Cell renewal and ground substance formation in replanted cat teeth

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The cellular dynamic pattern of pulpal healing 4, 10, 30, and 60 days after replantation of 47 apicoectomized cat incisors was studied after pulse labeling with ^{3}H-thymidine and ^{35}S-sulfate, autoradiography, and routine histology. In the control teeth the labeling index was less than 0.05%. The apical pulpal cells were capable of ground substance formation and cell proliferation already 4 days after replantation, with a labeling index of 7%, which increased up to 43% within 10 days. A gradual postoperative restitution and reorganization within the pulpal cellular compartment was seen. The maximum cell density, reached after 30 days, was reduced to on average 60% compared with the controls. The tissue reorganization was near completion within all pulpal zones after 60 days, and the labeling index was reduced to 2.5%. In some instances internal resorption in cervical pulpal areas negatively influenced the favorable healing. The present study shows that the pulpal healing in replanted teeth follows a consistent basic pattern in cellular dynamics and in histologic changes. The replanted tooth thus seems to be a suitable model for studies of healing and repair in connective tissues.
□ *Autoradiography; cell proliferation; dental pulp; ^{35}S-sulfate; ^{3}H-thymidine*

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Experimental and clinical studies of replanted teeth have demonstrated that under favorable conditions the pulpal tissue possesses a high potential for healing and repair (1–4). Although numerous histologic investigations have studied the tissue reactions, different views still prevail with regard to the pulpal healing pattern and the possible source of the renewing cells in replanted teeth (5–7).

Limited information is available concerning functional biological aspects in the pulp after tooth replantation (6, 7). Furthermore, knowledge about the mitotic activity in mature uninjured pulpal tissue is rather scarce (8, 9). Data on ground substance formation after general pulpal traumatic injury do not seem to have been previously described.

Information about the capacity for cellular renewal and the formation of basic tissue components contributes to a better understanding of the reaction pattern and dynamics in pulpal healing and repair. The purposes of this study were therefore as follows:

1. To study the cellular renewals at different sequences of pulpal healing and tissue reorganization after tooth replantation by means of ^{3}H-thymidine single-pulse labeling and autoradiography.
2. To investigate the influence of a general trauma on the ability of ground substance formation in the pulpal cells visualized by ^{35}S-sulfate and autoradiography.
3. To relate the cellular proliferative activity and ability of ground substance formation to the histologic sequences of events in replanted teeth.
4. To estimate the physiologic turnover rate in pulpal cell populations in cat incisors with completed roots.
5. Using replanted teeth as a dental experimental model system, to study the tissue reaction sequences after injury.

Materials and methods

Seventy-five mature 3rd incisors from 20 cats aged 7–9 months were used in the study. Forty-seven teeth were replanted (Table 1),

Table 1. Distribution of replanted teeth related to various observation periods and type of isotope used

Isotope	Teeth, *n*	Observation periods			
		4 days	10 days	30 days	60 days
^{3}H-Thymidine	33	7*	5*	12**	9
^{35}S-Sulfate	14	2	4*	8	
Total	47	9	9	20	9

* Represents one tooth with pulp necrosis.

whereas 28 contralateral teeth served as controls. Preoperative radiographs were taken to verify that the roots were completed.

Experimental procedure

The cats were anesthetized intraperitoneally with pentobarbital (Mebumal®), 50 mg/kg body weight, and additional doses of 2–4 mg Mebumal were given intravenously as needed. Tooth extraction, apicoectomy, and replantation procedures were performed as described earlier by Kvinnsland & Heyeraas (4). Ditardopen Leo Vet (Løwens Kjemiske Fabrik, Norway), 1 ml/kg body weight, was administered at replantation and the 2nd day postoperatively. During the 1st week after replantation the animals were kept on a soft diet. After postoperative periods of 4, 10, 30, and 60 days, the animals were reanesthetized, and the isotopes administered intravenously.

Fifteen cats received injection of 0.5 μCi ^{3}H-thymidine, specific activity 5 Ci/mmol (Amersham International, England) per gram body weight. Five cats were injected with 0.5 μCi ^{35}S-sulfate, specific activity 4.1 Ci/mmol (Institutt for Energiteknikk, Kjeller, Norway) per gram body weight.

One hour after isotope injection the animals were killed with an overdose of anesthetic followed by perfusion with 1% glutaraldehyde and 4% formaldehyde after flushing with saline containing 0.003% heparin. Teeth with surrounding tissues were removed and postfixed for 24 h in the previously used fixative.

The specimens were demineralized in 0.5 M ethylenediaminetetraacetic acid (EDTA) sucrose, pH 7.2. The end point of the demineralization was radiographically determined. Thereafter the paraffin-embedded specimens were serially sectioned in the axiobuccolingual direction at a thickness of 5 μm.

Alternate sections were prepared for autoradiography and routine histology after staining with hematoxylin–eosin. Sections for autoradiography were mounted on glass slides and dip-coated in liquid photographic emulsion (Kodak NTB-2, Nuclear Track Emulsion, Eastman Kodak Co., USA). The autoradiographs were exposed over an 8-day period at 4°C, developed in Kodak D-10 rapid developer (Eastman Kodak Co.), fixed (Kodak Unifix, Eastman Kodak Co.), stained with cresyl violet, and covered with a cover glass.

Alternate sections from 21 of the replanted teeth in the present material have previously been used to study dentin and osteodentin formation after replantation (4).

Registration procedure

For the registration procedures, central sections from the teeth were used, where pulpal tissue in total length was represented. In the control teeth the pulp was subdivided transversally in four equal zone lengths: the coronal, the cervical, the intermediate, and the apical zone (Fig. 1). For the experimental apicoectomized teeth the corresponding zones, except the apical, were measured.

Autoradiographic registrations

^{3}H-Thymidine-labeled material. The autoradiographs were examined in a Leitz microscope fitted with an eyepiece grid reticular,

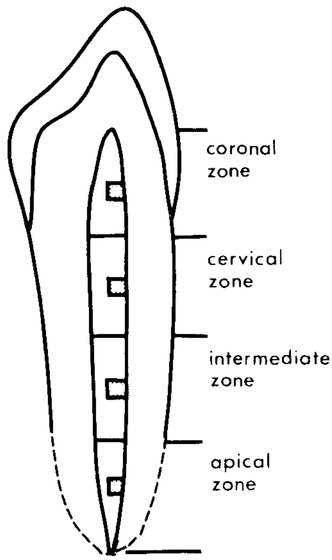


Fig. 1. Schematic drawing of a cat incisor indicating the areas of registration of cell density and labeled cells within the different pulpal zones. Coronal, cervical, and intermediate zones in the replanted teeth and, additionally, the apical zone in the control teeth.

which delimited an area of 0.016 mm^2, using ×40 objective. The microscopic field delineated by the counting chamber included all the pulpal cell populations—that is, odontoblasts, cells in the subodontoblastic layer, and cells in the main pulpal tissue. The total numbers of cells and labeled cells were counted within the defined tissue area in each pulpal zone, as indicated in Fig. 1. Labeled cells were defined as cells having more than five grains over the nucleus (10). The labeling index was calculated as the ratio between the number of labeled cells and total cell number in the area delimited by the counting chamber. The labeling index was expressed as percentage by multiplying by 100.

To estimate the low labeling index in control teeth, an average number of cells per section was calculated as follows: The cell number within one grid field was multiplied by the number of fields obtained in one representative central pulpal section. Labeled cells in the corresponding pulpal section was counted, and the labeling index given in percentage.

^{35}S-Sulfate-labeled material. The presence or absence of labeled ground substance was registered within the defined areas in the pulpal zones in control and replanted teeth (Fig. 1). Representative micrographs of the extent of intra- and extra-cellular ground substance labeling in control teeth were compared with the labeling extent in the replanted teeth.

To assess the cellular abilities of ground substance formation in replanted teeth, the extent of label present was graded as equal to, superior to, or inferior to the labeling in control pulps within the corresponding pulpal zones.

Histologic evaluation

The tissue reorganization and relationship among different tissue structures were evaluated histologically in experimental and control teeth. The following criteria were used: a) the odontoblast layer: normal structure, reduced or missing cell layer; b) the main pulp tissue: normal tissue structure including all cell types, altered tissue structure with reduced or increased number of pulpal cells, loss of tissue structure with presence of single cells and tissue fragments, tissue necrosis with karyorrhexis and cell pyknosis; c) absence or presence of inflammatory cells graded as mild, moderate, or severe; and d) presence of internal and external resorptions.

The presence or absence of normal dentin, osteodentin, cell inclusions, and dentinal tubules in 21 of the replanted teeth from the present material is registered and discussed in a previous paper (4).

When appropriate, registration differences were tested with Student's t test or Wilcoxon's signed rank test, $P = 0.05$. The registrations were made by the same investigator.

Results

Control teeth

^3H-Thymidine-labeled material. The proliferating cells showed in most instances a

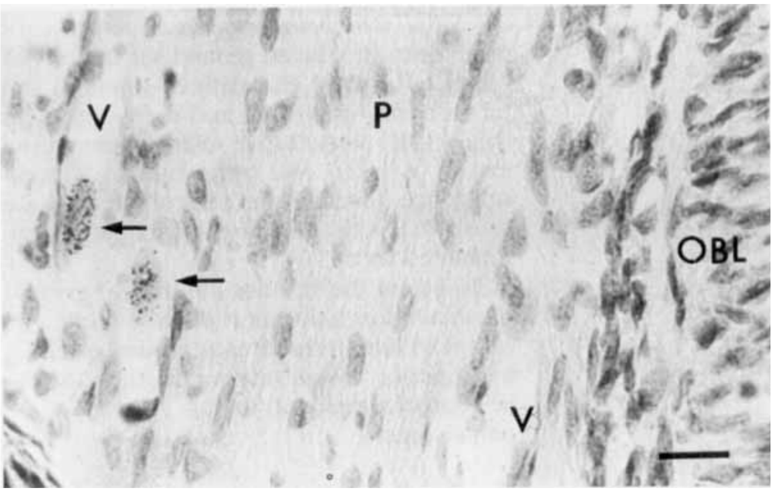


Fig. 2. ^{3}H-Thymidine-labeled endothelial cells (arrows) in pulpal tissue of a control tooth. OBL = odontoblast layer; P = dental pulp; V = vessel (autoradiograph). Bar = 20 μm.

uniform morphology. They were large, plump, and rich in cytoplasm, with a well-defined and ovoid nucleus (Fig. 2).

Fewer than 1 labeled cell from a total of 2000 pulpal cells per section was registered, giving a labeling index less than 0.05%. The odontoblasts were never labeled. The endothelial cells seemed to be the source of the cell renewing compartment rather than the fibroblasts (Fig. 2). However, labeled fibroblasts could occasionally be observed in the subodontoblastic cell layers.

In the control teeth the mean value of the cell population number in the different pulpal zones was rather uniform with no statistically significant differences ($P < 0.05$) (Fig. 3). No significant difference in the cell number per grid between the different control teeth was found.

^{35}S-Sulfate-labeled material. Labeled ground substance was present mainly within the odontoblast layer and was only occasionally observed within the main pulpal tissue (Fig. 4).

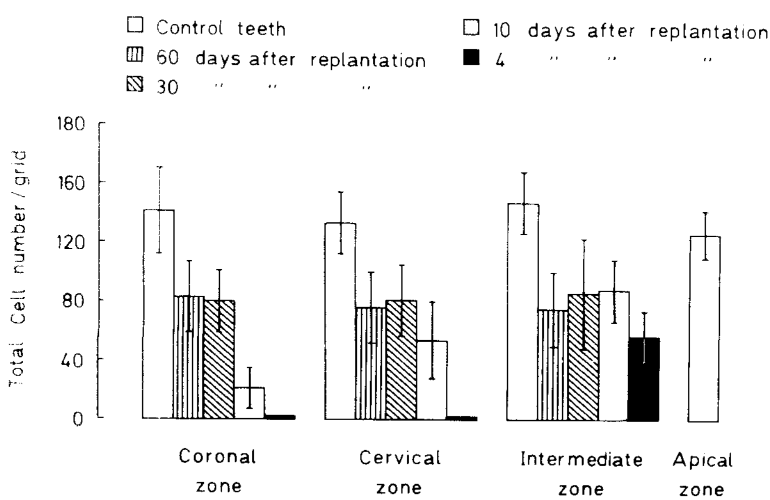


Fig. 3. The mean cell number per grid in coronal, cervical, and intermediate zones in control teeth and in experimental teeth 4, 10, 30, and 60 days after replantation. Additionally, the mean cell number per grid for the apical zone in the control teeth is given.

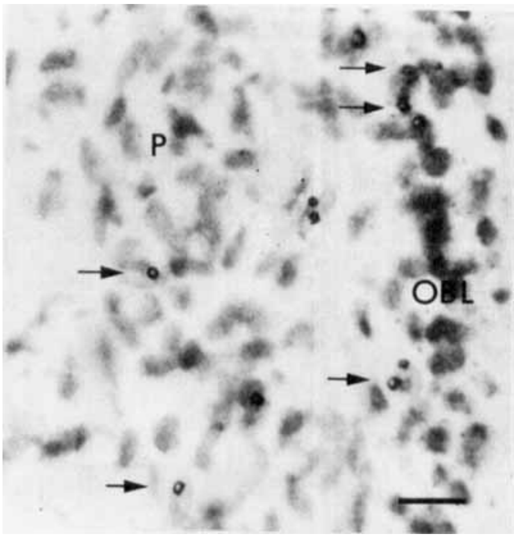


Fig. 4. Incorporation of ^{35}S-sulfate in pulpal tissue of a control tooth 1 h after isotope administration. The label (arrows) was most frequently seen within the odontoblast layer. OBL = odontoblast layer; P = main pulp (autoradiograph). Bar = 20 μm.

Histologic observations. The control teeth showed a normal pulpal structural arrangement without a subodontoblastic cell-free zone, as shown in Figs. 14 and 15.

Replanted teeth

The distribution of the replanted teeth related to the various observation periods and types of isotope used is given in Table 1.

Four days postoperatively

^{3}*H-Thymidine labeling* (n = 7). The pulp of one tooth showed absence of labeled cells. In the other teeth labeled fibroblasts and endothelial cells were distributed throughout the total intermediate zone (Figs. 5 and 6). In the cervical zone proliferating cells could be observed, but the number could not be counted because of accumulation of inflammatory cells and tissue degradation products. The coronal zone did not show labeled cells (Table 2). In the intermediate zone the mean total cell number within the delineated grid areas was nearly half the corresponding cell number of the control teeth (Fig. 3). The labeling index in percentage is given in Fig. 7.

^{35}*S-Sulfate labeling* (n = 2). A superior incorporation of radioactive sulfate was present in the intermediate pulpal zone compared with the controls, whereas an inferior ^{35}S-sulfate labeling could be observed within the cervical zone. The coronal zone in one pulp showed absence of ^{35}S-sulfate labeling. Surprisingly, labeled cells and intercellular ground substance were found arranged in rows in the coronal zone of one pulp (Fig. 8).

Histologic observations. Tissue degeneration and degradation and areas with histologic features of healing and repair were observed. One pulp was severely inflamed in the total length and seemed to become necrotic (Table 1). The odontoblastic layer was missing in all teeth. The tissue reaction in the coronal zone was dominated by karyorrhexis and cell pyknosis (Fig. 16), with scattered inflammatory cells. However, in the coronal zone of one pulp connective tissue cells were arranged in rows (Fig. 8). In the cervical zone a highly vascularized tissue was present, with fibroblasts and a moderate accumulation of inflammatory cells, together

Table 2. Mean number of ^{3}H-thymidine-labeled cells per grid in various pulpal zones 4, 10, 30, and 60 days after tooth replantation

Pulpal zones	Mean no. of labeled cells per grid (±SD)			
	4 days	10 days	30 days	60 days
Coronal zone	0	4 (1)	25 (8)	2 (0.9)
Cervical zone	*	14 (11)	25 (8)	1 (0.8)
Intermediate zone	4 (3)	38 (28)	30 (10)	1 (1)

* Presence of labeled cells (see Materials and methods).

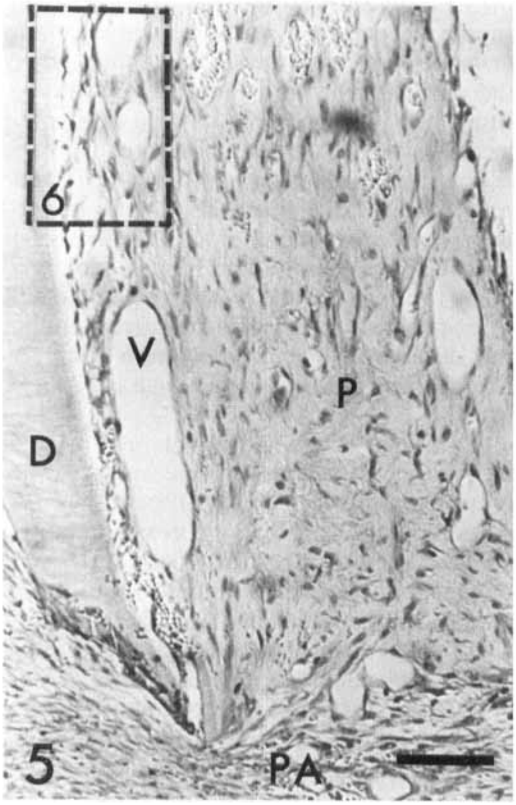


Fig. 5. Autoradiograph from the intermediate pulpal zone in a replanted tooth 4 days postoperatively. D = dentin; P = dental pulp; PA = periapical area; V = vessel. Bar = 100 μm.

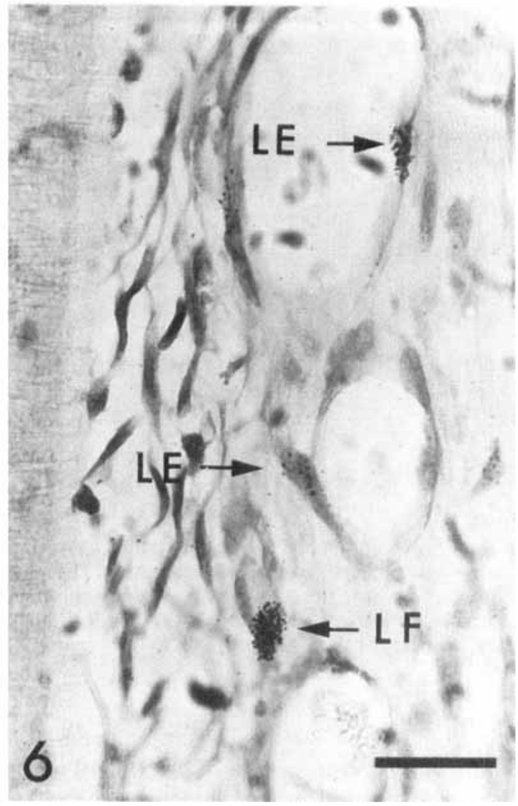


Fig. 6. Outlined area in Fig. 5 at higher magnification. ^{3}H-Thymidine-labeled pulpal fibroblast (LF) and endothelial cells (LE) are seen (arrows). Bar = 20 μm.

with tissue degradation products (Fig. 17). The intermediate zone comprised fibroblasts and numerous endothelial cells. Except for a few single inflammatory cells observed close to the dentin, no inflammatory cells were present in this zone.

Ten days postoperatively

^{3}H-Thymidine labeling (n = *5*). Labeled cells were present within all pulpal zones in four of five teeth, with a decreasing number of proliferating cells in coronal direction (Table 2, Fig. 7). The mean of the total cell number in the different pulpal zones decreased towards the incisal pulpal area (Fig. 3). The cell number within the intermediate zone seemed to have reached its maximum compared with longer observation periods (Fig. 3). In the intermediate zone the labeling index showed a dramatic increase, and compared with the 4-day group cells in the other pulpal zones also showed considerable proliferative activity (Fig. 7).

^{35}S-Sulfate labeling (n = *4*). A pronounced increase in labeling was present in the intermediate zone at this time (Fig. 9), whereas the label incorporation within the cervical zone was still inferior compared with the controls. Single labeled cells and scattered intercellular labeling could occasionally be observed in the coronal zone. One pulp showed no ^{35}S-sulfate labeling.

Histologic observations. The coronal zone

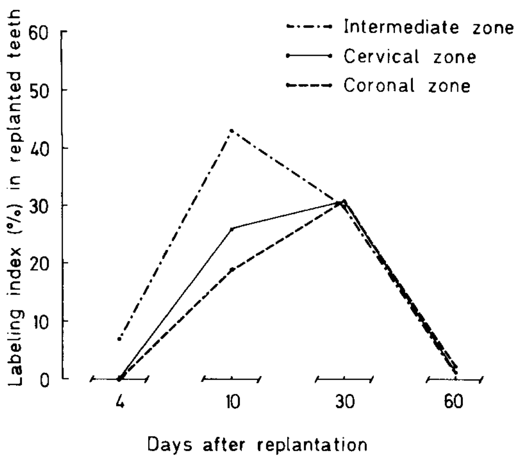


Fig. 7. The labeling index, given in percentage, for the different pulpal zones after pulse labeling with ^{3}H-thymidine 4, 10, 30, and 60 days after tooth replantation.

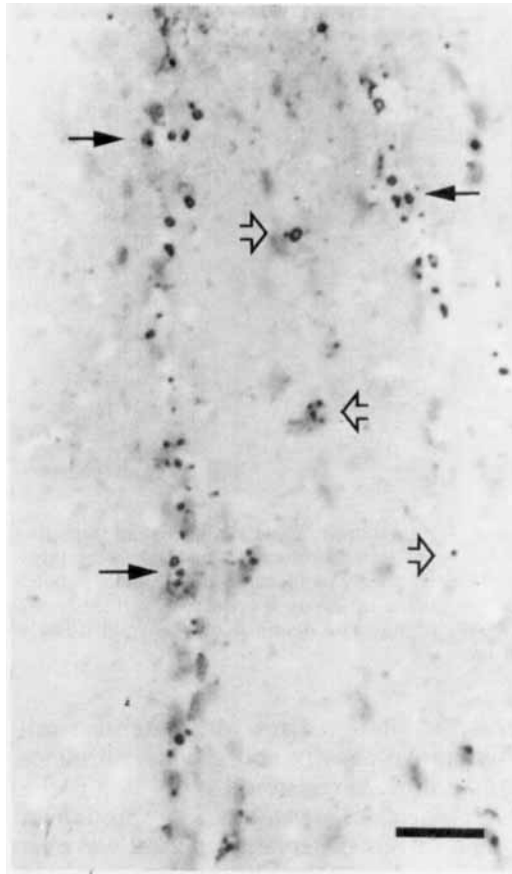


Fig. 8. ^{35}S-Sulfate labeling of intra- and extra-cellular ground substance (arrows) within the coronal pulpal zone 4 days after replantation. Labeled cells arranged in rows (closed arrows) or single-labeled cells and intercellular substance (open arrows) are seen (autoradiograph). Bar = 20 µm.

had a histologic appearance similar to the reactions observed within the cervical zone 4 days after replantation. The cellular inflammation was less pronounced and graded as mild. The reactions within the cervical zone after 10 days corresponded well with the findings in the intermediate zone 4 days postoperatively, with practically no inflammatory cells. The intermediate zone showed no inflammatory cells. The connective tissue compartment seemed to rearrange and organize, with fibroblast-like cells lining up along the dentin most apically in five out of seven teeth (Fig. 9), and in one tooth also within the cervical zone. An odontoblast layer was not observed. In two teeth the pulp was necrotic (Table 1).

Thirty days postoperatively

^{3}H-Thymidine labeling (n = *12*). There was no difference in the mean number of labeled cells in the pulpal zones (Table 2). As can be seen in Fig. 7, approximately every third cell within the pulp showed proliferative activity. The mean of the total cell number per grid had reached its maximum in all pulpal zones (Fig. 3). In two pulps no labeled cells were observed.

^{35}S-Sulfate labeling (n = *8*). All teeth except the coronal zone of two maxillary teeth showed labeling of the ground substance in the total pulpal length after 1 month. Compared with the control teeth the ^{35}S-sulfate labeling was superior in all pulpal zones. The most pronounced isotope incorporation was observed within the cervical and intermediate zones. The cells and extracellular compartment close to dentinal surfaces seemed to be more extensively labeled than areas located more centrally in the pulp.

In the pulps with internal resorption, which in most instances were located adjacent to an outer cervical lesion, circumscribed

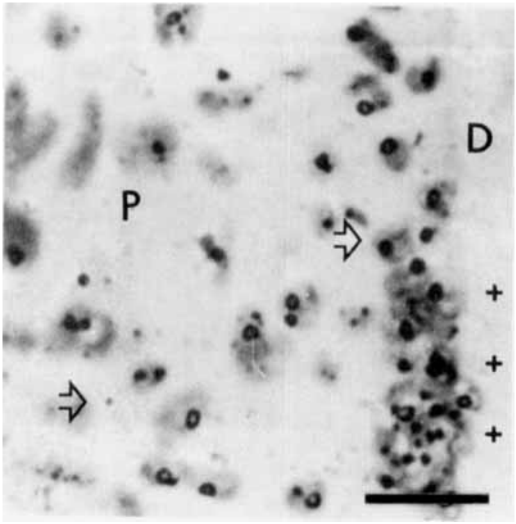
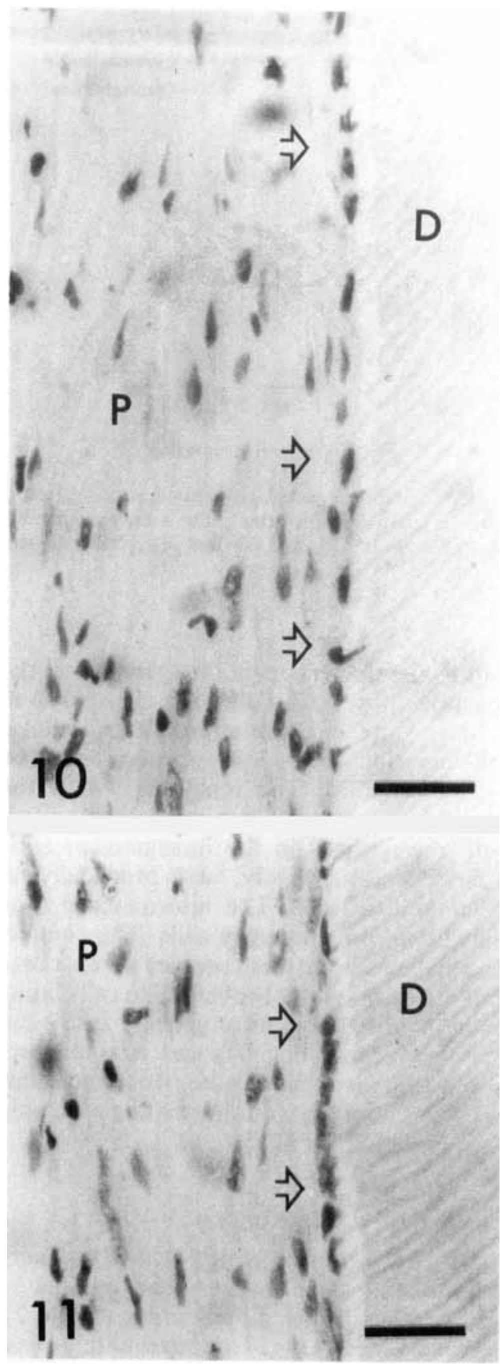


Fig. 9. A pronounced ^{35}S-sulfate labeling of intra- and extra-cellular ground substance (arrows) in the intermediate pulpal zone 10 days after replantation. Labeled cells are lining up along the dentinal surface (++). P = dental pulp; D = dentin (autoradiograph). Bar = 20 μm.

areas of different sizes with extensive cell proliferative activity and ground substance formation were registered.

Histologic observations. A prominent finding in this observation period was that reorganization of the cells had proceeded in the total pulpal length. As shown in Figs. 10 and 11, fibroblast-like cells were closing up along the dentin surface also within cervical and coronal zones, in 13 of 18 healing pulps.

In eight teeth a reduced odontoblast-like cell layer was present in the intermediate zone. In general, the whole pulp was almost free of inflammatory cells. However, the coronal zone in one tooth showed a moderate inflammatory reaction, and one pulp was severely inflamed in the total length. Two teeth were necrotic (Table 1). Five teeth showed internal resorption. In four of these the resorption was located in the pulpal area on the border between the cervical and coronal zone. Bony tissue was formed within the intermediate zone in one pulp.



Figs. 10 and 11. Thirty days after replantation cells are lining up (arrows) along the dentinal surface in both the coronal (Fig. 10) and the cervical pulpal zones (Fig. 11). D = dentin; P = dental pulp. Bars = 20 μm.

Sixty days postoperatively

^{3}H-Thymidine labeling (n = *9*). The num-

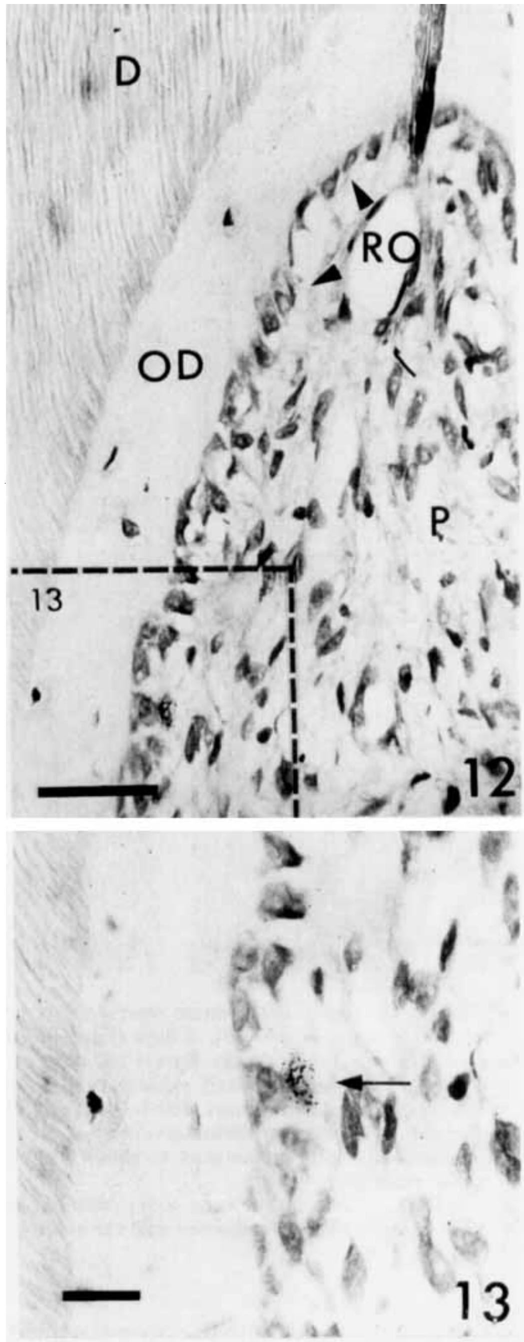
ber of labeled cells was remarkably reduced throughout the entire pulpal tissue after 2 months (Table 2). However, the labeling index was still about 50 times higher than in the control teeth, partly due to lower cell density. Compared with 30 days earlier, the labeling index was dramatically reduced (Fig. 7), whereas the mean total cell number was not changed (Fig. 3). Mainly endothelial cells and a few fibroblasts adjacent to an odontoblast-like cell layer was found to be labeled (Figs. 12 and 13). However, in five teeth with localized inflamed areas related to internal resorption, several connective tissue cells were labeled.

Histologic observations. Tissue reorganization with a reduced odontoblast-like cell layer was seen in seven of nine teeth (Figs. 18 and 19). In the intermediate zone of four teeth and in the coronal zone of two teeth an apparently complete odontoblast-like cell layer was observed. Two maxillary incisors were severely inflamed, and three teeth showed a moderate inflammation within the cervical zone related to internal resorption. One pulp was partly filled with bony tissue in confluence with the periapical bone.

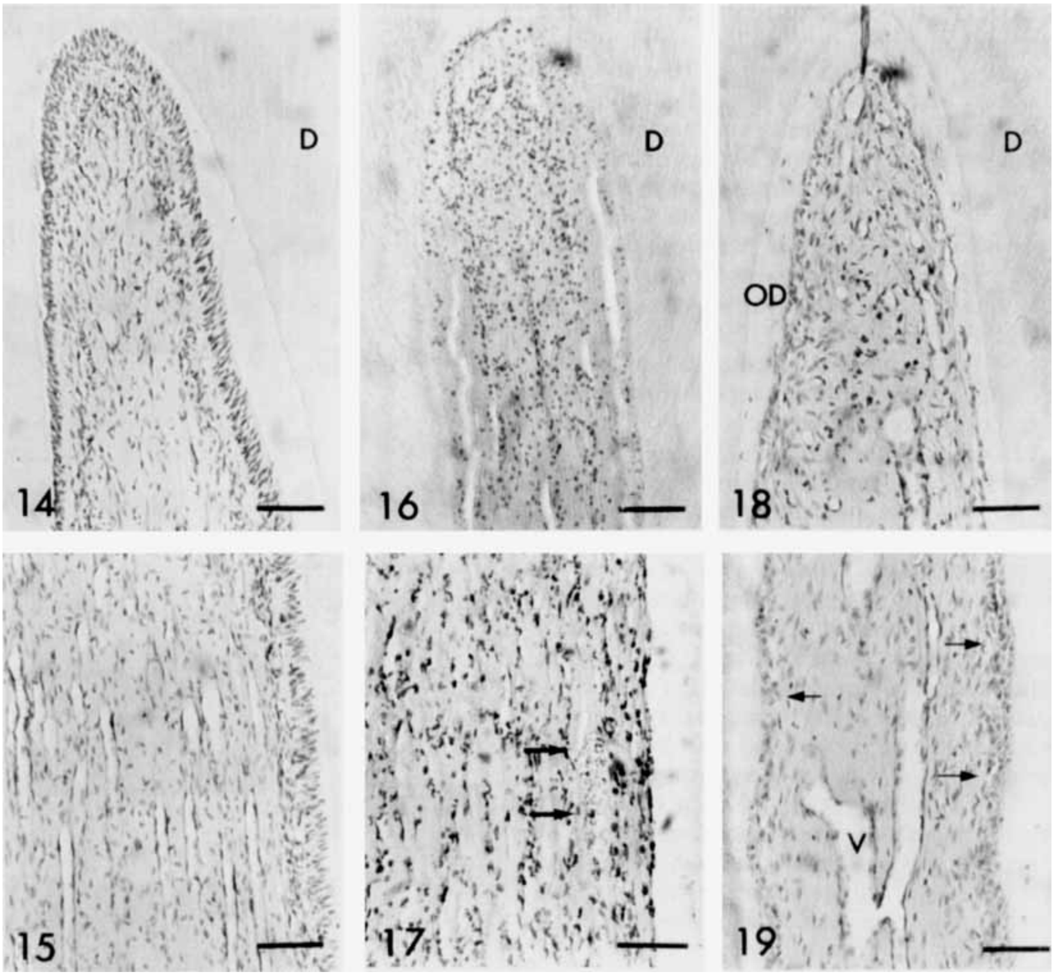
In the present study 10 of a total of 47 teeth showed internal resorption. In nine of these the resorption was seen in relation to an outer cervical lesion in the root surface. External root resorption was observed in all teeth with pulp necrosis ($n = 5$) and in eight teeth with regenerated pulp tissue.

Discussion

Functional dynamic aspects of the pulpal tissue response in replanted teeth are demonstrated in the present study. The cellular renewal and healing showed a rather consistent reaction pattern at the different observation periods with regard to both cellular kinetic activities and histologic tissue changes. Already 4 days after replantation cells situated in the apical pulpal parts possessed a considerable capacity for cell proliferation and ground substance formation. During a 2-month period a gradual renewal and reorganization of the pulpal cell compartment was at completion.



Figs. 12 and 13. Autoradiograph of the coronal pulpal zone in a replanted tooth 60 days postoperatively after ^{3}H-thymidine pulse labeling (Fig. 12). D = dentin; OD = osteodentin; P = dental pulp. Bar = 50 µm. Outlined area in Fig. 12 is shown in Fig. 13. A labeled fibroblast (arrow) is situated close to the reduced odontoblast layer. Bar = 20 µm.



Figs. 14–19. The figures demonstrate representative histologic findings in coronal and cervical pulpal zones in a control tooth (Figs. 14 and 15), 4 days (Figs. 16 and 17) and 60 days (Figs. 18 and 19) after replantation (hematoxylin–eosin). D = dentin. Bars = 100 μm.
Fig. 16. Four days postoperatively pyknotic cells with loss of tissue structure are seen in the coronal zone.
Fig. 17. The cervical zone shows vessels filled with erythrocytes (arrows) and fibroblasts and accumulation of inflammatory cells and degradation products.
Fig. 18. Sixty days after replantation an almost restored cellular pulpal structure lined with osteodentin (OD) is seen most coronally.
Fig. 19. The cervical zone shows an odontoblast-like cell layer (arrows), large vessels (V) and a restored cellular structure in the main pulp compared with the control tooth (Fig. 15).

The mature dental pulp has been classified as a cell population with a very low turnover rate (11). However, studies giving data about the turnover rate or labeling index in mature pulpal tissue are scarce (8, 9). The present estimated labeling index in mature cat incisors, less than 1 labeled cell per 2000, agrees well with the labeling index found in mature rat molars (8).

As shown in several replantation studies, a decisive factor for a successful pulpal healing is an open tooth apex (1, 2, 12–14) facilitating the transient nutrition of the pulpal cells and revascularization of the tissue (15–

17). The apicoectomy procedure has been reported to promote the healing capacity in replanted mature dog teeth (5, 17), whereas the same procedure used in monkeys is shown to reduce the pulpal healing in both mature and immature replanted teeth (18). In the present study in cat teeth, however, the healing proceeded at the same rate as reported previously in non-apicoectomized immature dog teeth (14). The difference in pulpal healing capacity demonstrated in dogs, monkeys, and cats may be related to species differences, tooth maturation, and pulpal length. Another important factor to be considered is that apicoectomy may increase the distance between pulpal cells and vascularized tissue and therefore to various extents may influence the survival of the apical pulpal cells.

Previous studies have reported no histologic changes in apical pulpal tissue in replanted teeth and in pulpal explants in culture media after postoperative periods of a few days (1, 19). In immature dog teeth the presence of oxidoreductase activity within the apical pulp has been reported to last for several days after replantation (20). Human pulpal tissue has shown the capacity for cell proliferation and ground substance and collagen formation as measured by liquid scintillation and autoradiography after 24 h in culture medium (21). In rat pulpal explants 5% of the cells are reported to be labeled with ^{3}H-thymidine after 3 days in culture medium (19). Therefore, previous results (1, 2, 4, 19–21) and present findings indicate that under favorable conditions the apical pulpal cells may survive the replantation trauma. Earlier suggestions (7, 22) that apical pulpal cells may be responsible for the cellular proliferation and renewal after tooth replantation thus fit in well with the present findings. Accordingly, a tubular postoperative hard tissue matrix may possibly be formed only by cells of pulpal origin.

A reiteration of the different sequences of pulpal healing in replanted teeth at various pulpal levels seemed to occur depending on the distance to the nutritional supply and the postoperative period. Within the early observation periods an inflammatory zone with cell proliferation, ground substance formation, and vessels filled with erythrocytes was a consistent finding, followed by a gradual tissue renewal and reorganization. These findings fit well with observations previously described in replanted human, cat, and dog teeth (1, 4, 14). After cessation of the inflammatory reaction in the different pulpal zones the cells showed a certain behavior in relation to the dentinal wall; that is, they lined up and accumulated along the dentin in the total pulpal length. This particular cell arrangement, also observed by Øhman (1), seems to follow the same pattern as pulpal cells after a local injury in capping experiments (23, 24).

As dentin represents a surface to which the pulp cells attach and polarize (25, 26) the sequences of healing after local and general pulpal injury correspond well. The main difference seems to be the time aspects for the different healing sequences. Cells along the dentin are also shown to direct the traffic of structural matrix components (26). This may explain why relatively undifferentiated cells along dentinal walls in the early stage of tissue reorganization could be embedded in their own matrix products (4, 14). At later observation periods a polarized and further differentiated cell may be able to form a postoperative tubular matrix, as demonstrated earlier (2, 4, 14).

Compared with the controls, the maximum pulpal cell density in replanted teeth was reduced. This corresponds with the repair of connective tissue in general when substantial cellular loss has to be restored (27).

Coincidentally with the maximum cell density within the different pulpal zones, a peak in the corresponding labeling index was demonstrated after ^{3}H-thymidine administration. Similar patterns are suggested by Fitzgerald (23) during healing of local pulpal injury in pulp capping experiments. The high labeling index during the 1st postoperative month indicates that there is a substantial tissue loss which has to be compensated for during healing. In the present study the labeling index showed the highest value in the intermediate zone 10 days postoperatively. However, this observation does not exclude the possibility that the labeling index may reach even higher values in the other pulpal zones in the postoperative period between 10 and 30 days.

Registration of labeled cells in autoradiographs is a semiquantitative measure and should not be regarded as absolute values. The explanation of the relatively broad variation within the SD values given in Table 2 may further be due to registration of variables within a biological material exposed to a substantial tissue loss.

This study demonstrates that the presence of the maximum cell density and the beginning of tissue reorganization seem to be two events clearly related to each other. It may therefore be justifiable to conclude that reorganization of pulpal tissue after a general trauma is dependent on the presence of sufficient cell density within the tissue. As shown in previous studies (4, 14), the osteodentin formation seems to start simultaneously with this reorganization of the pulpal cells along dentinal walls.

In conclusion, the sequence of events in pulpal response to replantation trauma is shown to follow a consistent reaction pattern in cell renewal, ground substance formation, and histologic changes. Although the healed pulp is less cellular, the tissue clearly demonstrates the capacity to form different tissue components necessary for a functioning pulpal tissue. A prerequisite for a successful pulpal healing seems to be an uninjured tooth surface. Apparently, under favorable conditions there are similarities in the healing sequences after tooth replantation and a local pulpal injury. Therefore, a replanted tooth seems suitable to use as a model system to study healing and repair within a connective tissue system.

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