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STUDIES ON THE ROOT FILLING CEMENT BI-OXOL

A CLINICAL, ROENTGENOLOGICAL AND HISTOLOGICAL INVESTIGATION

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Twenty-five human incisors and canines with healthy pulps were used. Partial pulpectomy and subsequent root filling with Bi-oxol was performed in 11 cases, while in 14 cases the entire pulp was removed and the root filling material intentionally pushed through the foramen. The teeth were examined clinically and radiographically throughout the observation period, which varied from 2-- to 32 1/2 months. Eighteen of these cases were also studied histologically.

It was found that Bi-oxol in contact with vital tissue caused inflammation of varying extent. Gross overfilling resulted in more extensive inflammation than mere contact of the root filling material with the residual pulp. The root filling material was resorbed in the canal in cases of partial pulpectomy. Resorption was somewhat more rapid when the material was implanted in the periapical region. Granulation tissue invaded the canal to replace Bi-oxol. In cases of partial pulpectomy, no radiographic changes were recorded, whereas total pulpectomy with overfilling produced radiographic changes. Overfilling with severe inflammation observed histologically also gave clinical symptoms. The length of the residual pulp was found to be less in the sections than indicated by radiographs.

The aim of this investigation has been to study the reaction of human tissue to the root filling cement Bi-oxol (*Nielsen*, 1963, 1965) and to compare the histological and clinical-radiographical findings.

Bi-oxol consists of a fluid chelating agent, 7-N-propyl-8-hydroxyquinoline, which reacts with bismuth oxide to form a cement with the following special properties (*Nielsen*, 1965): 1) expands during setting, 2) is resistant to bicarbonate ions in lymph and interstitial fluid, so that it is, unlike ZnO/eugenol, not destroyed by any seepage into the canal, 3) is impervious to bacteria, 4) is bactericidal, 5) yields excellent X-ray contrast.

With respect to the biological properties of this cement, *Nielsen* (1965) stated that subcutaneous injection of thin suspensions of Bi-oxol in mice

elicited decidedly less tissue reaction than ZnO/eugenol. This was contradictory to the findings of *Curson* and *Kirk* (1968) where 10 different root filling cements, both set and unset, were inserted intramuscularly in rats. Bi-oxol was then found to elicit the strongest reaction of all cements, including ZnO/eugenol.

MATERIAL AND METHOD

The material comprised 25 incisors and canines selected in patients due for maxillary immediate full denture. The patients comprised 14 women and 10 men aged 34 to 62 years, with an average age of 47 years. All the teeth were examined clinically and radiographically at half-yearly intervals after treatment. Eighteen cases were also studied histologically. The total observation period varied from 2 to 32 1/2 months. (Table I.)

Teeth with more than 70 % bone loss, gingival pockets deeper than 2/3 of the root length or complicated caries were excluded. All teeth were vital, and bleeding occurred in all cases upon pulp exposure. Leostesin-noradrenaline® 2 % was used for local anaesthesia.

During the endodontic procedure rubber dam was applied, and the field of operation was swabbed with 3 % hydrogen peroxide for 1 min., followed by 2 % benzalkonium chloride for 1 min. Two differing procedures were used, one aiming at a partial filling, the other at overfilling. The pulp was removed by means of a blunted Hedström file to a depth of 1/2 to 4 mm from the apical foramen as indicated by radiography. In those cases where overfilling was aimed at, the apical foramen was enlarged with a blunted Hedström file no. 3 or no. 4.

During filing, the canal was irrigated with 0.9 % sodium chloride. Haemorrhage which persisted after drying with sterile paper points was arrested with 3 % or 35 % hydrogen peroxide. No bacteriological test was carried out before filling.

Bi-oxol was rotated into the canal with a Lentulo spiral on a contra-angle handpiece, and a pre-fitted gutta-percha point was inserted. Care was taken to ensure that only the cement was in contact with residual pulp or periapical tissue, the gutta-percha point acting merely as a piston.

Root resection at the end of the observation period was performed according to the method described by *Nygaard-Ostby* (1939), in which a cone-shaped block with the base in the facial cortical bone, containing the root apex and surrounding bone, is removed surgically from the jaw. The block was fixed in 4 % aqueous formaldehyde solution and decalcified in a formic acid

Table I
Survey of the material and the results

Case number	Partial pulpectomies													Total pulpectomies																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25									
Observation period in months	7	2½	15	18	15	11½	3	13	32½	24	2	12	14	26½	10	18	8	16	16	15	16½	12	16	22	16									
<i>Clinical symptoms</i>	—	—	+	+	+	+	*	+	+	—	—	—	—	—	—	+	—	—	+	—	+	+	—	—	+									
After 8 days	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—									
At time of resection	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—									
At conclusion of observation period	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—									
<i>Radiographical changes</i>																																		
Enlarged periodontal membrane, broken lamina dura	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—								
Area of rarefaction	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—								
Resorption of root apex	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—								
Periapical resorption of Bi-oxol	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—								
Resorption of Bi-oxol in the canal	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—								
<i>Histological assessment</i>																																		
No inflammation	+																																	
Slight inflammation in residual pulp	+	+	+	+	+	(+)																												
Slight inflammation in the periodontal membrane													+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			
Severe inflammation in the periodontal membrane													+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

*) Clinical and radiographical information lacking.

sodium citrate solution of pH 2.4. After washing for 24 hours in running water, the tissue was double embedded in celloidin and paraffin wax. Sections 8–10 μm thick were then stained in Mayer's or Harris' haematoxylin-eosin.

RESULTS

Clinical assessment. Out of the 11 teeth in which partial pulpectomy had been performed, occlusion was painful in six within the first 8 days after extirpation, but no symptoms were recorded in the remaining observation period (Table I). In one case (no. 7), information is lacking.

Out of the 14 teeth where overfilling had been performed, symptoms were present within the first 8 days in seven, varying from pain on occlusion in five cases to spontaneous pain in two cases (nos. 19, 21).

In two cases (nos. 21, 22) the teeth were slightly tender to percussion and apical finger pressure throughout the observation period. In both these cases, and one further case (no. 20), perforation of the facial bone lamella and suppuration was revealed on resection.

Radiographical assessment. All teeth with partial pulpectomies (with the exception of no. 9) were assessed favourably throughout the observation period, no increase in the width of the periodontal membrane or broken lamina dura being observed.

Information was lacking in one case (no. 7). Bi-oxol seems to have been partially resorbed in the canal in two cases (nos. 3, 9).

In those cases where the canal was overfilled (with the exception of no. 12), a broken lamina dura, an increase in the width of the periodontal membrane, periapical radiolucency, resorption of the root apex and resorption of Bi-oxol periapically or in the canal were found, as shown in Table I.

HISTOLOGICAL ASSESSMENT

I. Partial pulpectomy. Only one (no. 1) of the seven teeth exhibited a normal residual pulp. Fig. 1 shows apposition of hard tissue to the wall along the entire length of the residual pulp, but in particular in relation to the numerous dentine particles lying between the pulp stump and the Bi-oxol.

In five cases (nos. 2–6), no inflammation was observed in the periodontal membrane. In one of these (no. 6), sections of the residual pulp were not obtained. In the other four specimens, the residual pulp was seen to be slightly inflamed, containing varying numbers of lymphocytes and plasma

Table II.
Length of residual pulp in millimetres

No.	Radiograph	Histological specimen
1	3	1.3
2	3	1.3
3	1	0.8
4	1	1.3
5	2	1.0
7	1/2	0.0

cells, especially in the immediate vicinity of the Bi-oxol (Fig. 2). Macrophages containing Bi-oxol were also found, (Fig. 3), not only in relation to the filling, but also sporadically in the rest of the pulp stump. In three cases (nos. 3, 4, 5), hard tissue apposition at the infundibulum was observed (Fig. 2).

In one case (no. 7), the histological section revealed that total pulpectomy had occurred, and the periodontal membrane was dominated by loose granulation tissue containing numerous lymphocytes and plasma cells.

Measurement on radiographs gave a length for the pulp stump of 1/2 to 4 mm. In six cases, its length was measured in the sections (Table II). In all cases (except no. 4, where special circumstances obtained, see Fig. 10), it was seen that the true length was less than the radiograph would indicate.

II. Total pulpectomy with overfilling. In eight cases (nos. 12–19) where overfilling had been carried out, granulation tissue was found in the periodontal area, more or less dominated by lymphocytes and plasma cells (Fig. 4). This has been characterized as slight inflammation in Table I. In a few specimens small accumulations of polymorphonuclear leucocytes were found in the immediate vicinity of Bi-oxol. In all the specimens, numerous Bi-oxol granules 2–3 μm in diameter were observed, both free and phagocytized by macrophages and multinuclear giant cells of foreign body type (Fig. 5). Resorption of root apices and alveolar bone was observed, with newly formed hard tissue occupying many of the lacunae thus formed. In those cases where Bi-oxol had been resorbed, newly formed collagenous connective tissue and numerous osteoblast strands were seen in the periodontal area. The Bi-oxol was in some cases (nos. 12, 14, 15, 16, 17, 19) resorbed in the canal and replaced by granulation tissue of the same type as that in the periodontal area (Fig. 4). In two cases (nos. 18, 19), the cavity in the periodontal tissue

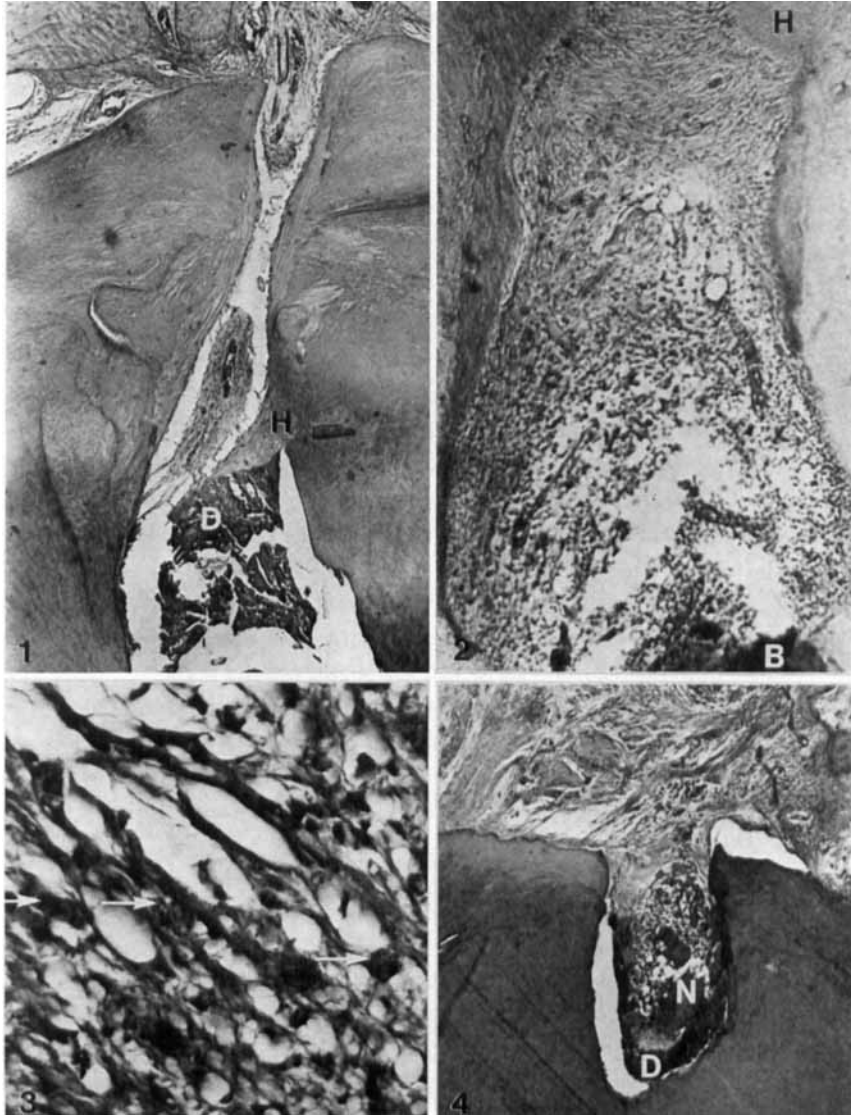


Fig. 1. No. 1. Partial pulpectomy — residual pulp ($\times 50$). Adjacent to dentine fragments (D), hard tissue apposition (H) has occurred after resorption. Similar tissue is also seen along the entire length of the remaining pulp. There are no inflammatory cells in the pulp, which contains blood vessels in the centre. The empty spaces are artefacts.

Fig. 2. No. 3. Partial pulpectomy — residual pulp ($\times 125$). Numerous lymphocytes are present and there is resorption in the wall along the Bi-oxol (B). Nearer the apex fewer inflammatory cells are seen, and hard tissue apposition (H) has occurred, tending to close the foramen.

Fig. 3. No. 4. Partial pulpectomy — residual pulp ($\times 500$). Macrophages (arrows) contain Bi-oxol. The empty spaces are due to the tumefacient effect of the acid on connective tissue.

which had been occupied by a gutta-percha point *in vivo* was seen to be surrounded by normal connective tissue without inflammatory cells (Fig. 6). In no. 19, Bi-oxol was seen to be undergoing resorption in the canal, between the gutta-percha point and the canal wall.

In one case where overfilling was moderate (no. 20), and in two cases where it was gross (nos. 21, 22), severe inflammation was seen, with the periodontal area dominated by inflammatory cells, mainly lymphocytes and plasma cells, which were also observed well out in the marrow space of the surrounding bone (Fig. 7). This type of inflammation was characterized as severe inflammation in Table I.

DISCUSSION

On account of the difficulty of finding suitable contralateral teeth, a direct evaluation of Bi-oxol relative to recognized root filling materials has not been carried out. Because the material comprised patients due for maxillary immediate full denture, the average age was relatively high. However, according to *Castagnola* (1952) and *Strindberg* (1956) this should have no influence on the result. *Ketterl* (1965) concluded, on the basis of clinical experience, that load affects the rate of healing after root canal treatment. All the patients in the present investigation had for a varying length of time only the incisors and canines in occlusion and articulation. This may have some bearing on the evaluation of the material as a whole, but there seems to be no indication that the severe inflammation observed in some of the cases was due to particularly unfortunate functional patterns. (All prosthetic records have been scrutinized with respect to occlusion and articulation.)

It was characteristic that Bi-oxol in contact with vital tissue, either residual pulp or periodontal tissue, produced inflammation of varying extent according to how much of the material was in tissue contact. Moreover, Bi-oxol was resorbed and could be demonstrated in macrophages and giant cells (Figs. 3, 5). Thus the root filling cement resembled the resorbable root filling pastes, which, however, quickly disappear from the periapical tissue.

Nicholls (1967) defined resorbable pastes as those which do not set after being introduced into the root canal and which are rapidly removed if forced

Fig. 4. No. 14. Total pulpectomy and overfilling with Bi-oxol. Granulation tissue has invaded the canal after the resorption of Bi-oxol ($\times 50$). Furthest up the canal are dentine fillings (D), followed by disintegrating Bi-oxol interspersed with necrotic tissue (N) and loose granulation tissue. In the periodontal area, granulation tissue is seen with occasional accumulations of lymphocytes and plasma cells.

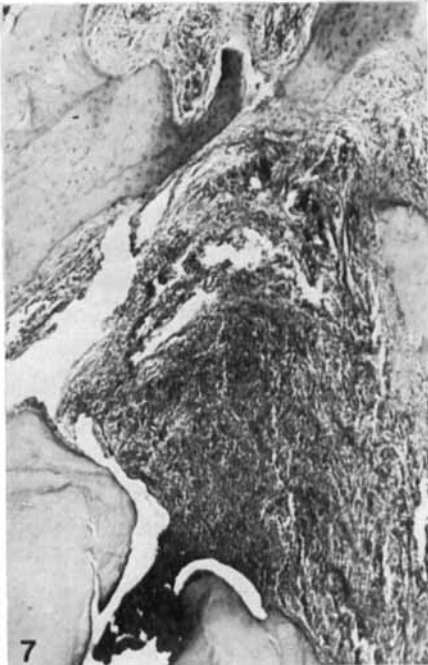
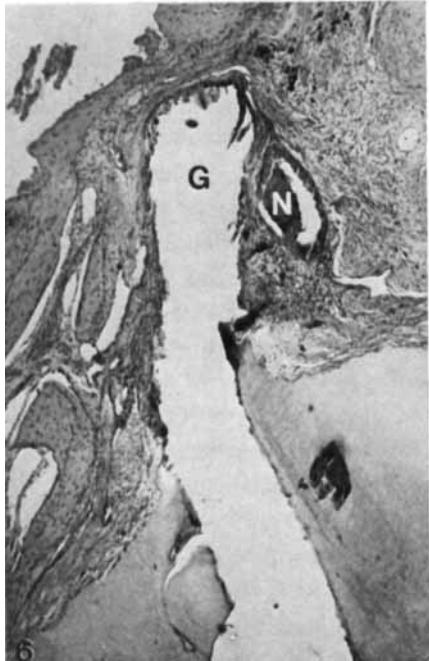
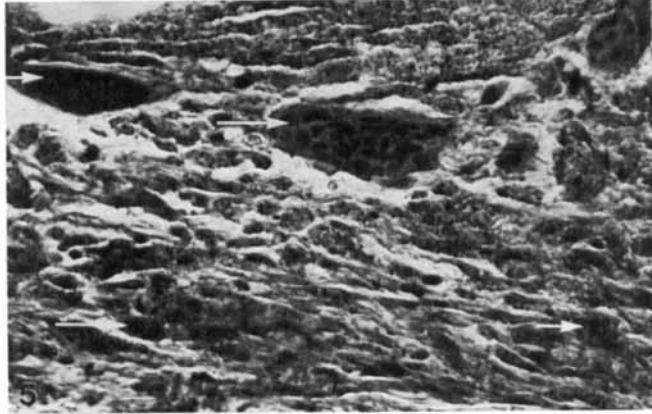


Fig. 5. No. 18. Giant cells and macrophages (arrows) containing Bi-oxol ($\times 400$). Necrotic tissue (N) with Bi-oxol is seen above.

Fig. 6. No. 18. Total pulpectomy and overfilling with a gutta-percha point and Bi-oxol ($\times 50$). The empty cavity (G), which has contained the gutta-percha point, is seen to be circumscribed by connective tissue without inflammation. To the right are inflammatory cells and necrotic tissue (N) with Bi-oxol. (Same specimen as Fig. 5.)

Fig. 7. No. 21. Total pulpectomy and overfilling with Bi-oxol ($\times 50$). The periodontal area is dominated by inflammatory cells, mainly lymphocytes. Also the marrow spaces contain granulation tissue with lymphocytes clustering around Bi-oxol residue.

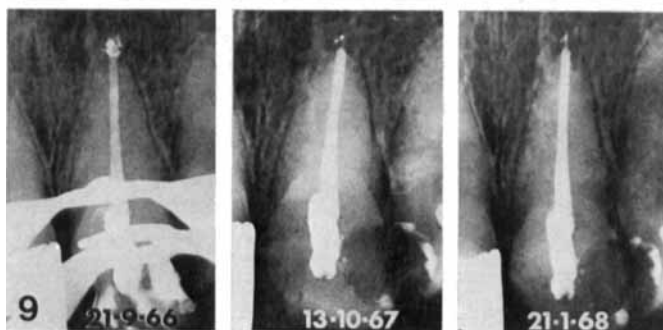
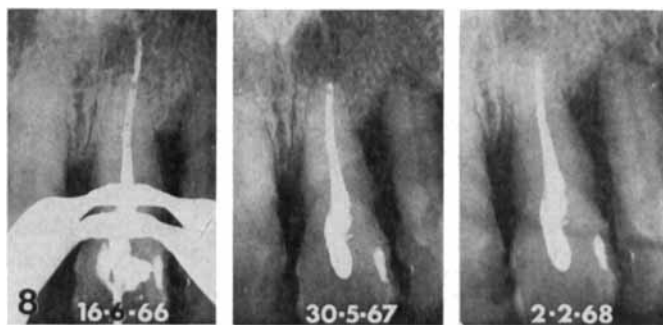
into the periapical region. This is in contrast to the so-called non-resorbable materials which, when in the form of cements, set after insertion, and whose gradual resorption does not extend into the canal itself. *Castagnola* (1952) required that any excess of root filling material be readily absorbable, while *Nygaard-Østby* (1939), for instance, propounded that if a root filling cement is resorbed beyond the root apex, it will also be resorbed inside the canal. *Hess* (1960) demonstrated that Walkhoff's resorbable root filling paste was followed into the canal by granulation tissue which developed into connective tissue, with a subsequent apposition of cementum at the apical foramen. *Honegger* showed as early as 1932, however, that the tissue which invades the canal after resorption of Walkhoff's paste may be inflamed. The present investigation has also demonstrated chronic non-specific inflammation of the invading tissue after resorption of Bi-oxol.

Resorption was most rapid in the periodontal space and bone and slower in the root canal, where there was a smaller contact surface between Bi-oxol and vital tissue (Fig. 8). This confirms the investigation of *Erausquin & Muruzábal* (1969) on resorbable root filling pastes in rat molars, where the slower resorption in the root canal was attributed to the poorer blood supply. Resorption of Bi-oxol might also be observed in cases of partial pulpectomy.

Feldman et al. (1965) and *Cutiérrez et al.* (1969) described resorption of gutta-percha points, the latter on the basis of implants in hares, where gutta-percha granules were demonstrated in macrophages. They concluded that overfilling with gutta-percha did not prevent healing, but delayed it. In *Nyborg & Tullin's* study (1965), two cases of total extirpation in human material were described, one with slight overfilling. Each tooth was filled with gutta-percha points and chloropercha. Unspecified root filling material was found intracellularly in giant cells, and in both cases the periapical tissue was characterized as granulation tissue, dominated by lymphocytes and plasma cells.

In the two present cases (nos. 18, 19), where the gutta-percha point was similarly forced out into the periapical tissue, no resorption of the point was observed (Fig. 6, 9). Neither did *Lantz & Persson* (1967) or *Strömberg* (1969) find resorption of gutta-percha points in their experiments on dogs.

Numerous investigations, radiographical (e.g. *Strindberg*, 1956; *Seltzer et al.*, 1965) as well as histological (both in man, e.g. *Nygaard-Østby*, 1969; *Ketterl*, 1965; *Nyborg & Tullin*, 1965; *Seltzer et al.*, 1969, and in animals, *Muruzábal & Erausquin*, 1966, *Rowe*, 1967; *Erausquin & Muruzábal*, 1968; *Bordoni & Erausquin*, 1970) have shown that overfilling gives more dubious prognosis than when the filling stops 1–2 mm short of the apical foramen. Undoubtedly the biological properties of the root filling material



affect the reaction in the pulp stump and the periodontal tissue. In addition, the extent of instrumentation is an important factor. *Seltzer et al.* (1968) have demonstrated in man and in animals that the trauma caused by instrumentation beyond the apex was greater than that resulting from extirpation confined to the pulp cavity.

In all cases where a partial pulpectomy had been carried out in the present investigation (except no. 9) an intact lamina dura was demonstrated throughout the observation period. Histologically, a slight chronic inflammation was seen in the residual pulp, whereas the periapical region was unaffected. The absence of inflammation in one residual pulp (no. 1, Fig. 1) was probably due to the fact that Bi-oxol was not in direct contact with the pulp tissue, but separated from it by numerous dentine particles.

The total pulpectomies with moderate or gross overfilling all showed (except no. 12) radiographical changes, as is apparent from Table I. Histologically, slight or severe inflammation, mainly of a chronic nature, was seen in the periapical region. In three cases with severe inflammation (nos. 20, 21, 22), clinical symptoms were reported at the time of resection. This means that as far as total pulpectomy is concerned, in contrast to *Ketterl's* (1963) results, radiographical and histological findings were to some extent correlated. However, only the most severe inflammations manifested themselves clinically.

It cannot entirely be ruled out that the severe reaction to overfilling with Bi-oxol in no. 22 was caused by hypersensitivity to hydroxyquinoline (*Leifer & Steiner*, 1951; *Hjorth*, 1967), as this patient was allergic to certain medicaments. It has not been possible to recall the patient for verification.

The present investigation thus seems to confirm the findings of *Curson and Kirk* (1968), that Bi-oxol is a strong irritant, although no direct comparison

Fig. 8. Radiographs from case No. 14. Total pulpectomy and overfilling with Bi-oxol. The surplus has been resorbed most rapidly in the periapical region and somewhat more slowly in the canal.

(Same specimen as Fig. 4.)

Fig. 9. Radiographs from case No. 18. Total pulpectomy and overfilling with a gutta-percha point and Bi-oxol. Bi-oxol has been resorbed, but not the gutta-percha point. (Same specimen as Figs. 5 and 6.)

Fig. 10. No. 4. Partial pulpectomy — residual pulp ($\times 50$). The pulp stump is longer than indicated by the radiograph, perhaps because of the curvature of the root canal. The root filling does not follow this, and residual pulp extends slightly coronally to the apical limit of the root filling. The length of the residual tissue will be obscured in the radiograph by the opaque root filling. (Same specimen as Fig. 3). Only a slight reaction to Bi-oxol is seen in this specimen, probably because of the presence of the numerous dentine particles (D) in contact with the residual pulp. Bi-oxol and necrotic tissue (N) are seen in the middle of the picture.

with other root filling materials was performed. There is no indication that Bi-oxol can be implanted without eliciting a tissue reaction.

It was also apparent that the length of the observation period as such was important only in the sense that over a longer period of time more Bi-oxol was resorbed from the periapical region, resulting in greater tendency to healing. In cases of partial pulpectomy, it is likely that the slight inflammation along the surface of the Bi-oxol will persist, and that the material will continue to be resorbed, although very slowly.

The relationship found between measurements on radiographs and sections (Table II) agrees with the findings of *Ketterl* (1963), *Nyborg & Halling* (1963), *Nyborg & Tullin* (1965) and *Engström & Spångberg* (1967).

The present study seems to show that however suitable a root filling cement Bi-oxol is in other respects, it falls short of the absolute requirement that a root filling material must be implantable in the body without causing persistent irritation.

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