Complications of Endodontic Irrigation: Dental, Medical, and Legal

6

Gary Glassman

Abstract

The objective of endodontic treatment is to treat and/or prevent apical periodontitis. Historically, there have been many irrigating agents that have been used to achieve this objective. Sodium hypochlorite, to date, still remains the irrigant of choice to break down the organic tissue of the dental pulp, debride necrotic tissue from the root canal space, and confirm negative bacteria cultures. Sodium hypochlorite while being an excellent endodontic irrigant can also cause devastating complications if extruded past the apex into the periradicular tissues.

This chapter will outline the complications and sequelae that potentially can occur if sodium hypochlorite is accidentally extruded past the apex and into the periradicular tissues. The mechanism of action of the irrigation accident will be detailed as well as preventative measures that can be employed to avoid such occurrences in addition to suggested treatment recommendations should such an accident occur. In addition, the legal and ethical implications with respect to the use and delivery of sodium hypochlorite during endodontic treatment will also be discussed.

Microbial Control: History

G. V. Black [1] recognized the significance of endodontic microbial control over a century ago, and by the mid-1920s, the importance of obtaining a "negative culture" prior to obturation was axiomatic [2]. Unfortunately, the early endodontic pioneers lacked the methods, techniques, and equipment to identify all varieties of microbiota and their symbiotic association within the root canal system. These shortcomings adversely affected the reasoning of many researchers like Bender and Seltzer who by 1964 questioned the need to culture [3, 4]. Fortunately, as microbiology assay methods improved, Sundqvist reestablished the importance of the endodontic microflora [5] and began the scientific path of discovery that would establish endodontic biofilm as the cause of apical periodontitis [6].

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Table 6.1 While 3 and 6 % NaOCl could eliminate biofilm from the dentinal walls, only 6 % NaOCl could prevent regrowth of the biofilm

Solution	SEM		Culture growth (%)
	Presence of bacteria	Biofilm status	
6 % NaOCl	–	Absent	0
3 % NaOCl	–	Absent	20
1 % NaOCl	+	Disrupted	90
1 % NaOCl/ MTAD	+	Disrupted	0
2 % CHX	+	Intact	0
+ Control	+	Intact	100
– Control	–	Absent	0

From Clegg [8]

Microbial Control: Biofilm and NaOCl

In 2005, Nair reported an abundance of biofilm within the root canal system after using copious amounts of 5.25 % NaOCl during canal preparation [7]. This finding immediately prompted Clegg to investigate the most currently available endodontic irrigation solutions so as to determine their ability to both eradicate biofilm and prevent its regrowth on dentinal walls [8]. His findings conclusively proved that 6 % NaOCl is required to achieve both objectives (Table 6.1). Although chlorhexidine effectively kills biofilm, it lacked the ability to hydrolyze it, thus failing to achieve one of the basic objectives of endodontic treatment – debridement. By default, 6 % NaOCl is the only known endodontic irrigant, to date, capable of addressing the problems associated with endodontic biofilm; therefore, this chapter will only address complications associated with using NaOCl during endodontic treatment.

NaOCl: Cytotoxicity

Unfortunately, the chemical characteristic responsible for complete hydrolysis of biofilm produces devastating effects on living tissue. In a classical 1985 study, Pashley et al. [9] investigated the effect on red blood cells (RBC) and found that 5.25 % NaOCl, when diluted with saline at a ratio of 1:1,000, produced 96.3 % hemolysis of an RBC sample. The study also included the intradermal injection effect using a rat model and 5.25 % NaOCl. The intradermal injections resulted in immediate hemorrhage within the entire area of solution contact, and the affected areas ulcerated after 24 h. Pashley et al. warned: "NaOCl, while a very effective proteolytic solvent, is extremely cytotoxic and should be used judiciously and with caution in endodontic treatment. Even the suggestion that NaOCl, at some dilution, will only affect necrotic tissue should be abandoned." Pashley et al. further noted that one of the serious clinical consequences of using NaOCl is the passage of some of the solution through the foramina, which sometimes occurs when the needle is momentarily wedged tightly into the canal during irrigation. Twenty-eight years after this warning, Pashley coauthored another publication that identified a far simpler and more dangerous cause of the NaOCl extrusion incident – direct intravenous injection via intraosseous infusion [10].

NaOCl: Complications

Complications from NaOCl extrusion includes (1) maxillary sinus incidents [11], (2) severe pain [12], (3) cellulitis [13], (4) life-threatening events [14], (5) permanent facial disfigurement [15], (6) permanent nerve damage [16], (7) secondary infection [17], and (8) acute kidney injury [18]. At the root of the problem is a broad misunderstanding of the reasons NaOCl is extruded from the apical foramen. It is generally believed that apical extrusion of NaOCl happens, as Pashley described, when an irrigation needle is wedged into a canal during irrigation; however, two studies disagree with this belief. First, in a survey of the diplomats of the American Board of Endodontics, only 20 % of the responding diplomats reported they felt the needle was wedged in the canal [19]. Second, in a one-of-a-kind clinical study, Hypaque (a radiopaque dye) was used as an irrigating solution [20]. It is important to note that the Hypaque investigators were aware of the possibility of forceful apical extrusion and reported that care was taken to insure that no irrigation needle was wedged into the walls, yet in both vital and nonvital teeth, apical extrusion of Hypaque was noted (Fig. 6.1). Considering the tissue toxicity of even the smallest amount of NaOCl, it seems reasonable that many patients would feel some degree of postoperative pain or discomfort following traditional endodontic irrigation. Gondim et al. proved this to be a statistically significant fact [21].

NaOCl: Reviewing the Extrusion Incident

A typical NaOCl extrusion is characterized in Fig. 6.2, but if an irrigant can escape the apical foramen as easily as demonstrated in Fig. 6.1, then why are these characteristic signs and symptoms of the NaOCl incident so rare? Furthermore, why isn't the facial area directly superficial to the involved root apex virtually ever affected; while very specific other parts of the face in Fig. 6.2 are usually always affected, and other areas like the cheek are never affected. This is apparent again with the patient shown in Fig. 6.3a. Curiously, almost no ecchymosis is apparent at or near the right alar lobule, and this is the area directly superficial to the apex of the treated tooth (upper right lateral incisor), yet ecchymosis is apparent up to the super palpebral vein (arrow in "A") and down to the angle of the mouth [22]. In July 2013, Boutsioukis et al. [23] published an extensive 16-page review paper that included 105 references and examined 40 case histories and stated: "*There is a lack of clinical studies focusing on irrigant extrusion during root canal irrigation. Currently available case reports provide limited data on the possible factors that may influence irrigant extrusion.*" It is important to note that the Boutsioukis' et al. review was published in July 2013, four months

Fig. 6.1 In a unique clinical study, Salzgeber used a radiopaque dye (Hypaque) as an endodontic irrigant delivered judicially and cautiously via a non-binding needle during canal preparation and final irrigation. Despite careful delivery, sometimes regardless of the pulp's vitality, the dye extended into the apical tissues. Regarding nonvital teeth: "When the Hypaque did extend into the periapical tissues in teeth with necrotic pulps, it seemed to respect no boundaries and occupied a random portion of the rarefied area." In a situation as shown here, due to tissue reaction with NaOCl, post-op pain is likely a consequence, a finding supported by Gondim et al. [21] (From Salzgeber and Brilliant [20])

Fig. 6.2 The pathognomonic appearance of a NaOCl extrusion incident typically includes hemifacial edema and ecchymosis involving (*A*) one or both eyelids and (*B*) upper and lower lips beginning at the angle of the mouth but (*C*) never includes the cheek area [18] (With permission from Saudi Journal of Kidney Diseases and Transplantation)

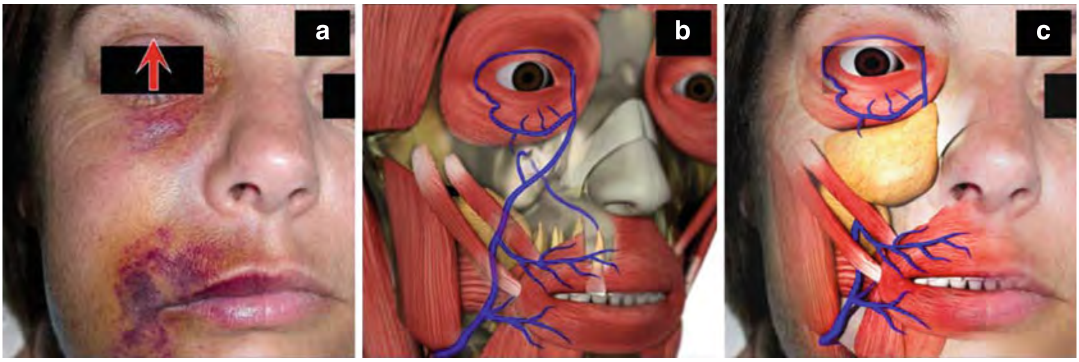

Fig. 6.3 (**a**) The classical pathognomonic facial appearance of NaOCl infusion resulting from the treatment of the maxillary right lateral incisor. Interestingly, although the right superior palpebral vein (*red arrow*) shows the hemorrhagic effect of NaOCl infusion, the midface area just below the eyelids and upper lip is virtually unaffected (From Witton and Brennan [22]). (**b**) The course of the anterior facial vein and its tributaries including the palpebral veins of the eyelids, the superior and inferior labia veins, and, most importantly – *an uncommon connection* [40] – with the superior alveolar vein(s) that normally drains blood from the teeth to the pterygoid plexus of the veins in the infratemporal fossa. (**c**) The area between the eyelids and the angle of the mouth is unaffected because the malar fat pad and the zygomatic muscles cover the anterior facial vein, thus hiding any hemorrhagic effect (Figs. **b & c** with Permission from SybronEndo)

before Pashley et al. described their novel theory of direct intravenous injection via intraosseous infusion.

The article immediately following Boutsioukis' July 2013 review was one of the three ex vivo studies published between April 2013 and May 2014 [24–26]. These ex vivo studies contained a method flaw obviously due to the investigator's lack of knowledge regarding the more recent findings of Pashley et al. The principle investigator with Pashley was Zhu [10], and their work was not referenced in any of Boutsioukis' ex vivo studies [24–26]. Additionally, two extremely important case histories [27, 28] were not included in the Boutsioukis' review; therefore, the method flaw and the case histories will be examined in detail. Finally, the review criticizes the ex vivo study by Desai and Himel [29] as not specifying a research hypothesis or aiming regarding "irrigan[t] extrusion," while in fact Desai stated: "*The specific aim of this in vitro study was to compare the relative safety of various intracanal irrigation systems.*" Furthermore, in Desai's discussion, he stated the following: "*The protocol for this study was designed to maximize the possibility of irrigant extrusion through an unrestricted, yet normal apex. It is understood that in clinical situations several factors might decrease the extent to which these systems extrude solutions. Periapical tissues and bone provide resistance to apical extrusion as well as non-patent canals. If quantities of periapical extrusion occurred clinically such as reported in this article, greater adverse treatment reactions associated with full-strength sodium hypochlorite would most likely occur. The model used most likely correlates, by design, to a canal that is open to atmospheric pressure, such as occurs when the apex of a tooth is extruding into the maxillary sinus with no apical covering or restriction.*"

Maxillary Sinus Considerations

The maxillary sinus is uniquely located in the immediate vicinity to the apices of maxillary teeth. With age, the alveolar bone surrounding these apices becomes thinner to the point where the root tips may project into the maxillary sinus and may not be covered with bony lamina dura or even the schneiderian membrane [30]. Furthermore, the ostium maxillae communicate directly with the nasal cavity and consequently normal atmospheric pressure. Provided the root canal is fully patent during treatment, this unique root canal system and maxillary sinus anatomical relationship offers no resistance to fluid extrusion during endodontic irrigation. Two previously cited studies [25, 29] used similar methods and materials. Each experiment used single straight-rooted teeth with open apical foramen exposed to normal atmospheric pressure. In the Boutsioukis' experiment, the canals were shaped to a #35/.06 and irrigated with open-ended (NaviTip) needles placed at WL – 1 mm with a delivery rate of 15.6 mL/min. Desai's canals were shaped larger to a #50/.04 and also irrigated with an open-ended (NaviTip) needles placed at WL – 1 mm but at a slower delivery rate of 7 mL/min. The percent extrusion was very similar: Boutsioukis ≈60 % and Desai (larger apical size) recorded ≈70 %. In summary, both studies found that an unrestricted apical foramen permits a very high irrigant extrusion escape from the root canal system as in the case of the maxillary sinus situation described earlier [30].

Maxillary Sinus: NaOCl Incident – Case Reports

One of the earliest case histories of NaOCl extruded into the maxillary sinus reported a relatively benign reaction; the authors stated: "The expected deleterious sequelae were not seen" [31]. The authors described a routine endodontic treatment that resulted in the extrusion event and did not report any needle binding nor any dramatic physiological response, just that the patient indicated the taste of NaOCl in his throat during treatment. Treating the extrusion event consisted of flushing sterile water through the palatal canal of the maxillary first molar and out the maxillary sinus via the ostium. Amoxicillin, a decongestant, and Motrin were prescribed for seven days. Except for a mild soreness associated with the tooth and congestion of the associated maxillary sinus and a brownish material expressed when blowing his nose, the patient made a full recovery. Other case reports were not so favorable; Kavanagh and Taylor [32] reported a similar case with a different outcome. During routine treatment of an upper right second bicuspid, NaOCl was inadvertently injected into the maxillary sinus resulting in acute severe facial pain and swelling. A futile attempt was made to aspirate the extruded NaOCl via the endodontic access opening, resulting in the need to admit the patient for a Caldwell-Luc procedure under general anesthesia. The tooth was eventually extracted three months after the hospital procedure. Recently, a never before described sequelae resulting from the extrusion of NaOCl into the maxillary sinus has been reported [33]. Sleiman, who maintains a practice limited to endodontics, was referred to a patient with a chief complaint concerning an uncomfortable feeling relative to her right maxillary molar region where she had received endodontic treatment several months earlier. The clinical examination was normal, and while the radiographic appearance of the molar region revealed that the maxillary first molar had been treated endodontically, the treatment appeared unremarkable having been properly prepared and obturated; the only exception noted radiographically was a vague appearance of something unusual within the maxillary sinus. This vague appearance resulted in a CBCT scan. The panoramic view (Fig. 6.4a) revealed that tissue filled half the volume of the affected maxillary sinus. A close examination of the posterior maxillary sinus wall (Fig. 6.4b) revealed areas of bone loss. Referring to Fig. 6.5 (red arrow), it must be noted that the posterior wall of the maxillary sinus forms part of the anterior boarder of the infratemporal fossa, an area rich with several complex nerves leaving the cranium, and that exposure to NaOCl has been reported to cause permanent nerve damage [16]. Sleiman postulated that *"Potentially, it could be the position of the patient during the root-canal procedure that made NaOCl stagnate on the posterior wall and aggravate[d] the damage."* When the patient was questioned about the procedure, she reported that during the treatment, she "had a chlorine taste in her throat arising from her nose as a liquid was dripping internally," and on her way home from the endodontic treatment,

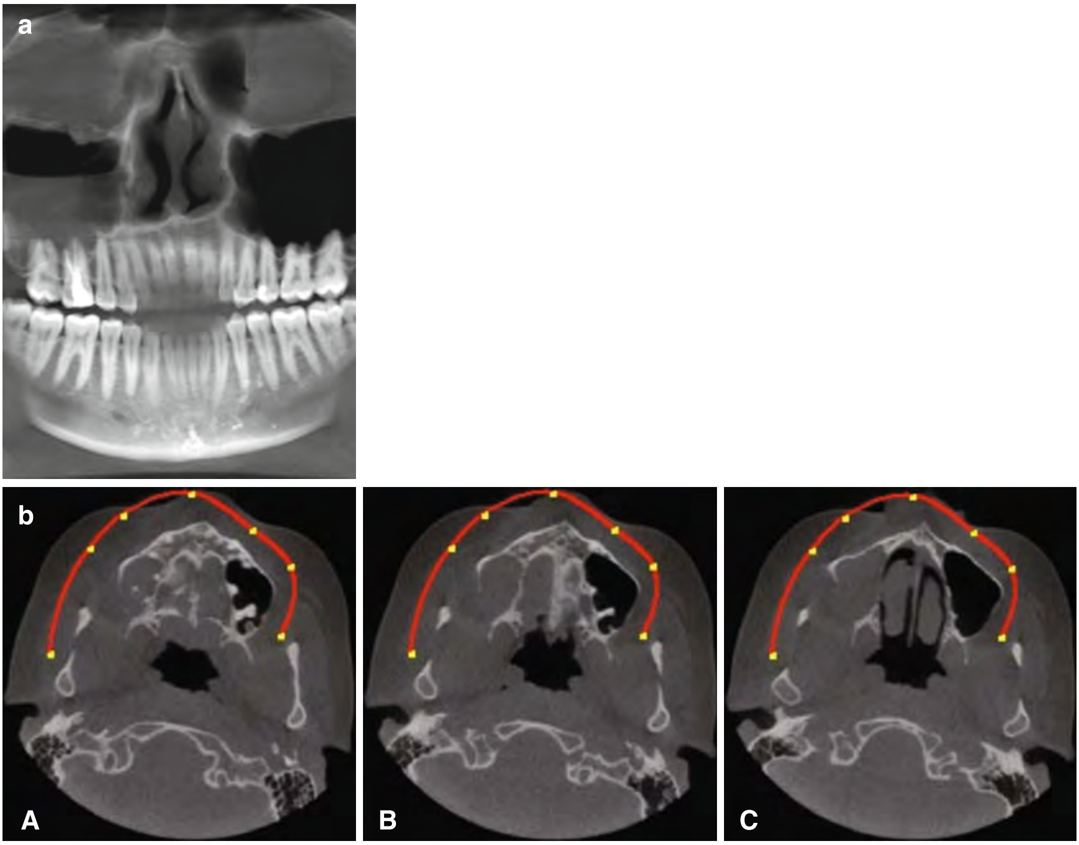

Fig. 6.4 (**a**) Panoramic CBCT scan demonstrates half of the maxillary sinus associated with endodontically treated tooth which is filled with inflammatory tissue (Courtesy of Dr. Philippe Sleiman, Beirut, Lebanon). (**b**) Sectional CBCT scan of same maxillary sinus demonstrates areas of the posterior wall that are nonexistent (Courtesy of Dr. Philippe Sleiman, Beirut, Lebanon)

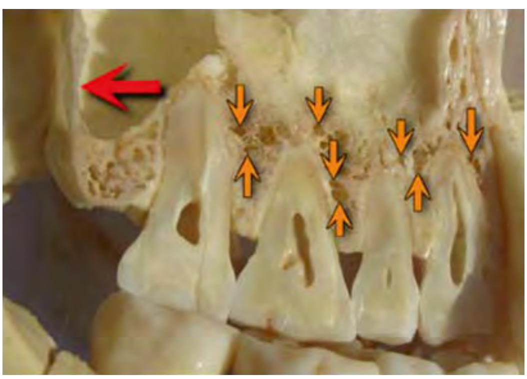

Fig. 6.5 (*Red arrow*) The posterior maxillary sinus wall is a critical anatomical feature because it forms a significant portion of the anterior boarder protecting the infratemporal fossa. In addition to the pterygoid venous plexus, the infratemporal fossa contains the following nerves: mandibular (inferior alveolar, lingual, buccal), plus the otic ganglion and chorda tympani (*Yellow Arrows*). A few of the many abundant sinusoid spaces are identified throughout the maxilla

the strange chlorine type liquid began to drip from her nose. Nothing of further consequence was reported. After viewing the CBCT results, the patient was referred to an otorhinolaryngologist for additional examination and treatment.

Maxillary Sinus: NaOCl Incidents – Treatment and Prevention

These three cited cases represent the spectrum of morbidity associated with extruding NaOCl into the maxillary sinus. Today's imaging technology can, and has revealed heretofore, unknown consequences of extruding NaOCl into the maxillary sinus; therefore, even the most seemingly inconsequential incidents involving extrusion of NaOCl into the maxillary sinus must be approached with caution. The literature universally suggested antibiotic and anti-inflammatory therapeutic treatment in the case of most NaOCl incidents [34, 35]; however, from the CBCT images presented in Fig. 6.4b, it is apparent that in some cases, a consultation with an otorhinolaryngologist may be appropriate in cases involving the maxillary sinus. Regarding prevention, as previously mentioned, the study conducted by Desai was modeled to simulate a root without any resistance to apical extrusion, and balanced to atmospheric as may occur in the maxillary sinus. Desai concluded: "This study concluded that the EndoVac *did not* extrude irrigant after deep intracanal delivery and suctioning the irrigant from the chamber to full working length." In concluding his case study, Sleiman opined: "One of the safest options that we currently have at our disposal is the EndoVac [Apical Negative Pressure] system, which is designed specifically to deliver fresh irrigant all along the root-canal system and, most importantly, to clean the last 3 mm of the root-canal system using the microcannula. It allows us to be certain that no chemicals can go beyond the limits of the root-canal space, nor cause any serious or even minor damage."

Pathognomonic Appearance of NaOCl Extrusion: A Problem

The facial appearance resulting from injecting NaOCl beyond the apical termination of the root canal does not agree with the 1985 Pashley intradermal injection findings. Consider a hypothetical situation whereby excessive amounts of NaOCl exceed the Hypaque extrusion in Fig. 6.1 [20]. If that was the root cause of the NaOCl incident, then according to Pashley in 1985, all of the superficial tissue should be ecchymotic and eventually ulcerate. That doesn't happen. Very specific parts of the face and neck are profoundly affected by ecchymosis: (1) the upper and lower eyelids on one (Fig. 6.6a) [27] or both sides of the face (Fig. 6.6b) [28], (2) the angle of the mouth

Fig. 6.6 (**a**) Upper left cuspid from Mehra et al. [27]. Most edematous and hemorrhagic effects of published NaOCl incidents are hemifacial. Although bilateral circumorbital ecchymosis is not uncommon, this case clearly demonstrates a vascular connection via superficial nasal veins (*arrow*) between both left and right circumorbital venous complexes suggesting that the NaOCl followed the venous connection across the bridge of the nose. (**b**) Upper right cuspid from Hülsmann [28]. There is no apparent venous connection between the orbits as shown in (**a**); thus, only the right side is affected. However, in this unique case, the anterior facial vein is positioned more toward the medial area of the face. Accordingly, *since part of it is not hidden under the malar fat pad*, the entire course of the anterior facial vein from the circumorbital veins to where it courses under the mandible joins the common facial vein which is apparent (Reproduced with permission of Elsevier)

Fig. 6.7 Upper right cuspid from de Sermeño et al. [36]. The ecchymotic pattern of this severe NaOCl incident is classically hemifacial, except where it crosses the bridge of the nose to include left circumorbital area as in Fig. 6.4b. Note the classical absence of ecchymosis in the area of the malar fat pad despite almost all of the middle, lower face and neck being affected

only on the affected side (Fig. 6.6a, b), (3) sometimes the inferior boarder of the mandible only on the affected side (Figs. 6.6b and 6.7) [36], and (4) while other parts of the face, specifically the cheek, are never affected (Fig. 6.7).

Pathognomonic Appearance of NaOCl Extrusion: A New Theory

In 2013 [10], a new theory hypothesized that the NaOCl extrusion incident is not the result of injecting excessive NaOCl into the periapical tissue alone, but rather its direct injection into the venous system, specifically (in most cases) the anterior facial vein and its associated complex of the veins (Fig. 6.3b). This theory evolved from the 1963 study by Rickles et al. [37] initiated by a fatal case history caused by air entering the circulatory system through the root canal space. Their study determined that when the air pressure inside the root canals was increased by using intracanal needles, air would enter the venous system, which would result in a fatal cardiac embolism. Twenty-seven years later, Davies and Campbell [38] reported three fatalities resulting from air entering the vascular system during implant surgery. They specifically stated that “For air embolism to occur there must be an open vessel, a gradient between extravascular and intravascular pressure, and a source of air. Bone tissue is very vascular….” A year prior to the Davies and Campbell paper, Manisali [39] reported an unusual case of canal overfilling (Fig. 6.8). In this unique case report, a radiopaque substance (iodoform paste) was injected into a lower second premolar and was forced out the apical foramen. At first it formed into a disorganized periapical mass similar to the appearance reported by Salzgber, but then within a few millimeters, it formed a second irregular mass that produced a well-defined wavy line extending distally. Manisali opined that the paste could have entered and coursed its way through a vein, not the inferior alveolar canal clearly shown positioned below the wavy line.

A careful examination of Fig. 6.3a shows an ecchymotic threadlike line extending across the upper eyelid. It is clearly the superior palpebral vein that is part of the anterior facial venous network (Fig. 6.3b). A direct vascular connection between the anterior facial vein and the maxillary teeth does, albeit rare, occur [40]. If NaOCl is extruded above a specific pressure gradient through patient’s maxillary right lateral incisor, it could enter a vein connected directly to the anterior facial vein and then spread through the venous complex affecting all areas extending from the upper eyelid to the angle of the mouth and beyond to the heart and the entire vascular system. The cheek would not be affected because the cheek fat pad (malar fat pad) and some of the zygomatic muscular fibers cover the anterior facial vein (Fig. 6.3c), therefore masking the hemorrhage. The case shown in Fig. 6.6b is very unique because it exhibits the full course of the anterior facial

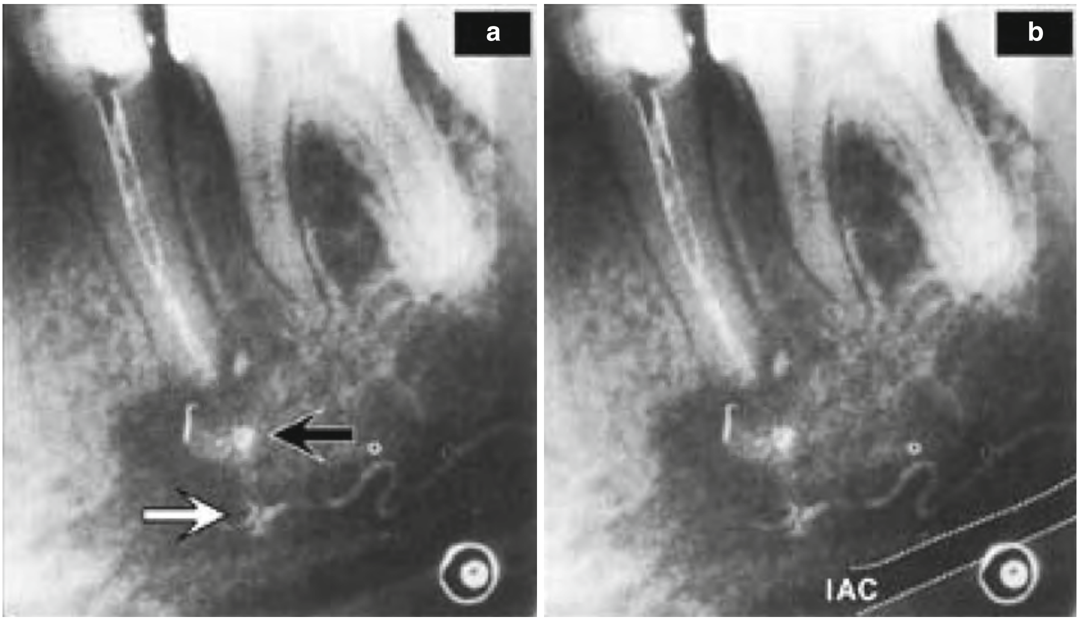

Fig. 6.8 From Manisali et al. [39], this figure shows overfill of iodoform paste which exhibits several unusual features. (**a**) The apical overfill of paste (*black arrow*) initially resembles the disorganized extrusion of Hypaque in Fig. 6.1, but a few millimeters below the initial overfill, a second mass (*white arrow*), appears again as another random mass then forms into a well-organized wavy line. (**b**) This line is not within the inferior alveolar canal (*dotted line*). Also note worthy is the faint radiopacity connecting the two masses. When viewed in its entirety, the paste overfill initially respects no boundaries upon leaving the apical foramen, then it becomes well organized as if running inside a blood vessel as it extends distally above the inferior alveolar canal

venous complex from the eyelids to the area where it courses under the mandible and joins the jugular vein; in this case, the anterior facial vein is positioned more laterally than usual and thus not hidden by the malar fat pad. Except for the inclusion of the other eye, Figs. 6.6a and 6.7 both share the pathognomonic characteristics of Fig. 6.3a including the absence of ecchymosis in the cheek area. Both circumorbital areas apparent in Figs. 6.6a and 6.7 are connected via a complex of superficial veins across the bridge of the nose (black arrow Fig. 6.6a). One apparent flaw in the theory is the fact that veins lack the elasticity of arteries and collapse easily, thus possibly nullifying the theory – but medullary sinusoids do not collapse, and they connect directly to veins. Schoeffel encountered another problem while investigating the uptake of ambient air by a healthy periodontal ligament [41]. He used the lower first premolar of young healthy dogs (Fig. 6.9a) and bonded a 21-gauge needle into a root canal space with an apical foramen prepared to 0.80 mm (Fig. 6.9b), and although the root canal space was pressurized to 175 mmHg above atmospheric pressure, no uptake was measured over 30 min.

Intraosseous Injection

In 1928, Drinker proposed that the intraosseous space be considered a non-collapsible vein [42]. Medullary bone contains thousands of small non-collapsible sinusoids that drain into larger veins [43–45]. The blood pressure in these spaces is approximately 30 mmHg, also known as the ¼ rule or 25 % of normal mammalian blood pressure [46, 47]. Since 1934, the interosseous (IO) space has been used to provide a reliable and safe method for allowing the introduction into systemic circulation [48–56]. Figure 6.10 shows a commercially available device used by the military and civilian medical personnel to establish

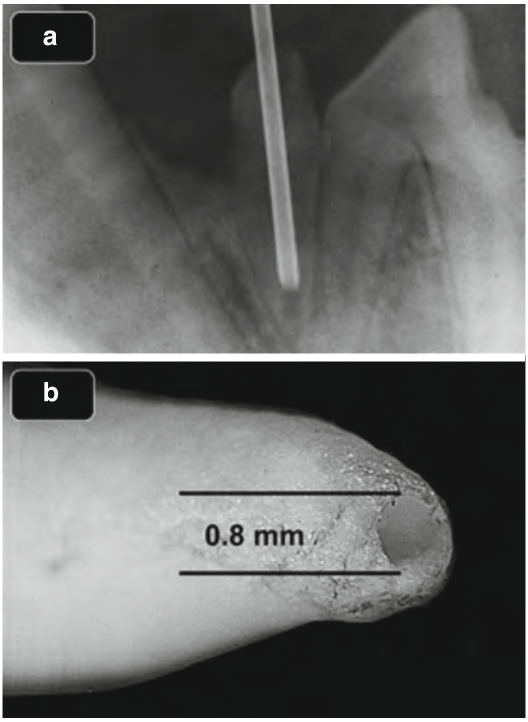

Fig. 6.9 (**a**) Radiograph of 21-gauge needle bonded into the root canal of live dog (From Schoeffel [41]). (**b**) Tooth after extraction demonstrating apical termination opened to 0.8 mm

Fig. 6.10 FAST device for interosseous infusion

rapid access to the venous system. Quoting from the FAST patent application 5,360,711: "It has long been recognized that access to the vascular system is available via bone marrow sinuses. See, e.g., Tocantins et al. [55], Turkel and Bethell, A New and Simple Instrument for Administration of Fluids Through Bone Marrow, *War Medicine*, pp. 222–25 (1944). Infusion of drugs or other fluids into the marrow (intraosseous infusion) results in rapid transmission of such fluids into the vascular system. This method of infusion can be quite important when the patient has very low blood pressure or collapsed veins." Additionally, the IO route is used routinely in dentistry to effect profound anesthesia [57]. Accordingly, constructing an ex vivo model as either "open" or "closed" ignores the very well-established medullary bone space anatomy and physiology relative to the circulatory system. Under the correct conditions, intraosseous injection can occur when the pressure gradient exceeds approximately 30 mmHg [10]. Schoeffel's observations in 1980 seem in conflict with Rickles findings, since he was using a model using a pressure gradient (170 mmHg); however, his observations were correct because the pressure approximated a healthy and intact periodontal ligament, not medullary sinusoids.

Pathognomonic Appearance of NaOCl Extrusion: A New Theory – Support

The Peck Case History

Although the pathognomonic features in Fig. 6.2 are indistinguishable from the classical endodontic NaOCl extrusion incident, the NaOCl extrusion was *not* the result of extrusion via the root canal system. This case resulted from the inadvertent injection of NaOCl instead of lidocaine into an anatomical area where a section of the anterior facial vein complex is located – the patient's right infraorbital space. The significant ecchymosis in the lower eyelid is understandable according to Pashley's 1985 findings, but the fact that the ecchymosis skips the cheek area and becomes apparent again at the angle of the mouth is easily explained by Pashley et al. later in 2013 theory of a direct intravenous injection, (Fig. 6.3b). Although Occam's razor proves nothing, it serves as a heuristic device; in this case history, the simplest solution is that NaOCl was injected directly into the anterior facial vein complex near the inferior palpebral vein and followed its natural course toward the heart.

This recent case history also provides a new and alarming insight regarding the systemic effects of a NaOCl extrusion. Due to the immediate facial swelling and hemorrhage, the patient was directed immediately to visit the emergency department of the nearest hospital. A few days after the event, urine microscopy showed the presence of granular casts. Accordingly, the patient was referred for nephrological evaluation that resulted in the diagnosis of acute kidney injury secondary to renal tubular injury. The nephrologists reported: "We speculate that direct tubular epithelial injury occurred as a result of sodium hypochlorite exposure. This is the first report demonstrating that ATN [acute tubular necrosis] is an important diagnosis to consider after systemic sodium hypochlorite exposure during a dental procedure" [18].

Pathognomonic Appearance of NaOCl Extrusion: Multivaried Factors

Although the long-term consequences of NaOCl extrusion have been reported to vary from benign to life-threatening, it is still a rare event. Why? Three conditions must occur together before an intravenous injection can occur: (1) the apical foramen must be patent, (2) an anatomical variation in the venous drainage must exist that directs the blood flow away from the pterygoid plexus of the veins, and (3) the periapical pressure gradient must communicate with and exceed the sinusoidal pressure of approximately 30 mmHg [10]. Excluding wedging the needle in the root canal system, the pressure gradient factor involves its own subset of contributory factors including (1) rate of delivery, (2) location of the irrigation needle relative to the apical foramen, (3) size and shape of the canal relative to the irrigation, (4) design of the irrigation needle, and (5) the use of positive or negative apical pressure. Interestingly, two recent peer-reviewed articles appeared in the April 2013 issue of the Journal of Endodontics, and both cited venous blood pressure as a possible threshold pressure gradient to be avoided [58, 59]. Park et al. opined: "The data of the present study show that it is quite easy to exceed capillary pressure when the needle is close to the working length even at low flow rates."

Pathognomonic Appearance of NaOCl Extrusion – Periapical Pressure

As previously stated, three basic factors must happen simultaneously in order to produce a NaOCl incident: a patent apex, unusual vasculature anatomy, and access to and pressure exceeding the intraosseous space. Periapical pressure presents the most confusion because several basic subfactors influence this issue: canal configuration, type and position of irrigation needle, irrigant delivery rate, and universal misunderstanding of the anatomy and physiology of the periapical region.

Periapical Pressure Gradient: Historical Misconceptions

Until the recent Zhu et al. [10] paper, many fluid dynamic studies modeled their experiments on the premise that "The apical foramen was simulated as a rigid and impermeable wall" [60–64]. More recent ex vivo studies consider the pressure resistance at the apical foramen to be either "low compliant" (atmospheric pressure) or high compliant (incompressible) [24–26]. With the publication of Zhu et al. in 2013, the dental profession has come to realize the efficacy of the intraosseous (IO) fluid delivery method and now must reevaluate safe periapical pressure gradients at the apical foramen by including the interseptal bone spaces that are so abundant in both arches.

Periapical Pressure Gradient: Irrigation Needle Position and Flow Rate

In an ex vivo study, Khan et al. [59] evaluated the apical pressure produced with different 30-gauge open and side-vented irrigation needles located at WL – 1 mm from the apical termination at different flow rates varying from 1 to >8 mL/min. The

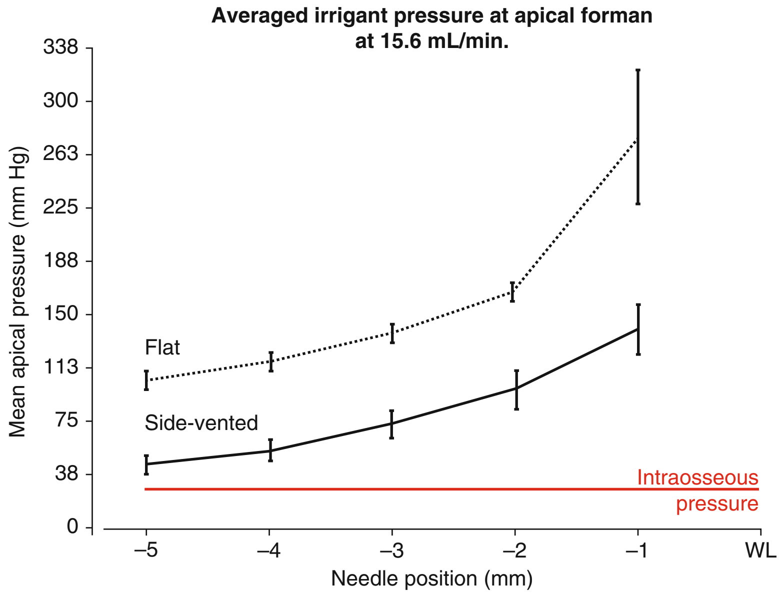

Fig. 6.11 Apical pressures were calculated at a constant *"clinically realistic"* delivery rate (15.6 mL/min.) by using an Unsteady Computational Fluid Dynamics Model. The variables were the depth of needle insertion (WL −1 to −5 mm), and needle configuration - Flat or Side-vented. Note: all pressures recorded exceed normal intraosseous pressure. (From Boutsioukis et al. [63])

Khan study used an ex vivo canal initially shaped to #35/.06 and finally to #40/.02. Boutsioukis et al. [63] employed a similar shape #45/.06 when building their computerized model and positioned their irrigation needles, also 30-gauge open or side-vented, at various working length but at constant flow rate 15.6 mL/min. In both cases, their variables (position or rate of delivery) produced similar results; regardless of needle configuration, the apically directed pressure increased proportionate to either the flow rate or depth of insertion (Figs. 6.11 and 6.12).

Periapical Pressure Gradient: Backflow Resistance – Needle vs. Canal Size

Khan et al. [59] used four different needle types for delivery irrigant via positive pressure; three had an outside diameter of 0.31 mm (Max-i-Probe, NaviTip, and Vpro StreamClean) while one had an outside diameter of 0.38 mm (Vpro EndoSafe). Irrigant was delivered at rates that varied from 1 to >8 mL/min. The recorded pressures are illustrated in Fig. 6.12. All positive pressure needles produced increasing apical >0 mmHg pressure proportionate to the rate of irrigant delivery. The three 0.31 needles produced virtually identical apical pressure, but the 0.38 needle produced dramatically higher apical pressure at the same flow rates, thus proving that resistance to backflow is a direct result of the total surface area available for the irrigant to backflow. The area available for backflow between the canal walls and the tip of a 0.31 needle is .065 mm^2 while the same area for a 0.38 needle is .030 mm^2 or 216 % less surface area. Noting that the thickness of a normal human hair is approximately .07 mm in diameter (the difference between the 0.31 and 0.38 needle), this illustrates that the slightest variation in size or depth of irrigation needles, in critical areas of the root canal, can have profound effects on the final apical pressure.

Periapical Pressure Gradient: Backflow Resistance – Canal Shape

The models used by Boutsioukis et al. [63] and Khan et al. [59] were configured as perfectly round and tapered canals. Although their data was consistent, the models were not representative of the true biological situation. Figure 6.13 demonstrates root canal variations at WL – 1 mm. In the mandibular molar mesial root in Fig. 6.13a, the left canal has limited area for backflow while

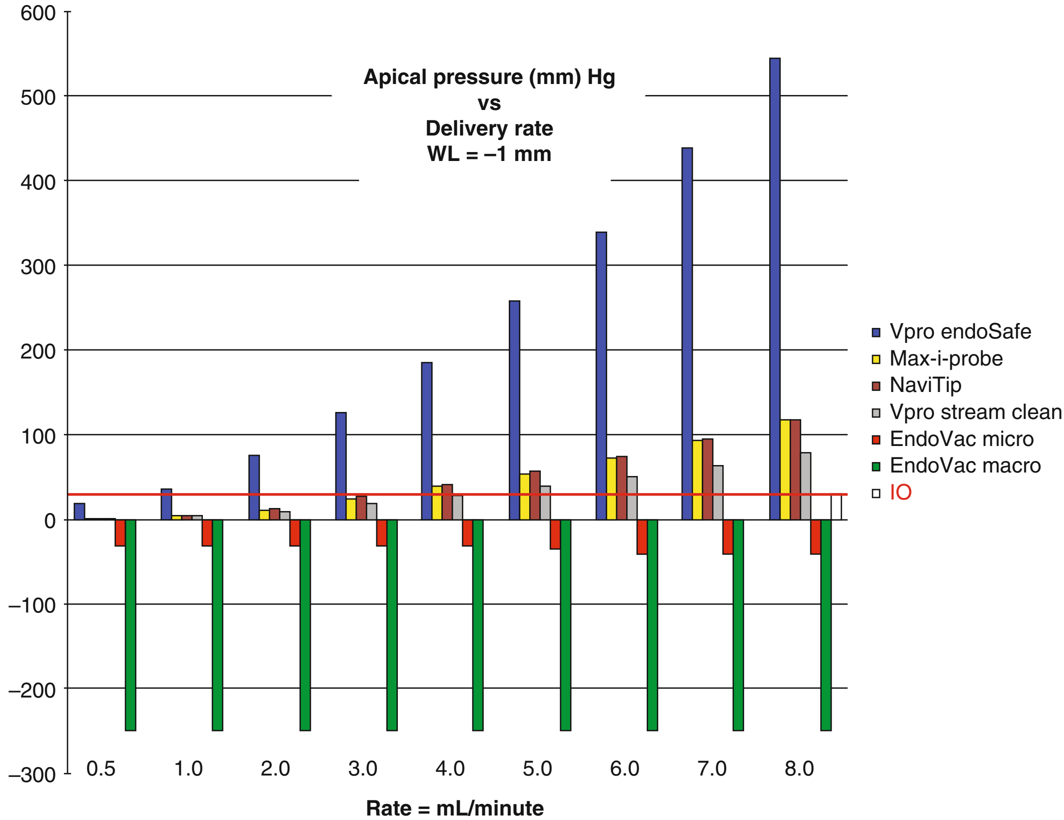

Fig. 6.12 A digital manometer was connected to the apical termination of a root canal model created according to the following parameters: (**a**) material = polycarbonate, (**b**) WL = 17 mm, (**c**) canal preparation #30/.06 followed by #40/.02 at apical seat, and (**d**) needle position = WL – 1 mm [except macro cannula which could not be positioned closer than WL – 4 mm]. Needle designs tested: (1) positive pressure group = Vpro EndoSafe, Max-i-Probe, NaviTip, and Vpro Stream Clean; (2) apical negative pressure group = EndoVac microcannula and macro cannula. In the case of positive pressure, the apical pressure was directly proportionate to increased flow rate. At a flow rate exceeding 3.5 mL/min, all positive pressure needles met or exceed the interosseous (IO) pressure. Conversely, regardless of irrigant flow rates, the negative pressure groups produced a consistent, negative pressures ≈ – 35 mmHg (microcannula) and ≈ – 250 mmHg (macro cannula) (From Khan et al. [59] and Goode et al. [79])

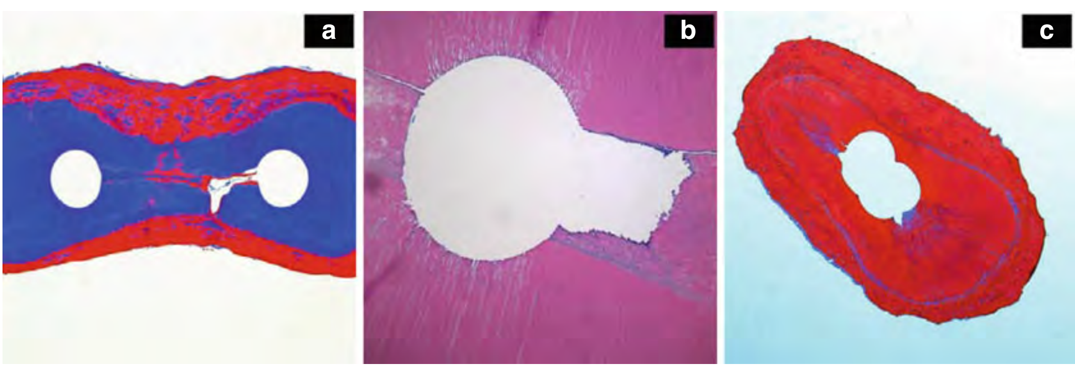

Fig. 6.13 Apical configurations at WL – 1 mm. In keeping with the findings that backflow space affects apical pressure, the intra- and intercanal configurations shown above illustrate different backflow scenarios: (**a**) mesial root lower molar, (**b**) maxillary central incisor, and (**c**) mesial root lower molar

its companion canal demonstrates a fin that obviously increases the backflow area, but if this "fin" is part of an isthmus complex, then entire companion canal could offer a backflow escape route. It is easy to see how two very different apical pressures could be recorded from the same root using the same needle and pressure. In the maxillary anterior root in Fig. 6.13b, although the canal is basically round, a large lateral fin is apparent thus producing a sizeable increased backflow escape area. In mesial root lower molar in Fig. 6.13c, in this situation, both the mesiobuccal and mesiolingual canals converge in the apical millimeter. Irrigant flow directed down either canal at this point will follow the path of least resistance up the companion canal rather than being forced apically. Hess [65] conclusively demonstrated the irregularities of the root canal system, and from the discussion in the previous paragraph, it is apparent that the most seemingly insignificant physical differences in internal anatomical configurations produce profoundly different results even when all other parameters remain constant. Unlike the findings of Boutsioukis and Khan, when reporting their results using human teeth, Park et al. [58] stated: "When the 30-gauge side-vented closed-ended needle was placed at 1 mm from the working length, the apical pressure was unpredictable and oscillated between low and moderate apical pressures."

Periapical Pressure Gradient: Subjective Pressure Factors

A further interesting observation was also reported in the Park experiment. The investigators prepared the mesiobuccal canals of mandibular molars to #35/.06 and used 30-gauge irrigation needles (0.31 mm diameter) placed at −1 mm from WL during one phase of the experiment. Accordingly, at WL – 1 mm, the diameter of the root canal would be 0.41 mm (0.35 + 0.06 mm) thus leaving free space of 0.10 mm (0.41–0.31 mm) and thus making it impossible for binding to occur. However, the investigators noted: "When the needles were placed at 1 mm from the apex, only two needles could be placed at this level in the root canal without binding of the needle tip. These needles included the 30-gauge blunt open-ended (FlexiGlide) needle and the 30-gauge side-vented closed-ended (ProRinse) needle." However, according to the actual preparation geometry vs. the size of the irrigation needle, binding would be physically impossible. The more likely scenario is that the operating clinician experienced the *sensation of binding* as the needles encountered root curvatures, thus demonstrating the highly subjective nature of clinical irrigation methods. It is also important to note that even though Boutsioukis et al. [64] reported an irrigant flow of 15.6 mL/min as a "clinically realistic" flow rate, every one of their apical pressures recording exceeded the intraosseous pressure. Furthermore, in an earlier experiment Boutsioukis et al. [66] surveyed a heterogeneous group of clinicians that included both genders practicing as either endodontists or general dentist and determined that their rates of irrigant delivery varied from 1.2 to 48 mL/min when using a 30-gauge needle, again demonstrating the subjective nature of irrigant delivery techniques.

Preventing the NaOCl Endodontic Incident

The next section will describe treating the NaOCl incident; however, it is imperative to note that since no specific treatment can reverse the initial damages caused due to NaOCl [67], emphasis must be placed on prevention. The previously discussed experiments all proved that flow rates, irrigation needle depth, canal shape, and clinician's subjective delivery technique each affected the periapical pressure. Additionally, until Zhu et al. explained the interosseous route of vasculature infusion, the profession had not been aware that the tissue surrounding the apical termination was not rigid and impermeable. Recalling that Davies and Campbell [38] and Rickles and Joshi [37] reported intravenous air emboli arising from dental procedures as causing patient death, it is important to examine the Bradford et al. [68] study that examined periapical pressures produced via air delivery. Bradford opined in (A) Results: "No needle design or gauge proved safe to use in either round or ovoid canals, regardless of stage of instrumentation" and (B) Discussion: "Vacuum rather than air under pressure, may be a superior means for canal drying."

Several studies have examined vacuum pressure as means of delivering irrigants to the apical termination under various clinical scenarios (Desai, Baumgartner, Khan, and Gondim). In the Desai study, using a totally open apex and equalized atmospheric pressure, no irrigant was expelled during any test. In the Khan study in Fig. 6.12 using a closed system, modeled after Bradford's method, all pressures using apical negative pressure recordings were less than zero meaning not only that irrigants could not be forced *out* of the root canal system but that exudate from the apical area can be aspirated *from* the periapical area (Fig. 6.14).

Treatment of the NaOCl Extrusion Incident

As previously stated, the initial damage from a NaOCl extrusion incident cannot be reversed; therefore, post-extrusion treatment is directed toward preventing further deterioration. Each incident must be evaluated on a case-by-case basis because a multitude of factors must be considered including severity of the incident, allergies to medications, side effects, dosing, and so on. Physiological and systemic concerns must be evaluated on an individual basis, for example, respiratory embarrassment, renal damage, and so on. Accordingly, the following general recommendations are summarized from six sources [28, 69, 70, 33, 18]:

1. Inform the patient regarding the nature of the incident including the possible risks and complications.
2. Hospitalization is required in all cases of respiratory embarrassment or uncontrolled

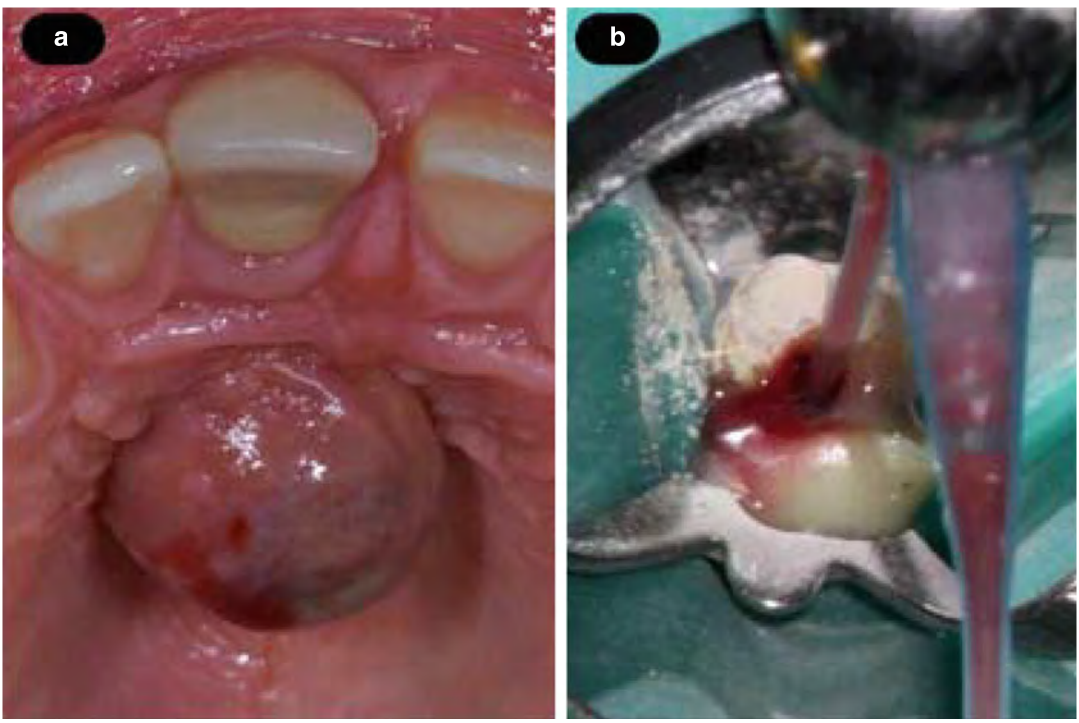

Fig. 6.14 (**a**) A large palatal lesion filled with purulent exudate is aspirated (**b**) using apical negative pressure via the root canal system of associated central incisor (Courtesy of Dr. Filippo Santarcangelo, Bari, Italy)

hemorrhage or when the need for intravenous medications is indicated.
3. Pain control can range from local anesthesia to analgesics.
4. Refer to an otolaryngologist when the maxillary sinus is involved or a nephrologist if the urine appears unusually dark.
5. Use external cold compresses for one day to reduce swelling.
6. After the first day, warm mouth rinses will stimulate blood flow.
7. Daily recall is required to monitor recovery.
8. Antibiotics are not always required but are reserved in cases of high risk or evidence of secondary infection.
9. Corticosteroids are often given, but their use is controversial.
10. Further treatment like surgical intervention, tooth extraction, or sinus procedures must be assessed.

Informed Consent

Fifty years ago, John Ingle published the first modern and extremely well-referenced endodontic textbook: *Endodontics* [71]. That all-inclusive work of the day explained the use of silver points, culturing techniques, and all that was known about NaOCl extrusion in a single sentence. "Care must be taken not to seat the needle tightly in the canal or the solution may be forced through the apical foramina and produce a painful apical periodontitis." Nine years later, the first published NaOCl report of apical extrusion through the apex of an upper second premolar was published; the authors described facial swelling and bleeding into the tissue causing the patient discomfort and distress, "However, recovery occurred in a few days" [72]. In the succeeding decades, endodontics materials, methods, and technology have advanced into the ultramodern age characterized by NiTi instrumentation, electronic apex locators, digital radiography, endodontic microscope, CBCT technology, and the realization that Becker's publication would be followed by NaOCl apical extrusion case histories that included severe sequelae including at least one life-threatening event [14] and some reports of permanent facial nerve damage [16]. In just the last two years, the profession has learned that the direct intraosseous infusion route can deliver NaOCl directly into the circulatory system, without the need to wedge a needle into the root canal [10].

Despite the professions' knowledge concerning the often morbid dangers relative to the NaOCl extrusion incident, it has failed to heed the obligation to warn the patient about the use of NaOCl. Pelka concluded his case history: "Because of this fact and the number of reported cases, it is very important to include the adverse reactions of NaOCl into the normal written information provided to the patient before endodontic treatment. Without such written consent, NaOCl should not be used as an irrigation solution during endodontic therapy." As of this writing, the American Association of Endodontists has a position statement on its website entitled: "Informed Consent Guidelines" [73]. Careful reading of this position paper does not mention a word about the NaOCl extrusion incident; it is quite vague about exactly what the patient needs to know, and it ends with a statement: "These guidelines are not to be considered legal advice. Members should consider their own particular needs and on the basis of those needs, draft forms and procedures for use in their own offices. Recognizing that state statutes regarding informed consent vary, it is recommended that members consult their state statutes when developing their own informed consent forms. A copy of your state statute can be obtained from your attorney or by writing to the local county bar association where you practice or reside."

Like the AAE's position statement, it's beyond this author's, editor's, or publisher's professional field to offer legal advice. That said, the clinician must also understand the therapeutic privilege that permits clinicians to tailor (and even withhold) information when, but only when, its disclosure would so upset a patient that he or she could not rationally engage in a conversation about therapeutic options and consequences. The therapeutic privilege itself can vary from state to state as exemplified in two different opinions. The first is entitled: "Legal and Ethical Myths About Informed Consent" [74]. The second is entitled: "Don't lie, but don't tell the whole truth: The Therapeutic Privilege is it ever justified?" [75]. Accordingly, in order to arrive at a correct and proper informed consent document relative to the NaOCl incident, every practicing dentist must consult his or her own attorney on a state-by-state basis when considering all aspects of informed consent, including the therapeutic privilege. The University of Washington School of Law maintains a convenient resource regarding informed consent laws in the United States on a state-by-state basis [76].

In the alternative to an informed consent document dealing with the NaOCl extrusion incident, Rochelle, an ABOTA [American Board of Trial Advocates], has published an opinion entitled: Has The Doctor's Duty To Warn Been Replaced By the Need For The Doctor To Simply Make The Best Decision For The Patient? The entire text can be read at this website [77]. Rochelle based his opinion on the Johnson v. American Standard, Inc. 43 Cal. 4th 56 (2008) case that recognized the "sophisticated user" doctrine as a defense to both negligence and shift product liability claims based on failure to warn. Rochelle states that the Johnson case is the latest in a trend of decisions that act to relieve the manufacturer of a duty to warn the ultimate user (patient) and places the duty on the doctor to warn the patient. Rochelle's opinion is quoted in Disinfection of Root Canal Systems [78]: "that doctor has the affirmative duty to discuss that product with the patient. Alternatively, has medical science progressed to the degree of specialization that the doctor has the duty to simply select the new, lesser risk device? An example of such a newer medical device recently described in the peer review literature is the EndoVac (Kerr (SybronEndo) Endodontics, Orange, CA) delivery system for endodontic irrigation. Previously, the device utilized for irrigation in the root canal was a simple syringe to introduce sodium hypochlorite into the root canal for irrigation and debridement, an important and standard part of endodontic treatment. While the occurrence of sodium hypochlorite extrusion is uncommon, under any analysis of product liability law, the EndoVac would be the preferred alternative device. It is superior in that, for a minimal cost, it does not sacrifice treatment efficacy and eliminates the risk of severe debilitating injury that can occur from sodium hypochlorite extrusion from positive pressure."

Conclusion

In light of the cytotoxicity of the sodium hypochlorite (NaOCl), its extrusion from the root canal will affect the periapical tissue and may cause the patient a series of complications of variable clinical significance, often beginning with postoperative pain [21].

This does not imply that NaOCl can or should be excluded as an endodontic irrigant; in fact, its use is essential to achieve adequate chemical debridement. What this does imply is that it must be delivered safely.

Apical negative pressure devices such as the EndoVac have been shown to enable irrigants to safely reach the apical one third in voluminous amounts and help overcome apical vapor lock (air entrapment at the apical one third) as well as remove tissue and bacteria throughout the root canal system [80–82].

Apart from being able to avoid air entrapment, the EndoVac system is also advantageous in its ability to deliver irrigants safely to working length without causing their undue extrusion into the periapex [29, 80, 83], as long as manufacturer's recommendations are followed, thereby avoiding NaOCl incidents.

Note and Acknowledgement Figure 11: The pressures recorded for the macro cannula were not reported in the Khan study [59] but were mentioned in Goode [79] as unpublished results. Goode coauthored the Khan study [59].

Dr. John Schoeffel, inventor and royalty recipient (SybronEndo/Kerr Endodontics) of the EndoVac system, originally envisioned the concept of NaOCl traveling in the venous system after scrutinizing the Bradford study [68] and the associated references. I am grateful for his help in explaining the concept of intraosseous fluid delivery and the intracanal fluid dynamics that affect periapical pressure as well as his assistance in organizing the logic path and graphics for this chapter.

Dr. Ovidiu Cioanu (www.ovidiu.ca) produced graphics 4 B and C.

References

1. Black GV. Special dental pathology. Chicago: Medico-Dental Publishing Co; 1915. p. 295.
2. Prinz H. Diseases of the soft structures of the teeth and their treatment. Philadelphia: Lea & Febiger; 1928. p. 225.
3. Bender IB, Seltzer S, Turkenkopf S. To culture or not to culture? Oral Surg Oral Med Oral Pathol. 1964;18:527–40.
4. Seltzer S, Bender IB. Cognitive dissonance in endodontics. Oral Surg Oral Med Oral Pathol. 1965;20:505–16.
5. Spånberg LSW. Editorial. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;102:577–8.
6. Ricucci D, Siqueira Jr JF. Biofilms and apical periodontitis: study of prevalence and association with clinical and histopathologic findings. J Endod. 2010;36(8):1277–88.
7. Nair PN, Henry S, Cano V, et al. Microbial status of apical root canal system of human mandibular first molars with primary apical periodontitis after "one-visit" endodontic treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2005;99:231–52.
8. Clegg MS, Vertucci FJ, Walker C, Belanger M, Britto LR. The effect of exposure to irrigant solutions on apical dentin biofilms in vitro. J Endod. 2006;32(5):434–7.
9. Pashley EL, Birdsong NL, Bowman K, Pashley DH. Cytotoxic effects of NaOCl on vital tissue. J Endod. 1985;11(12):525–8.
10. Zhu WC, Gyamfi J, Niu LN, Schoeffel GJ, Liu SY, Santarcangelo F, Khan S, Tay KC, Pashley DH, Tay FR. Anatomy of sodium hypochlorite accidents involving facial ecchymosis – a review. J Dent. 2013;41(11):935–48.
11. Zairi A, Lambrianidis T. Accidental extrusion of sodium hypochlorite into the maxillary sinus. Quintessence Int. 2008;39(9):745–8.
12. Oreadi D, Hendi J, Papageorge MB. A clinicopathologic correlation. J Mass Dent Soc. 2010;59(3):44–6.
13. Wang S, Chung M, Cheng J, Chen C, Shieh Y. Sodium hypochlorite accidentally extruded beyond the apical foramen. J Med Sci. 2010;30(2):61–5.
14. Bowden J, Ethunandan M, Brennan P. Life-threatening airway obstruction secondary to hypochlorite extrusion during root canal treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;101:402–4.
15. Markose G, Cotter CJ, Hislop WS. Facial atrophy following accidental subcutaneous extrusion of sodium hypochlorite. Br Dent J. 2009;206(5):263–4.
16. Pelka M, Petschelt A. Permanent mimic musculature and nerve damage caused by sodium hypochlorite: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;106(3):e80–3.
17. Bosch-Aranda ML, Vázquez-Delgado E, Gay-Escoda C. Atypical odontalgia: a systematic review following the evidence-based principles of dentistry. Cranio. 2011;29(3):219–26.
18. Peck BW, Workeneh B, Kadikoy H, Abdellatif A. Sodium hypochlorite-induced acute kidney injury. Saudi J Kidney Dis Transpl. 2014;25(2):381–4.
19. Kleier DJ, Averbach RE, Mehdipour O. The sodium hypochlorite accident: experience of diplomates of the American Board of Endodontics. J Endod. 2008;34(11):1346–50.
20. Salzgeber RM, Brilliant JD. An in vivo evaluation of the penetration of an irrigating solution in root canals. J Endod. 1977;3(10):394–8.
21. Gondim Jr E, Setzer F, dos-Carmo CD, Kim S. Postoperative pain after the application of two different irrigation devices in a prospective randomized clinical trial irrigation devices in a prospective randomized clinical trial. J Endod. 2010;36(8):1295–301.
22. 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(12):749–50.
23. Boutsioukis C, Psimma Z, van der Sluis LW. Factors affecting irrigant extrusion during root canal irrigation: a systematic review. Int Endod J. 2013;46(7):599–618.
24. Psimma Z, Boutsioukis C, Vasiliadis L, Kastrinakis E. A new method for real-time quantification of irrigant extrusion during root canal irrigation ex vivo. Int Endod J. 2013;46(7):619–31.
25. Psimma Z, Boutsioukis C, Kastrinakis E, Vasiliadis L. Effect of needle insertion depth and root canal curvature on irrigant extrusion ex vivo. J Endod. 2013;39(4):521–4.
26. Boutsioukis C, Psimma Z, Kastrinakis E. The effect of flow rate and agitation technique on irrigant extrusion ex vivo. Int Endod J. 2014;47(5):487–96.
27. Mehra P, Clancy C, Wu J. Formation of a facial hematoma during endodontic therapy. J Am Dent Assoc. 2000;131(1):67–71.
28. Hülsmann M, Rödig T, Nordmeye S. Complications during root canal irrigation. Endod Topics 2009. 2007;16(1):27–63.
29. Desai P, Himel V. Comparative safety of various intracanal irrigation systems. J Endod. 2009;35(4):545–9.
30. Hauman CH, Chandler NP, Tong DC. Endodontic implications of the maxillary sinus: a review. Int Endod J. 2002;35(2):127–41.
31. Ehrich DG, Brian Jr JD, Walker WA. Sodium hypochlorite accident: inadvertent injection into the maxillary sinus. J Endod. 1993;19(4):180–2.
32. Kavanagh CP, Taylor J. Inadvertent injection of sodium hypochlorite into the maxillary sinus. Br Dent J. 1998;185(7):336–7.
33. Sleiman P. Irrigation for the root canal and nothing but the root canal. Roots. 2012;4:32–33.
34. Mehdipour O, Kleier DJ, Averbach RE. Anatomy of sodium hypochlorite accidents. Compend Contin Educ Dent. 2007;28(10):544–6.
35. Hülsmann M, Hahn W. Complications during root canal irrigation – literature review and case reports. Int Endod J. 2000;33(3):186–93.
36. de Sermeño RF, da Silva LA, Herrera H, Herrera H, Silva RA, Leonardo MR. Tissue damage after sodium hypochlorite extrusion during root canal treatment.

Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2009;108(1):e46–9.
37. 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.
38. Davies JM, Campbell LA. Fatal air embolism during dental implant surgery: a report of three cases. Can J Anaesth. 1990;37(1):112–21.
39. Manisali Y, Yücel T, Erişen R. Overfilling of the root. A case report. Oral Surg Oral Med Oral Pathol. 1989;68(6):773–5.
40. Drake R, Vogl AW, Mitchell AWM. Gray's anatomy for students. 2nd ed. London: Churchill Livingstone/Elsevier; 2009. Chapter 8.
41. Schoeffel GJ. The dynamic response characteristics of the periodontal ligament at the apical foramen to increased intracanal gaseous pressure. Harvard University Master Thesis, Boston; 1980, A-5.
42. Drinker CK, Drinker KR, Lund CC. The circulation in the mammalian bone marrow. Am J Physiol. 1922;62:1–92.
43. Draenert K, Draenert Y. The vascular system of bone marrow. Scan Electron Microsc. 1980;4:113–22.
44. Oni OO, Stafford H, Gregg PJ. An investigation of the routes of venous drainage from the bone marrow of the human tibial diaphysis. Clin Orthop Relat Res. 1988;230:237–44.
45. de Saint-Georges L, Miller SC. The microcirculation of bone and marrow in the diaphysis of the rat hemopoietic long bones. Anat Rec. 1992;233:169–77.
46. Kofoed H. Intraosseous pressure, gas tension and bone blood flow in normal and pathological situations: a survey of methods and results. Bone Circulation and Vascularization in Normal and Pathological Conditions. NATO ASI Ser. 1993;247:101–11.
47. Gurkan UA, Akkus O. The mechanical environment of bone marrow: a review. Ann Biomed Eng. 2008;36:1978–91.
48. Helm M, Breschinski W, Lampl L, et al. Intraosseous puncture in preclinical emergency medicine. Experiences of an air rescue service. Anaesthesist. 1996;45(12):1196–202.
49. Josefson A. A new method of treatment – intraosseous injections. Acta Med Scand. 1934;81:550–64.
50. Arbeiter HI, Greengard J. Tibial bone marrow infusion in infants. J Pediatr. 1944;25:1–12.
51. Elston JT, Jayne RV, Kaump DH, et al. Intraosseous infusions in infants. Am J Clin Pathol. 1947;17:143–50.
52. Heinild S, Sondergaard T, Tudvad F. Bone marrow infusion in childhood: experiences from a thousand infusions. J Pediatr. 1947;30:400–12.
53. Tocantins LM. Rapid absorption of substances injected into the bone marrow. Proc Soc Exp Biol Med. 1940;45:292–6.
54. Tocantins LM, O'Neil JF. Infusions of blood and other fluids into the general circulation via the bone marrow. Surg Gynecol Obstet. 1941;73:281–7.
55. Tocantins LM, O'Neil JF, Jones HW. Infusions of blood and other fluids via the bone marrow. JAMA. 1941;117:1229–34.
56. Tocantins LM, O'Neil JF. Complications of intraosseous therapy. Ann Surg. 1945;122:266–77.
57. Brown R. Intraosseous anesthesia: a review. J Calif Dent Assoc. 1999;27:785–92.
58. Park E, Shen Y, Khakpour M, Haapasalo M. Apical pressure and extent of irrigant flow beyond the needle tip during positive-pressure irrigation in an in vitro root canal model. J Endod. 2013;39(4):511–5.
59. Khan S, Niu LN, Eid AA, Looney SW, Didato A, Roberts S, et al. Periapical pressures developed by nonbinding irrigation needles at various irrigation delivery rates. J Endod. 2013;39(4):529–33.
60. Boutsioukis C, Lambrianidis T, Kastrinakis E. Irrigant flow within a prepared root canal using various flow rates: a computational fluid dynamics study. Int Endod J. 2009;42(2):144–55.
61. Boutsioukis C, Gogos C, Verhaagen B, Versluis M, Kastrinakis E, Van der Sluis LW. The effect of apical preparation size on irrigant flow in root canals evaluated using an unsteady computational fluid dynamics model. Int Endod J. 2010;43(10):874–81.
62. Boutsioukis C, Gogos C, Verhaagen B, Versluis M, Kastrinakis E, Van der Sluis LW. The effect of root canal taper on the irrigant flow: evaluation using an unsteady computational fluid dynamics model. Int Endod J. 2010;43(10):909–16.
63. Boutsioukis C, Lambrianidis T, Verhaagen B, Versluis M, Kastrinakis E, Wesselink PR, van der Sluis LW. The effect of needle-insertion depth on the irrigant flow in the root canal: evaluation using an unsteady computational fluid dynamics model. J Endod. 2010;36(10):1664–8.
64. Boutsioukis C, Verhaagen B, Versluis M, Kastrinakis E, Wesselink PR, van der Sluis PR. Evaluation of irrigant flow in the root canal using different needle types by an unsteady computational fluid dynamics model. J Endod. 2010;36(5):875–97.
65. Hess W. The anatomy of the root-canals of the teeth of the permanent dentition. New York: Wood; 1925.
66. 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(7):504–13.
67. Tegginmani VS, Chawla VL, Kahate MM, Jain VS. Hypochlorite accident – a case report. Endodontology (Indian Endod Soc). 2011;23:89–94.
68. Bradford CE, Eleazer PD, Downs KE, Scheetz JP. Apical pressures developed by needles for canal irrigation. J Endod. 2002;28(4):333–5.
69. Spencer HR, Ike V, Brennan PA. Review: the use of sodium hypochlorite in endodontics—potential complications and their management. Br Dent J. 2007;202(9):555–9.
70. Hales JJ, Jackson CR, Everett AP, Moore SH. Treatment protocol for the management of a sodium hypochlorite accident during endodontic therapy. Gen Dent. 2001;49:278–81.
71. Ingle JI. Endodontics. Philadelphia: Lea & Febiger; 1965. p. 175–6.

72. Becket GL, Cohen S, Borer R. The sequelae of accidentally injecting sodium hypochlorite beyond the root apex. Oral Surg. 1974;38:633–8.
73. http://www.aae.org/uploadedfiles/publications_and_research/guidelines_and_position_statements/informedconsent.pdf.
74. Meisel A, Kuczewski M. Legal and ethical myths about informed consent. Arch Intern Med. 1996;156(22):2521–6.
75. Edwin AK. Don't lie but don't tell the whole truth: the therapeutic privilege is it ever justified? Ghana Med J. 2008;42(4):156–61.
76. http://uwtortswikimiller.wikifoundry.com/page/California [Note to reader: Opening this website will open on California, but the other states are listed on the left].
77. http://rochellegriffith.com/2009/11/02/has-the-doctors-duty-to-warn-been-replaced-by-the-need-to-simply-make-the-best-decision-for-the-patient-endovac-use-in-root-canals.
78. Cohenca N. Disinfection of root canal systems: the treatment of apical periodontitis. Ames: Wiley; 2014. p. 163.
79. Goode N, Khan S, Eid AA, Niu LN, Gosier J, Susin LF, Pashley DH, Tay FR. Wall shear stress effects of different endodontic irrigation techniques and systems. J Dent. 2013;41(7):636–41.
80. Nielsen BA, Craig Baumgartner J. Comparison of the EndoVac system to needle irrigation of root canals. J Endod. 2007;33:611–5.
81. Ribeiro EM, Silva-Sousa YTC, Souza-Gabriel AE, Sousa-Neto MD, Lorencetti KT, Silva SRC. Debris and smear removal in flattened root canals after use of different irrigant agitation protocols. Microsc Res Tech. 2012;75:781–90.
82. Shin S-J, Kim H-K, Jung I-Y, Lee C-Y, Lee S-J, Kim E. Comparison of the cleaning efficacy of a new apical negative pressure irrigating system with conventional irrigation needles in the root canals. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109:479–84.
83. Malentacca A, Uccioli U, Zangari D, Lajolo C, Fabiani C. Efficacy and safety of various active irrigation devices when used with either positive or negative pressure: an in vitro study. J Endod. 2012;38:1622–6.