSGG) create pressure waves in intracanal irrigants, which might force the solutions through the apical foramen (77). To review the possible side-effects of all types of lasers available for use in endodontics lies far beyond the scope of this review.

Concluding remarks

The endodontic literature contains several case reports on complications during root canal irrigation, including inadvertent injection of sodium hypochlorite or hydrogen peroxide into the periapical tissues, air emphysema, and allergic reactions to the solutions. Most of the cases occurred because of incorrect determination of endodontic working length, iatrogenic widening of the apical foramen, lateral perforation, or wedging of the irrigating needle. Clearly, precautions must be undertaken to prevent such mishaps. The irrigating needle has to be fixed to the syringe and must not be wedged into the root canal. During irrigation, a low and constant pressure should be used and the operator must ensure that excess irrigant leaves the root canal coronally via the access cavity, where it should be suctioned off immediately. However, it has been shown that contact between the periapical tissues and the irrigant cannot be completely avoided (70, 218). Therefore, a diluted concentration of the irrigant that still retains adequate disinfective properties is recommended. In a concentration of 0.5%, NaOCl is non-toxic to vital tissues and immediately washed away by the circulating blood (15, 16).

In case of an irrigation incident, the dentist should remain calm and assist the patient, who will inevitably become concerned about the dramatic sequelae. The dentist should immediately inform the patient of the cause and the nature of the incident. No standard therapy for further management of the complication has been described. Any intervention depends on the nature and severity of the incident. In many cases, no or only minimal intervention is necessary. To reduce the acute pain, local anesthesia may be helpful along with the prescription of analgesics. Antibiotics are recommended in cases where there is a high risk of the spread of infection; they are not necessary in minor cases. The patient should be informed that healing will take some days, or even weeks, and that symptoms in most cases will resolve completely. When the acute symptoms have resolved or diminished, endodontic treatment may be completed in most cases. The use of a mild, non-irritating irrigation solution (sterile saline, CHX gluconate) is recommended in such cases. In the majority of cases, there is no need or indication for extraction or surgical treatment of the involved tooth.

Acknowledgements

The authors thank the following colleagues for their valuable contributions in the form of cases, photographs, and literature: Prof. T. Lambrianidis (Greece), Prof. E. Schäfer, Dr. A. Hager, Dr. Gerner, Dr. Gehrig, Dr. Wettlin, Prof. C. Kockapan, Prof. C. Löst, Prof. J. Wiltfang, Dr. J. Versümer, Dr. A. Schönbach, and Dr. Essig (all Germany).

References

1. Zehnder M. Root canal irrigants. *J Endod* 2006: **32**: 389–398.
2. Grossman LI. *Endodontic Practice*, 10th edn. Philadelphia: Lea & Febiger, 1981.
3. Harrison JW. Irrigation of the root canal system. *Dent Clin North Am* 1984: **28**: 797–808.
4. Barbakow F, Lutz F, Toth L. Materials and techniques in root canal treatments in Switzerland – a determination of their status (in German). *Schweiz Monatsschr Zahnmed* 1995: **105**: 1265–1271.
5. Pashley EL, Birdsong NL, Bowman K, Pashley DH. Cytotoxic effects of NaOCl on vital tissue. *J Endod* 1985: **11**: 525–528.
6. Senia ES, Marraro RV, Mitchell JL, Lewis AG, Thomas L. Rapid sterilization of gutta-percha cones with 5.25% sodium hypochlorite. *J Endod* 1975: **1**: 136–140.
7. Zielke DR, Heggers JP, Harrison JW. A statistical analysis of anaerobic versus aerobic culturing in endodontic therapy. *Oral Surg Oral Med Oral Pathol* 1976: **42**: 830–837.
8. Byström A, Sundqvist G. The antibacterial action of sodium hypochlorite and EDTA in 60 cases of endodontic therapy. *Int Endod J* 1985: **18**: 35–40.
9. Byström A, Sundqvist G. Bacteriologic evaluation of the effect of 0.5 percent sodium hypochlorite in endodontic therapy. *Oral Surg Oral Med Oral Pathol* 1983: **55**: 307–312.
10. Byström A, Sundqvist G. Bacteriologic evaluation of the efficacy of mechanical root canal instrumentation in endodontic therapy. *Scand J Dent Res* 1981: **89**: 321–328.
11. Ørstavik D, Haapasalo M. Disinfection by endodontic irrigants and dressings of experimentally infected dentinal tubules. *Endod Dent Traumatol* 1990: **6**: 142–149.
12. Jeansonne MJ, White RR. A comparison of 2.0% chlorhexidine gluconate and 5.25% sodium hypochlorite as antimicrobial endodontic irrigants. *J Endod* 1994: **20**: 276–278.
13. Heling I, Chandler NP. Antimicrobial effect of irrigant combinations within dentinal tubules. *Int Endod J* 1998: **31**: 8–14.
14. Zehnder M, Kosicki D, Luder H, Sener B, Waltimo T. Tissue-dissolving capacity and antibacterial effect of buffered and unbuffered hypochlorite solutions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002: **94**: 756–762.
15. Spångberg L, Engström B, Langeland K. Biologic effects of dental materials. III. Toxicity and antimicrobial effect of endodontic antiseptics in vitro. *Oral Surg Oral Med Oral Pathol* 1973: **36**: 856–871.
16. Baumgartner JC, Cuenin PR. Efficacy of several concentrations of sodium hypochlorite for root canal irrigation. *J Endod* 1992: **18**: 605–612.
17. Hauman CH, Love RM. Biocompatibility of dental materials used in contemporary endodontic therapy: a review. Part 1. Intracanal drugs and substances. *Int Endod J* 2003: **36**: 75–85.
18. Cunningham WT, Joseph SW. Effect of temperature on the bactericidal action of sodium hypochlorite endodontic irrigant. *Oral Surg Oral Med Oral Pathol* 1980: **50**: 569–571.
19. Cunningham WT, Balekjian AY. Effect of temperature on collagen-dissolving ability of sodium hypochlorite endodontic irrigant. *Oral Surg Oral Med Oral Pathol* 1980: **49**: 175–177.
20. Abou-Rass M, Oglesby SW. The effects of temperature, concentration, and tissue type on the solvent ability of sodium hypochlorite. *J Endod* 1981: **7**: 376–377.
21. Moorer WR, Wesselink PR. Factors promoting the tissue dissolving capability of sodium hypochlorite. *Int Endod J* 1982: **15**: 187–196.
22. Sirtes G, Waltimo T, Schaetzle M, Zehnder M. The effects of temperature on sodium hypochlorite short-

term stability, pulp dissolution capacity, and antimicrobial efficacy. *J Endod* 2005: **31**: 669–671.
23. Clarkson RM, Moule AJ. Sodium hypochlorite and its use as an endodontic irrigant. *Aust Dent J* 1998: **43**: 250–256.
24. Grossman LI. Irrigation of root canals. *J Am Dent Assoc* 1943: **30**: 1915–1917.
25. Svec TA, Harrison JW. The effect of effervescence on debridement of the apical regions of root canals in single-rooted teeth. *J Endod* 1981: **7**: 335–340.
26. Schäfer E. Irrigation of the root canal. *ENDO – Endod Pract Today* 2007: **1**: 11–28.
27. Masillamoni CR, Kettering JD, Torabinejad M. The biocompatibility of some root canal medicaments and irrigants. *Int Endod J* 1981: **14**: 115–120.
28. Scelza MF, Daniel RL, Santos EM, Jaeger MM. Cytotoxic effects of 10% citric acid and EDTA-T used as root canal irrigants: an *in vitro* analysis. *J Endod* 2001: **27**: 741–743.
29. Koulaouzidou EA, Margelos J, Beltes P, Kortsaris AH. Cytotoxic effects of different concentrations of neutral and alkaline EDTA solutions used as root canal irrigants. *J Endod* 1999: **25**: 21–23.
30. Serper A, Çalt S, Dogan AL, Guç D, Ozçelik B, Kuraner T. Comparison of the cytotoxic effects and smear layer removing capacity of oxidative potential water, NaOCl and EDTA. *J Oral Sci* 2001: **43**: 233–238.
31. Sousa SM, Bramante CM, Taga EM. Biocompatibility of EDTA, EGTA and citric acid. *Braz Dent J* 2005: **16**: 3–8.
32. Malheiros CF, Marques MM, Gavini G. *In vitro* evaluation of the cytotoxic effects of acid solutions used as canal irrigants. *J Endod* 2005: **31**: 746–748.
33. Amaral KF, Rogero MM, Fock RA, Borelli P, Gavini G. Cytotoxicity analysis of EDTA and citric acid applied on murine resident macrophages culture. *Int Endod J* 2007: **40**: 338–343.
34. Okino LA, Siqueira EL, Santos M, Bombana AC, Figueiredo JA. Dissolution of pulp tissue by aqueous solution of chlorhexidine digluconate and chlorhexidine digluconate gel. *Int Endod J* 2004: **37**: 38–41.
35. Chang YC, Huang FM, Tai KW, Chou MY. The effect of sodium hypochlorite and chlorhexidine on cultured human periodontal ligament cells. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001: **92**: 446–450.
36. Faria G, Celes MR, De Rossi A, Silva LA, Silva JS, Rossi MA. Evaluation of chlorhexidine toxicity injected in the paw of mice and added to cultured L929 fibroblasts. *J Endod* 2007: **33**: 715–722.
37. Lamers AC, van Mullem PJ, Simon M. Tissue reactions to sodium hypochlorite and iodine potassium iodide under clinical conditions in monkey teeth. *J Endod* 1980: **6**: 788–792.
38. Barnhart BD, Chuang A, Lucca JJ, Roberts S, Liewehr F, Joyce AP. An *in vitro* evaluation of the cytotoxicity of various endodontic irrigants on human gingival fibroblasts. *J Endod* 2005: **31**: 613–615.
39. Wilcox LR, Wiemann AH. Effect of a final alcohol rinse on sealer coverage of obturated root canals. *J Endod* 1995: **21**: 256–258.
40. Stevens RW, Strother JM, McClanahan SB. Leakage and sealer penetration in smear-free dentin after a final rinse with 95% ethanol. *J Endod* 2006: **32**: 785–788.
41. Torabinejad M, Khademi AA, Babagoli J et al. A new solution for the removal of the smear layer. *J Endod* 2003: **29**: 170–175.
42. Zhang W, Torabinejad M, Li Y. Evaluation of cytotoxicity of MTAD using the MTT-tetrazolium method. *J Endod* 2003: **29**: 654–657.
43. Hsieh YD, Gau CH, Kung Wu SF, Shen EC, Hsu PW, Fu E. Dynamic recording of irrigating fluid distribution in root canals using thermal image analysis. *Int Endod J* 2007: **40**: 11–17.
44. Ram Z. Effectiveness of root canal irrigation. *Oral Surg Oral Med Oral Pathol* 1977: **44**: 306–312.
45. Chow TW. Mechanical effectiveness of root canal irrigation. *J Endod* 1983: **9**: 475–479.
46. Sedgley CM, Nagel AC, Hall D, Applegate B. Influence of irrigant needle depth in removing bioluminescent bacteria inoculated into instrumented root canals using real-time imaging *in vitro*. *Int Endod J* 2005: **38**: 97–104.
47. Abou-Rass M, Piccinino MV. The effectiveness of four clinical irrigation methods on the removal of root canal debris. *Oral Surg Oral Med Oral Pathol* 1982: **54**: 323–328.
48. Druttman AC, Stock CJ. An *in vitro* comparison of ultrasonic and conventional methods of irrigant replacement. *Int Endod J* 1989: **22**: 174–178.
49. Nguy D, Sedgley C. The influence of canal curvature on the mechanical efficacy of root canal irrigation *in vitro* using real-time imaging of bioluminescent bacteria. *J Endod* 2006: **32**: 1077–1080.
50. Moser JB, Heuer MA. Forces and efficacy in endodontic irrigation systems. *Oral Surg Oral Med Oral Pathol* 1982: **53**: 425–428.
51. Boutsioukis C, Lambrianidis T, Kastrinakis E, Bekiaroglou P. Measurement of pressure and flow rates during irrigation of a root canal *ex vivo* with three endodontic needles. *Int Endod J* 2007: **40**: 504–513.
52. Boutsioukis C, Lambrianidis T, Vasiliadis L. Clinical relevance of standardization of endodontic irrigation needle dimensions according to the ISO 9,626:1991 and 9,626:1991/Amd 1:2001 specification. *Int Endod J* 2007: **40**: 700–706.
53. Salzgeber RM, Brilliant JD. An *in vivo* evaluation of the penetration of an irrigating solution in root canals. *J Endod* 1977: **3**: 394–398.
54. Mohorn HW, Dowson J, Blankenship JR. Odontic periapical pressure following vital pulp extirpation. *Oral Surg Oral Med Oral Pathol* 1971: **31**: 536–544.
55. Weine FS. The enigma of the lateral canal. *Dent Clin North Am* 1984: **28**: 833–852.

56. Seltzer S, Bender IB, Ziontz M. The interrelationship between pulp and periodontal disease. *Oral Surg Oral Med Oral Pathol* 1963: **16**: 1474–1490.
57. Miyashita M, Kasahara E, Yasuda E, Yamamoto A, Sekizawa T. Root canal system of the mandibular incisor. *J Endod* 1997: **23**: 479–484.
58. Kasahara E, Yasuda E, Yamamoto A, Anzai M. Root canal system of the maxillary central incisor. *J Endod* 1990: **16**: 158–161.
59. Venturi M, Di Lenarda R, Prati C, Breschi L. An *in vitro* model to investigate filling of lateral canals. *J Endod* 2005: **31**: 877–881.
60. Fairbourn DR, McWalter GM, Montgomery S. The effect of four preparation techniques on the amount of apically extruded debris. *J Endod* 1987: **13**: 102–108.
61. Ruiz-Hubard EE, Gutmann JL, Wagner MJ. A quantitative assessment of canal debris forced periapically during root canal instrumentation using two different techniques. *J Endod* 1987: **13**: 554–558.
62. Martin H, Cunningham WT. The effect of endosonic and hand manipulation on the amount of root canal material extruded. *Oral Surg Oral Med Oral Pathol* 1982: **53**: 611–613.
63. McKendry DJ. Comparison of balanced forces, endosonic, and step-back filing instrumentation techniques: quantification of extruded apical debris. *J Endod* 1990: **16**: 24–27.
64. Myers GL, Montgomery S. A comparison of weights of debris extruded apically by conventional filing and Canal Master techniques. *J Endod* 1991: **17**: 275–279.
65. AlOmari MA, Dummer PM. Canal blockage and debris extrusion with eight preparation techniques. *J Endod* 1995: **21**: 154–158.
66. Tanalp J, Kaptan F, Sert S, Kayahan B, Bayirl G. Quantitative evaluation of the amount of apically extruded debris using 3 different rotary instrumentation systems. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006: **101**: 250–257.
67. Ferraz CC, Gomes NV, Gomes BP, Zaia AA, Teixeira FB, Souza-Filho FJ. Apical extrusion of debris and irrigants using two hand and three engine-driven instrumentation techniques. *Int Endod J* 2001: **34**: 354–358.
68. Beeson TJ, Hartwell GR, Thornton JD, Gunsolley JC. Comparison of debris extruded apically in straight canals: conventional filing versus profile .04 Taper series 29. *J Endod* 1998: **24**: 18–22.
69. Zarrabi MH, Bidar M, Jafarzadeh H. An *in vitro* comparative study of apically extruded debris resulting from conventional and three rotary (Profile, Race, FlexMaster) instrumentation techniques. *J Oral Sci* 2006: **48**: 85–88.
70. Brown DC, Moore BK, Brown CE Jr, Newton CW. An *in vitro* study of apical extrusion of sodium hypochlorite during endodontic canal preparation. *J Endod* 1995: **21**: 587–591.
71. Hinrichs RE, Walker WA III, Schindler WG. A comparison of amounts of apically extruded debris using handpiece-driven nickel–titanium instrument systems. *J Endod* 1998: **24**: 102–106.
72. Lambrianidis T, Tosounidou E, Tzoanopoulou M. The effect of maintaining apical patency on periapical extrusion. *J Endod* 2001: **27**: 696–698.
73. Er K, Sümer Z, Akpinar KE. Apical extrusion of intracanal bacteria following use of two engine-driven instrumentation techniques. *Int Endod J* 2005: **38**: 871–876.
74. Tinaz AC, Alacam T, Uzun O, Maden M, Kayaoglu G. The effect of disruption of apical constriction on periapical extrusion. *J Endod* 2005: **31**: 533–535.
75. Williams CE, Reid JS, Sharkey SW, Saunders WP. *In vitro* measurement of apically extruded irrigant in primary molars. *Int Endod J* 1995: **28**: 221–225.
76. Kustarci A, Akpinar KE, Kürsat E. Apical extrusion of intracanal debris and irrigant following the use of various instrumentation techniques. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008: **105**: 257–262.
77. George R, Walsh LJ. Apical extrusion of root canal irrigants when using Er:YAG and Er,Cr:YSGG lasers with optical fibers: an *in vitro* dye study. *J Endodont* 2008: **34**: 706–708.
78. Hauman CH, Chandler NP, Tong DC. Endodontic implications of the maxillary sinus: a review. *Int Endod J* 2002: **35**: 127–141.
79. Ariji Y, Obayashi N, Goto M et al. Roots of the maxillary first and second molars in horizontal relation to alveolar cortical plates and maxillary sinus: computed tomography assessment for infection spread. *Clin Oral Investig* 2006: **10**: 35–41.
80. Selden HS. The interrelationship between the maxillary sinus and endodontics. *Oral Surg Oral Med Oral Pathol* 1974: **38**: 623–629.
81. Eberhardt JA, Torabinejad M, Christiansen EL. A computed tomographic study of the distances between the maxillary sinus floor and the apices of the maxillary posterior teeth. *Oral Surg Oral Med Oral Pathol* 1992: **73**: 345–346.
82. Selden HS, August DS. Maxillary sinus involvement – an endodontic complication. Report of a case. *Oral Surg Oral Med Oral Pathol* 1970: **30**: 117–122.
83. Selden HS. The endo-antral syndrome: an endodontic complication. *J Am Dent Assoc* 1989: **119**: 397–402.
84. Pataky L, Nitsche H, Cseh L, Szendrey T. Radiographic survey of the maxillary sinus complications through endodontic treatment. *Dentomaxillofac Radiol* 1978: **7**: 87–91.
85. Ehrich DG, Brian JD Jr, Walker WA. Sodium hypochlorite accident: inadvertent injection into the maxillary sinus. *J Endod* 1993: **19**: 180–182.
86. Kavanagh CP, Taylor J. Inadvertent injection of sodium hypochlorite into the maxillary sinus. *Br Dent J* 1998: **185**: 336–337.
87. Ørstavik D, Brodin P, Aas E. Paraesthesia following endodontic treatment: survey of the literature and report of a case. *Int Endod J* 1983: **16**: 167–172.

88. Denio D, Torabinejad M, Bakland LK. Anatomical relationship of the mandibular canal to its surrounding structures in mature mandibles. *J Endod* 1992: **18**: 161–165.
89. Littner MM, Kaffe I, Tamse A, Dicapua P. Relationship between the apices of the lower molars and mandibular canal – a radiographic study. *Oral Surg Oral Med Oral Pathol* 1986: **62**: 595–602.
90. Hillerup S. Iatrogenic injury to oral branches of the trigeminal nerve: records of 449 cases. *Clin Oral Investig* 2007: **11**: 133–142.
91. Rowe AH. Damage to the inferior dental nerve during or following endodontic treatment. *Br Dent J* 1983: **155**: 306–307.
92. Koçkapan C. Overfilling into the mandibular canal as an endodontic complication. A review. *Schweiz Monatsschr Zahnmed* 1993: **103**: 20–28.
93. Grötz KA, Al Nawas B, de Aguiar EG, Schulz A, Wagner W. Treatment of injuries to the inferior alveolar nerve after endodontic procedures. *Clin Oral Investig* 1998: **2**: 73–76.
94. Morse DR. Endodontic-related inferior alveolar nerve and mental foramen paresthesia. *Compend Contin Educ Dent* 1997: **18**: 963–968, 976.
95. Reeh ES, Messer HH. Long-term paresthesia following inadvertent forcing of sodium hypochlorite through perforation in maxillary incisor. *Endod Dent Traumatol* 1989: **5**: 200–203.
96. Hülsmann M, Hahn W. Complications during root canal irrigation – literature review and case reports. *Int Endod J* 2000: **33**: 186–193.
97. Witton R, Brennan PA. Severe tissue damage and neurological deficit following extravasation of sodium hypochlorite solution during routine endodontic treatment. *Br Dent J* 2005: **198**: 749–750.
98. Witton R, Henthorn K, Ethunandan M, Harmer S, Brennan PA. Neurological complications following extrusion of sodium hypochlorite solution during root canal treatment. *Int Endod J* 2005: **38**: 843–848.
99. Becking AG. Complications in the use of sodium hypochlorite during endodontic treatment. Report of three cases. *Oral Surg Oral Med Oral Pathol* 1991: **71**: 346–348.
100. Mehdipour O, Kleier DJ, Averbach RE. Anatomy of sodium hypochlorite accidents. *Compend Contin Educ Dent* 2007: **28**: 544–550.
101. Becker GL, Cohen S, Borer R. The sequelae of accidentally injecting sodium hypochlorite beyond the root apex. Report of a case. *Oral Surg Oral Med Oral Pathol* 1974: **38**: 633–638.
102. Gatot A, Arbelle J, Leiberman A, Yanai-Inbar I. Effects of sodium hypochlorite on soft tissues after its inadvertent injection beyond the root apex. *J Endod* 1991: **17**: 573–574.
103. Neaverth EJ, Swindle R. A serious complication following the inadvertent injection of sodium hypochlorite outside the root canal system. *Compendium* 1990: **11**: 474, 476, 478–481.
104. Sabala CL, Powell SE. Sodium hypochlorite injection into periapical tissues. *J Endod* 1989: **15**: 490–492.
105. Mehra P, Clancy C, Wu J. Formation of a facial hematoma during endodontic therapy. *J Am Dent Assoc* 2000: **131**: 67–71.
106. Linn JL, Messer HH. Hypochlorite injury to the lip following injection via a labial perforation. Case report. *Aust Dent J* 1993: **38**: 280–282.
107. Schwerin C, Gerlach K. Iatrogene Zwischenfälle bei der Wurzelkanalspülung mit Natriumhypochlorit. *Quintessenz* 2007: **58**: 1041–1044.
108. Bhat KS. Tissue emphysema caused by hydrogen peroxide. *Oral Surg Oral Med Oral Pathol* 1974: **38**: 304–307.
109. Nygaard-Østby B. Chelation in root canal therapy: ethylenediamine tetraacetic acid for cleansing and widening of root canals. *Odont Tidsk* 1957: **65**: 3–11.
110. Bowden JR, Ethunandan M, Brennan PA. Life-threatening airway obstruction secondary to hypochlorite extrusion during root canal treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006: **101**: 402–404.
111. Joffe E. Complication during root canal therapy following accidental extrusion of sodium hypochlorite through the apical foramen. *Gen Dent* 1991: **39**: 460–461.
112. Cymbler DM, Ardakani P. Sodium hypochlorite injection into periapical tissues. *Dent Update* 1994: **21**: 345–346.
113. Tosti A, Piraccini BM, Pazzaglia M, Ghedini G, Papadia F. Severe facial edema following root canal treatment. *Arch Dermatol* 1996: **132**: 231–233.
114. Balto H, Al-Nazhan S. Accidental injection of sodium hypochlorite beyond the root apex. *Saudi Dent J* 2002: **14**: 36–38.
115. Gernhardt CR, Eppendorf K, Kozlowski A, Brandt M. Toxicity of concentrated sodium hypochlorite used as an endodontic irrigant. *Int Endod J* 2004: **37**: 272–280.
116. Sennhenn-Kirchner S, Hülsmann M. Spülzwischenfall mit NaOCl – Ein Fallbericht. *Endodontie* 2008: **17**: 243–250.
117. Pynn BR, Amato D, Walker DA. Subcutaneous emphysema following dental treatment: a report of two cases and review of the literature. *J Can Dent Assoc* 1992: **58**: 496–499.
118. Watts A, Paterson RC. Atypical apical lesions detected during a study of short-term tissue responses to three different endodontic instrumentation techniques. *Endod Dent Traumatol* 1993: **9**: 200–210.
119. Spencer HR, Ike V, Brennan PA. Review: the use of sodium hypochlorite in endodontics – potential complications and their management. *Br Dent J* 2007: **202**: 555–559.
120. Hales JJ, Jackson CR, Everett AP, Moore SH. Treatment protocol for the management of a sodium hypochlorite accident during endodontic therapy. *Gen Dent* 2001: **49**: 278–281.

121. Grob R. An incident with sodium hypochlorite – only my error? *Schweiz Monatsschr Zahnmed* 1984: **94**: 661–662.
122. Walker JE. Emphysema of soft tissues complicating endodontic treatment using hydrogen peroxide: a case report. *Br J Oral Surg* 1975: **13**: 98–99.
123. Patterson CJ, McLundie AC. Apical penetration by a root canal irrigant: a case report. *Int Endod J* 1989: **22**: 197–199.
124. Essig H, Wiltfang J, Warnke PH. H_2O_2-induziertes emphysem. *Zahnärztl Mitt* 2007: **97**: 254–255.
125. Seidner S. Durch H_2O_2 hervorgerufenes emphysem der Gesichtshaut. *Z Stomatol* 1938: **36**: 204–205.
126. Pöllmann L. Emphysem nach Wurzelkanalbehandlung. *Dtsch Zahnärztl Z* 1980: **35**: 835.
127. Kaufman E, Leviner E, Galili D, Garfunkel AA. Subcutaneous air emphysema – a rare condition (four case reports). *J Oral Med* 1984: **39**: 47–50.
128. Kaufman AY. Facial emphysema caused by hydrogen peroxide irrigation: report of a case. *J Endod* 1981: **7**: 470–472.
129. Hülsmann M, Denden JM. Iatrogene Zwischenfälle bei der Wurzelkanalspülung – Literaturübersicht und Falldarstellung. *Endodontie* 1997: **6**: 191–205.
130. Nahlieli O, Neder A. Iatrogenic pneumomediastinum after endodontic therapy. *Oral Surg Oral Med Oral Pathol* 1991: **71**: 618–619.
131. Patterson SS. *In vivo* and *in vitro* studies of the effect of the disodium salt of ethylenediamine tetraacetate on human dentine and its endodontic implications. *Oral Surg Oral Med Oral Pathol* 1963: **16**: 83–103.
132. Segura JJ, Calvo JR, Guerrero JM, Sampedro C, Jimenez A, Llamas R. The disodium salt of EDTA inhibits the binding of vasoactive intestinal peptide to macrophage membranes: endodontic implications. *J Endod* 1996: **22**: 337–340.
133. Segura JJ, Calvo JR, Guerrero JM, Jimenez-Planas A, Sampedro C, Llamas R. EDTA inhibits *in vitro* substrate adherence capacity of macrophages: endodontic implications. *J Endod* 1997: **23**: 205–208.
134. Çehreli ZC, Onur MA, Tasman F, Gümrükçüoglu A, Artuner H. Effects of current and potential dental etchants on nerve compound action potentials. *J Endod* 2002: **28**: 149–151.
135. Harris WE. Unusual endodontic complication: report of case. *J Am Dent Assoc* 1971: **83**: 358–363.
136. Osmundsen PE. Contact dermatitis due to sodium hypochlorite. *Contact Dermatitis* 1978: **4**: 177–178.
137. Al-Hamri K, Kreusch T. Allergische Reaktionen nach Wurzelkanalspülung mit Natriumhypochlorit-Lösung. *Dtsch Zahnärztl Z* 2005: **60**(Suppl): A160–A162.
138. Eun HC, Lee AY, Lee YS. Sodium hypochlorite dermatitis. *Contact Dermatitis* 1984: **11**: 45.
139. Habets JM, Geursen-Reitsma AM, Stolz E, van Joost T. Sensitization to sodium hypochlorite causing hand dermatitis. *Contact Dermatitis* 1986: **15**: 140–142.
140. Andersen M, Lund A, Andreasen JO, Andreasen FM. *In vitro* solubility of human pulp tissue in calcium hydroxide and sodium hypochlorite. *Endod Dent Traumatol* 1992: **8**: 104–108.
141. Hasselgren G, Olsson B, Cvek M. Effects of calcium hydroxide and sodium hypochlorite on the dissolution of necrotic porcine muscle tissue. *J Endod* 1988: **14**: 125–127.
142. Krautheim AB, Jermann TH, Bircher AJ. Chlorhexidine anaphylaxis: case report and review of the literature. *Contact Dermatitis* 2004: **50**: 113–116.
143. Autegarden JE, Pecquet C, Huet S, Bayrou O, Leynadier F. Anaphylactic shock after application of chlorhexidine to unbroken skin. *Contact Dermatitis* 1999: **40**: 215.
144. Ebo DG, Stevens WJ, Bridts CH, Matthieu L. Contact allergic dermatitis and life-threatening anaphylaxis to chlorhexidine. *J Allergy Clin Immunol* 1998: **101**: 128–129.
145. Snellman E, Rantanen T. Severe anaphylaxis after a chlorhexidine bath. *J Am Acad Dermatol* 1999: **40**: 771–772.
146. Pham NH, Weiner JM, Reisner GS, Baldo BA. Anaphylaxis to chlorhexidine. Case report. Implication of immunoglobulin E antibodies and identification of an allergenic determinant. *Clin Exp Allergy* 2000: **30**: 1001–1007.
147. Scully C, Ng YL, Gulabivala K. Systemic complications due to endodontic manipulations. *Endodontic Topics* 2003: **4**: 60–68.
148. Tupker RA, Schuur J, Coenraads PJ. Irritancy of antiseptics tested by repeated open exposures on the human skin, evaluated by non-invasive methods. *Contact Dermatitis* 1997: **37**: 213–217.
149. Lee SK, Zhai H, Maibach HI. Allergic contact dermatitis from iodine preparations: a conundrum. *Contact Dermatitis* 2005: **52**: 184–187.
150. Kaufman AY, Keila S. Hypersensitivity to sodium hypochlorite. *J Endod* 1989: **15**: 224–226.
151. Çaliskan MK, Türkün M, Alper S. Allergy to sodium hypochlorite during root canal therapy: a case report. *Int Endod J* 1994: **27**: 163–167.
152. Dandakis C, Lambrianidis T, Boura P. Immunologic evaluation of dental patient with history of hypersensitivity reaction to sodium hypochlorite. *Endod Dent Traumatol* 2000: **16**: 184–187.
153. Crincoli V, Scivetti M, Bisceglie D, Pilolli GP, Favia G. Unusual case of adverse reaction in the use of sodium hypochlorite during endodontic treatment: a case report. *Quintessence Int* 2008: **39**: e70–e73.
154. Ribeiro DA. Do endodontic compounds induce genetic damage? A comprehensive review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2008: **105**: 251–256.
155. Herrmann JW, Heicht RC. Complications in therapeutic use of sodium hypochlorite. *J Endod* 1979: **5**: 160.

156. Pontes F, Pontes H, Adachi P, Rodini C, Almeida D, Pinto D Jr. Gingival and bone necrosis caused by accidental sodium hypochlorite injection instead of anaesthetic solution. *Int Endod J* 2008: **41**: 267–270.
157. Gursoy UK, Bostanci V, Kosger HH. Palatal mucosa necrosis because of accidental sodium hypochlorite injection instead of anaesthetic solution. *Int Endod J* 2006: **39**: 157–161.
158. Hülsmann M, Schäfer E. *Probleme in der Endodontie. Prävention, Identifikation und Management*. Berlin: Quintessenz Verlag, 2007.
159. Goffin V, Pierard GE, Henry F, Letawe C, Maibach HI. Sodium hypochlorite, bleaching agents, and the stratum corneum. *Ecotoxicol Environ Saf* 1997: **37**: 199–202.
160. Lambrianidis T. Irrigation related risks. In: Lambrianidis T, ed. *Risk Management in Root Canal Treatment*. Thessaloniki: University Studio Press, 2001: 163–173.
161. Ingram TA. Response of the human eye to accidental exposure to sodium hypochlorite. *J Endod* 1990: **16**: 235–238.
162. Gasset AR, Ishii Y. Cytotoxicity of chlorhexidine. *Can J Ophthalmol* 1975: **10**: 98–100.
163. Hamill MB, Osato MS, Wilhelmus KR. Experimental evaluation of chlorhexidine gluconate for ocular antisepsis. *Antimicrob Agents Chemother* 1984: **26**: 793–796.
164. Green K, Livingston V, Bowman K, Hull DS. Chlorhexidine effects on corneal epithelium and endothelium. *Arch Ophthalmol* 1980: **98**: 1273–1278.
165. Serper A, Ozbek M, Calt S. Accidental sodium hypochlorite-induced skin injury during endodontic treatment. *J Endod* 2004: **30**: 180–181.
166. Arevalo-Silva C, Eliashar R, Wohlgelernter J, Elidan J, Gross M. Ingestion of caustic substances: a 15-year experience. *Laryngoscope* 2006: **116**: 1422–1426.
167. Yarington CT Jr. The experimental causticity of sodium hypochlorite in the esophagus. *Ann Otol Rhinol Laryngol* 1970: **79**: 895–899.
168. Weeks RS, Ravitch MM. The pathology of experimental injury to the cat esophagus by liquid chlorine bleach. *Laryngoscope* 1971: **81**: 1532–1541.
169. Foulkes DM. Some toxicological observations on chlorhexidine. *J Periodontal Res* 1973: **12**(Suppl): 55–60.
170. Ricciardolo FL. Mechanisms of citric acid-induced bronchoconstriction. *Am J Med* 2001: **111**(Suppl 8A): 18S–24S.
171. Battrum DE, Gutmann JL. Implications, prevention and management of subcutaneous emphysema during endodontic treatment. *Endod Dent Traumatol* 1995: **11**: 109–114.
172. Shovelton DS. Surgical emphysema as a complication of dental operations. *Br Dent J* 1957: **102**: 125–129.
173. Heyman SN, Babayof I. Emphysematous complications in dentistry, 1960–1993: an illustrative case and review of the literature. *Quintessence Int* 1995: **26**: 535–543.
174. Lambrianidis T. Ephysema. In: Lambrianidis T, ed. *Risk Management in Root Canal Treatment*. Thessaloniki: University Studio Press, 2001: 323–336.
175. Bradford CE, Eleazer PD, Downs KE, Scheetz JP. Apical pressures developed by needles for canal irrigation. *J Endod* 2002: **28**: 333–335.
176. Eleazer PD, Eleazer KR. Air pressures developed beyond the apex from drying root canals with pressurized air. *J Endod* 1998: **24**: 833–836.
177. Nehlsen B. Ein anderer Fall von Emphysem der Wange bei einer Wurzelkanalbehandlung. *Zahnärztl Rdsch* 1927: **36**: 21–22.
178. Berg A. Emphysembildung im Anschluss an die Behandlung wurzelkranker Zähne. *Z Stomatol* 1928: **26**: 904–916.
179. Müller-Stade P. Ausgedehntes Hautemphysem nach Einblasen von Luft in einen Zahnwurzelkanal. *Z Stomatol* 1931: **29**: 880–882.
180. Salvas C. A case of emphysema. *Dent Cosmos* 1931: **73**: 307.
181. Langegger PA. Emphysem bei der Zahnbehandlung. *Z Stomatol* 1950: **47**: 133–137.
182. Glahn M. Akutes Emphysem nach Einblasen von Luft durch den Wurzelkanal. *Dt Zahn-, Mund-, Kieferheilk* 1953: **18**: 252.
183. Magnin J. Oedeme palpebral apres insufflation d'air dans le canal d'une incisive centrale superieure. *Schweiz Monatsschr Zahnmed* 1958: **68**: 437.
184. Lloyd RE. Surgical emphysema as a complication in endodontics. *Br Dent J* 1975: **138**: 393–394.
185. Harnisch H. Lidemphysem bei zahnärztlicher Behandlung. *Zahnärztl Welt/Reform* 1976: **27**: 501.
186. Spaulding CR. Soft tissue emphysema. *J Am Dent Assoc* 1979: **98**: 587–588.
187. Arnold WH. Die Wurzelkanalbehandlung als Kausalfaktor eines Emphysems. *Quintessenz* 1979: **30**: 46.
188. Hirschmann PN, Walker RT. Facial emphysema during endodontic treatment – two case reports. *Int Endod J* 1983: **16**: 130–132.
189. Falomo OO. Surgical emphysema following root canal therapy. Report of a case. *Oral Surg Oral Med Oral Pathol* 1984: **58**: 101–102.
190. Wright KJ, Derkson GD, Riding KH. Tissue-space emphysema, tissue necrosis, and infection following use of compressed air during pulp therapy: case report. *Pediatr Dent* 1991: **13**: 110–113.
191. Sikora U. Über Hautemphyseme im Kiefer-Gesichts-Bereich. *Dtsch Stomatol* 1966: **16**: 648–652.
192. Rickles NH, Joshi BA. A possible case in a human and an investigation in dogs of death from air embolism during root canal therapy. *J Am Dent Assoc* 1963: **67**: 397–404.
193. Harrison JW, Svec TA, Baumgartner JC. Analysis of clinical toxicity of endodontic irrigants. *J Endod* 1978: **4**: 6–11.
194. Harrison JW, Baumgartner CJ, Zielke DR. Analysis of interappointment pain associated with the combined

use of endodontic irrigants and medicaments. *J Endod* 1981: 7: 272–276.
195. Torabinejad M, Shabahang S, Bahjri K. Effect of MTAD on postoperative discomfort: a randomized clinical trial. *J Endod* 2005: **31**: 171–176.
196. Heyden G. Relation between locally high concentration of chlorhexidine and staining as seen in the clinic. *J Periodontal Res* 1973: **12**(Suppl): 76–80.
197. Vivacqua-Gomes N, Ferraz CC, Gomes BP, Zaia AA, Teixeira FB, Souza-Filho FJ. Influence of irrigants on the coronal microleakage of laterally condensed gutta-percha root fillings. *Int Endod J* 2002: **35**: 791–795.
198. Basrani BR, Manek S, Sodhi RN, Fillery E, Manzur A. Interaction between sodium hypochlorite and chlorhexidine gluconate. *J Endod* 2007: **33**: 966–969.
199. Yeung SY, Huang CS, Chan CP, Lin CP, Lin HN, Lee PH, Jia HW, Huang SK, Jeng JH, Chang MC. Antioxidant and pro-oxidant properties of chlorhexidine and its interaction with calcium hydroxide solutions. *Int Endod J* 2007: **40**: 837–844.
200. Marchesan MA, Pasternak JB, Afonso MM, Sousa-Neto MD, Paschoalato C. Chemical analysis of the flocculate formed by the association of sodium hypochlorite and chlorhexidine. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007: **103**: e103–e105.
201. Tay FR, Mazzoni A, Pashley DH, Day TE, Ngoh EC, Breschi L. Potential iatrogenic tetracycline staining of endodontically treated teeth via NaOCl/MTAD irrigation: a preliminary report. *J Endod* 2006: **32**: 354–358.
202. Rotstein I, Karawani M, Sahar-Helft S, Mor C, Steinberg D. Effect of sodium hypochlorite and EDTA on mercury released from amalgam. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001: **92**: 556–560.
203. Walters MJ, Baumgartner JC, Marshall JG. Efficacy of irrigation with rotary instrumentation. *J Endod* 2002: **28**: 837–839.
204. Setlock J, Fayad MI, BeGole E, Bruzick M. Evaluation of canal cleanliness and smear layer removal after the use of the Quantec-E irrigation system and syringe: a comparative scanning electron microscope study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003: **96**: 614–617.
205. Hauser V, Braun A, Frentzen M. Penetration depth of a dye marker into dentine using a novel hydrodynamic system (RinsEndo). *Int Endod J* 2007: **40**: 644–652.
206. Nielsen BA, Craig BJ. Comparison of the EndoVac system to needle irrigation of root canals. *J Endod* 2007: **33**: 611–615.
207. Fukumoto Y, Kikuchi I, Yoshioka T, Kobayashi C, Suda H. An *ex vivo* evaluation of a new root canal irrigation technique with intracanal aspiration. *Int Endod J* 2006: **39**: 93–99.
208. Fukumoto Y. Intracanal aspiration technique for root canal irrigation: evaluation of smear layer removal (in Japanese). *Kokubyo Gakkai Zasshi* 2005: **72**: 13–18.
209. Lussi A, Messerli L, Hotz P, Grosrey J. A new non-instrumental technique for cleaning and filling root canals. *Int Endod J* 1995: **28**: 1–6.
210. Lussi A, Nussbacher U, Grosrey J. A novel noninstrumented technique for cleansing the root canal system. *J Endod* 1993: **19**: 549–553.
211. Lussi A. The cleaning and obturation of the root canal system without conventional instruments. A position definition. *Schweiz Monatsschr Zahnmed* 2000: **110**: 248–261.
212. Attin T, Buchalla W, Zirkel C, Lussi A. Clinical evaluation of the cleansing properties of the non-instrumental technique for cleaning root canals. *Int Endod J* 2002: **35**: 929–933.
213. Lussi A, Portmann P, Nussbächer U, Imwinkelried S, Grosrey J. Comparison of two devices for root canal cleansing by the noninstrumentation technology. *J Endod* 1999: **25**: 9–13.
214. Hems RS, Gulabivala K, Ng YL, Ready D, Spratt DA. An *in vitro* evaluation of the ability of ozone to kill a strain of *Enterococcus faecalis*. *Int Endod J* 2005: **38**: 22–29.
215. Lynch E. *Ozone: Revolution in Dentistry.* Berlin: Quintessenz Publishing, 2004.
216. Meire M, DeMoor R. Lasers in endodontics: laser disinfection, an added value? *ENDO – Endodontic Practice Today* 2007: **1**: 159–172.
217. Stabholz A, Sahar-Helft S, Moshonov J. Lasers in endodontics. *Dent Clin North Am* 2004: **48**: 809–832, vi.
218. Vande Visse JE, Brilliant JD. Effect of irrigation on the production of extruded material at the root apex during instrumentation. *J Endod* 1975: **1**: 243–246.