Dental Traumatology 2007; doi: 10.1111/j.1600-9657.2006.00481.x
All rights reserved

Copyright © Blackwell Munksgaard 2006
DENTAL TRAUMATOLOGY

Influence of enamel matrix derivative (Emdogain®) and sodium fluoride on the healing process in delayed tooth replantation: histologic and histometric analysis in rats

Poi WR, Carvalho RM, Panzarini SR, Sonoda CK, Manfrin TM, Rodrigues TS. Influence of enamel matrix derivative (Emdogain®) and sodium fluoride on the healing process in delayed tooth replantation: histologic and histometric analysis in rats.
© Blackwell Munksgaard, 2006.

Abstract – Although it has already been shown that enamel matrix derivative (Emdogain®) promotes periodontal regeneration in the treatment of intrabony periodontal defects, there is little information concerning its regenerative capacity in cases of delayed tooth replantation. To evaluate the alterations in the periodontal healing of replanted teeth after use of Emdogain®, the central incisors of 24 Wistar rats (*Rattus norvegicus albinus*) were extracted and left on the bench for 6 h. Thereafter, the dental papilla and the enamel organ of each tooth were sectioned for pulp removal by a retrograde way and the canal was irrigated with 1% sodium hypochlorite. The teeth were assigned to two groups: in group I, root surface was treated with 1% sodium hypochlorite for 10 min (changing the solution every 5 min), rinsed with saline for 10 min and immersed in 2% acidulated-phosphate sodium fluoride for 10 min; in group II, root surfaces were treated in the same way as described above, except for the application of Emdogain® instead of sodium fluoride. The teeth were filled with calcium hydroxide (in group II right before Emdogain® was applied) and replanted. All animals received antibiotic therapy. The rats were killed by anesthetic overdose 10 and 60 days after replantation. The pieces containing the replanted teeth were removed, fixated, decalcified and paraffin-embedded. Semi-serial 6-μm-thick sections were obtained and stained with hematoxylin and eosin for histologic and histometric analyses. The use of 2% acidulated-phosphate sodium fluoride provided more areas of replacement resorption. The use of Emdogain® resulted in more areas of ankylosis and was therefore not able to avoid dentoalveolar ankylosis. It may be concluded that neither 2% acidulated-phosphate sodium fluoride nor Emdogain® were able to prevent root resorption in delayed tooth replantation in rats.

Wilson Roberto Poi[1], Roberta Martinelli Carvalho[2], Sônia Regina Panzarini[1], Celso Koogi Sonoda[1], Thais Mara Manfrin[2], Thais da Silveira Rodrigues[2]

[1]Department of Surgery and Integrated Clinics, Faculty of Dentistry of Araçatuba, São Paulo State University (UNESP), Araçatuba, SP; [2]Faculty of Dentistry of Araçatuba, São Paulo State University (UNESP), Araçatuba, SP, Brazil

Key words: tooth replantation; dental enamel proteins; enamel matrix derivate; sodium fluoride

Dr Wilson Roberto Poi, Departamento de Cirurgia e Clínica Integrada, Disciplina de Clínica Integrada, Faculdade de Odontologia do Campus de Araçatuba, UNESP, Rua José Bonifácio 1193, CEP: 16015-050, Araçatuba, SP, Brazil
Tel.: +55 18 3636 3240
Fax: +55 18 3636 3332
e-mail: poi@foa.unesp.br

Accepted 13 December, 2005

The ideal treatment for an avulsed permanent tooth is its immediate replantation into the socket. However, in spite of its recognized therapeutic value, in practice, immediate replantation is performed only in few cases because of factors associated with the accident itself, such as the patient's emotional status at the moment of trauma and lack of knowledge or confidence about replantation procedures (1–3).

The findings of recent clinical and laboratory studies have led to a new definition of immediate replantation, changing from 30 min to <5 min of extra-alveolar time (4). Consequently, delayed replantation has become a clinical reality for dentists, considering the moment that the patient arrives at the dental office.

Periodontal ligament (PDL) regeneration is the best result expected for a replanted tooth. Nevertheless, successful PDL regeneration depends on factors such as the storage conditions and extra-alveolar time elapsed before replantation (5). Tooth dehydration, for example, is devastating for PDL fibers. A longitudinal study (5) has shown that PDL regeneration was evident in 73% of the cases of immediately replanted teeth. However, only half the teeth replanted 10 min after avulsion exhibited a normal PDL. Lekic & Mcculloch (6) have demonstrated *in vitro* that, after 15 min, progenitor PDL cell populations exhibited quite limited proliferation ability and that this became impossible after 30 min.

Pulp necrosis is present in almost all cases of dental avulsion. The root canal will invariably be infected if endodontic treatment is not effectively performed. The combination of bacterial infection within the root canal and cementum lesion on the external root surface will result in an external inflammatory root resorption, which may lead to loss of the replanted tooth (7).

All the proposed treatment protocols are aimed at avoiding or minimizing this inflammatory process, which is directly proportional to the periodontal damage extension and pulp infection (7). In cases where this damage cannot be reduced and replacement resorption is almost certain, measures should be enacted to increase root resistance, in an attempt to keep the tooth in the oral cavity. This is particularly important for young patients during craniofacial growth because the replanted tooth might be able to maintain the height and thickness of alveolar ridge until the patient reaches the proper age to receive a more comprehensive prosthetic rehabilitation (8).

This has been the intent of several authors who have recommended the use of fluorides for surface root treatment for avulsed teeth, both for delayed replantation and storage in a dry medium (9–11).

Some questions have been raised on whether the therapies that regulate or promote proliferation and differentiation of PDL cells, such as the use of growth factors, surface adhering molecules and/or the extracellular matrix components, could improve the prognosis of avulsed teeth (12).

This is the context where Emdogain® (Biora AB, Malmö, Sweden) belongs. It is a therapeutic gel consisting of an enamel matrix derivative (EMD) in a propylene glycol alginate vehicle that is applied during periodontal surgeries to achieve biological regeneration of lost tooth attachment by promoting migration, proliferation and differentiation of PDL fibroblasts to cover exposed root surfaces (13–16).

The purpose of this study was to assess, by histologic and histometric analyses, the influence of Emdogain® and sodium fluoride used as root surface treatment on the healing process after delayed tooth replantation in rats.

Materials and methods

The research proposal was first submitted to review by the local Ethics in Animal Research Committee and the designed methodology was approved. Twenty-four male Wistar rats (*Rattus norvegicus albinus*), weighing 250–300 g were used in this study. The animals were obtained from the vivarium of the Faculty of Dentistry of Araçatuba (UNESP), Brazil and were housed under climate-controlled conditions (12 h light : 12 h dark; 22 ± 3°C) with free access to ground solid ration and water.

Before the surgical procedures, xylazine chlorhydrate (Anasedan; AgriBrands Ltda, Campinas, Brazil) was administered i.m. [0.03 ml $(100\ g)^{-1}$ body weight] to attain muscular relaxation and the animals were then anesthetized with ketamine chlorhydrate (Dopalen; AgriBrands Ltda, Campinas, SP, Brazil) at a dose of 0.07 ml $(100\ g)^{-1}$ body weight.

The rats had their upper right incisors extracted. The teeth were held by their crowns, fixed on a red wax plate and kept dry at room temperature for 6 h. Afterwards, the dental papilla and the enamel organ of each tooth were sectioned and removed with a no. 11 scalpel blade (Medico International Trading, Tianjin, China). The pulp was extirpated through a retrograde via with a slightly curved size 40 K-file (Sybron Kerr Corporation, Orange, CA, USA). Root canal was irrigated with 1% sodium hypochlorite, aspirated and dried with absorbing paper points (Dentsply Ind. e Com. Ltda., Petrópolis, RJ, Brazil). Thereafter, the teeth were randomly assigned to two groups ($n = 12$), according to the root surface treatment protocols accomplished before replantation.

In group I, root surfaces were treated with 50 ml of 1% sodium hypochlorite for 10 min (changed

after the first 5 min), rinsed with 50 ml of saline for 10 min and immersed in 50 ml of 2% acidulated-phosphate sodium fluoride solution, pH 5.5 (0.1 M phosphoric acid pH 2.0 diluted in 2% sodium fluoride solution pH 8.0 (Apothicário Farmácia de Manipulação, Araçatuba, SP, Brazil) for additional 10 min. The root canals were filled with a calcium hydroxide (Calcium Hydroxid Für Analyse, Criedel, de Rainag Seelge, Hannover, Germany) and propyleneglycol paste, packed in a cartridge and injected with a Carpule syringe. The teeth were replanted into their sockets, which were not treated, except for removal of blood clots with saline.

In group II, the roots were also treated with 1% sodium hypochlorite and saline, for 10 min each. Pulpectomy was carried out and the root canals were irrigated, dried and filled in the same way as described above. In this group, however, instead of immersion in sodium fluoride, Emdogain® gel (Biora AB) was applied to the lingual surface of the roots with a syringe and the teeth were replanted.

No suture or contention was performed on the replanted teeth (17) and all animals received a single intraperitoneal dose of benzathine G penicillin 20 000 IU (Fontoura-Wyeth SA, São Paulo, SP, Brazil).

The rats were sacrificed by anesthetic overdose 10 days ($n = 6$ per group) and 60 days ($n = 6$ per group) postsurgery. The pieces containing the replanted teeth were removed, immersed in 10% formalin for 24 h for fixation, decalcified in a 4.13% EDTA solution, pH 7.0 and paraffin-embedded. Longitudinal 6-μm thick semi-serial sections were obtained and stained with hematoxylin and eosin for histologic and histometric analyses.

Histomorphometric analysis was carried out according to the protocol proposed by Panzarini et al. (18). Ten sections were analyzed from 10 different slides of each experimental group, only at the 60th postoperative day. The chosen sections were digitalized using an optical scanner (HP 4C/T; Hewlett-Packard Development Company, Palo Alto, CA, USA) and the images were saved using an image management software [ImageLab 2000; Laboratório de Informática Dedicado à Odontologia (LIDO), USP, São Paulo, SP, Brazil]. For accurate identification and selection of representative resorption areas, the digital images were compared with the same slides examined under light microscopy.

Results

The results were drawn from qualitative analysis after observation of the following structures: gingival mucosa, PDL, cementum, dentin, bone wall and bottom of the socket, 10 and 60 days after replantation.

Ten days

In group I (2% acidulated-phosphate sodium fluoride) the gingival epithelium was located slightly below the cementoenamel junction. The underlying connective tissue exhibited moderate number of blood vessels and fibroblasts and some lymphocytes. The connective tissue in the PDL space was poorly organized and exhibited moderate number of fibroblasts and blood vessels, along with some macrophages and lymphocytes. Cementum and dentin remained intact along the three alveolar thirds. The alveolar bone wall presented bone apposition throughout its extension, which caused narrowing of the PDL space (Fig. 1). There was new trabecular bone formation at the bottom of the socket and great amount of connective tissue with no bone differentiation and moderate number of fibroblasts.

In group II (Emdogain®), the gingival epithelium was located close to the cementoenamel junction. The underlying connective tissue presented discrete inflammatory infiltrate and small number of fibroblasts. The PDL space was narrowed along the entire alveolus extension; it was quite cellularized and exhibited a slight fibrilar aspect. Collagen fibers were disposed parallel to cementum surface and presented several islets of neoformed bone tissue, which were narrowing the PDL space. Two specimens presented areas of ankylosis. Cementum and dentin remained intact along the three alveolar thirds. The alveolar bone wall presented bone apposition, mainly in the middle third, which caused narrowing of PDL space (Fig. 2). At the

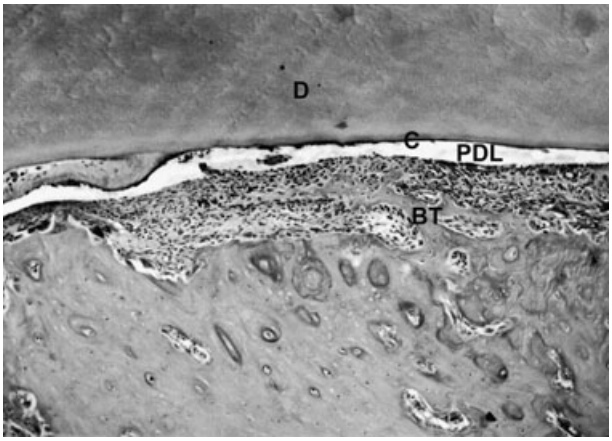

Fig. 1. Group I (sodium fluoride; 10 days): bone apposition (BT) resulting in narrowing of the periodontal ligament space (PDL). Notice cementum (C) and dentin (D) integrity. H&E (original magnification ×63).

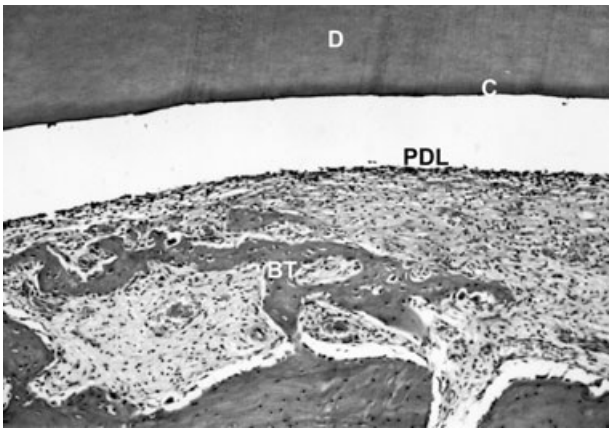

Fig. 2. Group II (Emdogain®; 10 days): middle third exhibiting thin trabecular bone (BT) in the periodontal ligament space (PDL) and intact dentin (D) and cementum (C). H&E (original magnification ×63).

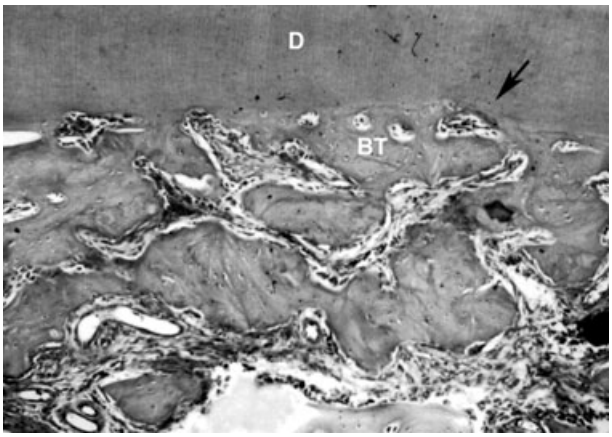

Fig. 3. Group I (sodium fluoride; 60 days): Periodontal ligament space (PDL) completely filled with neoformed bone tissue (BT). Note the presence of some replacement resorption areas (narrow). H&E (original magnification ×63).

bottom of the socket, close to the filling material, there was poorly organized loose connective tissue, with great number of fibroblasts and cells characteristic of a mononuclear inflammatory infiltrate.

Sixty days

In group I (2% acidulated-phosphate sodium fluoride), the gingival epithelium was located below the cementoenamel junction. The underlying connective tissue was well developed and exhibited a discrete number of fibroblasts. The PDL space close to the cervical third was partially occupied by neoformed bone tissue in contact with dentin surface. The connective tissue without bone differentiation presented moderate number of blood vessels and fibroblasts. Dentin and cementum presented ceased surface resorption, which was repaired by bone tissue neoformation. Some areas exhibited small amount of intact cementum in contact with neoformed bone tissue. The alveolar bone wall showed several areas of bone apposition, which filled almost completely the PDL space and was in contact with dentin surface (Fig. 3). The bottom of the socket was partially filled with trabecular bone and connective tissue without bone differentiation.

In group II (Emdogain®), the gingival epithelium was located below the cementoenamel junction. The underlying connective tissue was well developed and exhibited discrete number of fibroblasts. The PDL space presented collagen fibers disposed perpendicular to the root surface in the middle and apical thirds. In part of the middle third, the PDL connective tissue was replaced by neoformed bone tissue, which almost completely filled the PDL space. Dentin and cementum presented small areas of inflammatory resorption in the cervical third and areas of superficial replacement resorption and ankylosis along the whole root surface. Except for the cervical third, the alveolar bone wall exhibited bone apposition that frequently filled almost completely the PDL space and contacted the root surface (Fig. 4). Neoformed trabecular bone could be seen at the bottom of the socket, close to the alveolar bone wall.

Data for statistical analysis were considered from histomorphometric findings obtained at the 60th postoperative day because, in both groups, no replacement resorption was observed at 10 days after replantation and inflammatory resorption occurred only in group II. Student's *t*-test used for comparison of the groups did not show statistically significant differences ($P > 0.05$).

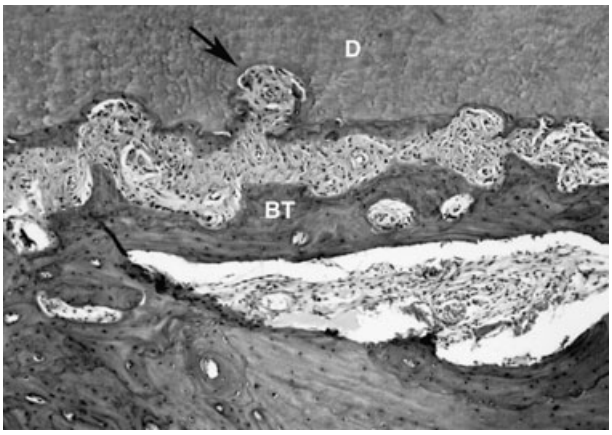

Fig. 4. Group II (Emdogain®; 60 days): areas of cementodentinal resorption close to the middle third of the root (narrow). H&E (original magnification ×63).

Discussion

In daily clinical practice, dental avulsion has a relatively small incidence and involves mainly the maxillary incisors of patients aged 10–18 years (3). In spite of not being a frequent event, the great number of published studies addressing dental avulsion over the last decades is explained by the uncertain prognosis of tooth replantation. All of these studies have sought to establish patterns of root resorption (superficial, inflammatory and replacement resorption) or provide measures that might prevent or at least minimize its occurrence and consequences.

It is well accepted that replantation, even if temporary, is the best treatment option for avulsed teeth. Taking into account that the most commonly affected population is within the age group of craniofacial growth, replantation of an avulsed tooth might allow maintenance of the height and thickness of the alveolar ridge, even if ankylosis and replacement resorption occur. This fact greatly favors prosthetic rehabilitation at the proper time (8).

As formerly mentioned and confirmed by the findings of Kenny et al. (19), cases of tooth avulsion usually reach the dental office when delayed replantation presents as the last possible resort. In addition to the long extra-alveolar time, inappropriate storage conditions of the avulsed tooth strongly compromise the PDL vitality (3).

Andreasen (7) reported the progression of replacement resorption when the extra-alveolar time in dry medium was >60 min. Based on the findings of their study, the authors affirmed that no cell would remain vital on root surface of teeth kept dry for over 120 min. Similar results were also observed by Blomlöf et al. (20) and Lekic & Mcculloch (6). In cases of teeth replanted after a 6-h extra-alveolar period in a dry medium, no cell vitality is expected on root surface. Therefore, the proposed treatments are aimed at attenuating the consequences of dry storage by increasing the resistance of root surface to resorption.

Several studies (18, 21, 22) have shown that treatment of root surface with 1% sodium hypochlorite preserves the integrity of the cementum layer, which was also observed in the present study, especially at 10 days after replantation. Hammarström et al. (23) have reported that root resorption following integration between alveolar bone and root surface increases slowly if the cementum remains intact.

Acidulated fluoride solutions have also been employed for treatment of root surface in cases of delayed tooth replantation (9–11, 18, 24). Panzarini et al. (18) have demonstrated that the association of 1% sodium hypochlorite and 2% acidulated-phosphate sodium fluoride solution reduced the ankylosis and replacement root resorption values, although this therapy was not able to avoid them completely. Similar findings were observed in the present study for group I at 60 days postreplantation. There were small areas of replacement resorption. Fewer areas of ankylosis were observed in comparison with the areas of replacement resorption.

Although the ideal treatment has not yet been defined, the most promising therapies seem to lie ever more among the methods that promote or regulate the proliferation of PDL cells, such as growth factors, surface adhering molecules and/or extra-cellular matrix constituents (12).

Emdogain® gel (Biora AB) is an EMD containing proteins that belong to the amelogenin family (19). Apparently, a period of enamel-related protein secretion precedes the formation of acellular cement (25). According to Lindskog et al. (26), as fibroblasts are not able to adhere to dentin surface, acellular cement formation is of paramount importance for rendering the PDL functional.

Therefore, considering that cementogenesis involves secretion of amelogenins and an acellular cementum is required for attachment of Sharpey fibers, it may be assumed that if root surface is covered by an EMD periodontal regeneration might be obtained. Following this reasoning, several studies have tried to extrapolate the promising results obtained in regenerative periodontal therapies (13–16, 27–32) to improve the prognosis of delayed tooth replantation (19, 24, 33–39) or retreat replanted teeth with ankylotic areas (36–39). In this study, Emdogain® was applied onto the root surface of teeth replanted after a 6-h dry storage.

Iqbal & Bamaas (33) reported that the incidence of periodontal regeneration was inversely proportional to the extra-alveolar time in dry medium (the largest period was 60 min). These authors make an important provision stating that the best results were observed on histological cuts obtained from the longest times (12 weeks postreplantation). According to these findings, the great number of ankylotic areas observed in the present study was somehow expected because the extra-alveolar time was even greater (6 h).

The outcomes of this study revealed that the ankylotic areas were more frequent than the replacement resorption areas, which is consistent with the findings of previous studies that used Emdogain® under the same conditions (19, 33–35, 38, 39). However, periodontal regeneration mediated by the PDL cells remaining on the alveolar bone was not observed in this study.

The great question to be addressed is to establish the difference between teeth with extensive bone loss (periodontitis), teeth replanted after a shorter

extra-alveolar time (up to 60 min) and teeth without any possibility of viable PDL remnants, after 6 h in a dry medium. This difference may possibly be explained by the presence of still viable differentiated PDL cells in the first two situations, which may be the crucial factor. Emdogain® is able to stimulate the migration and adherence of cells on root surface (12), but it seems not to be able to stimulate their differentiation. This material has wider cell specificity, similar to that of fibronectin. If root surface is colonized by osteoblasts in the first place, these cells will define the repair pattern.

Conclusion

According to the methodology proposed and based on the results of this study, it may be concluded that neither 2% acidulated-phosphate sodium fluoride nor Emdogain® were able to prevent root resorption in delayed tooth replantation in rats.

References

1. Hamilton FA, Hill FJ, Mackie IC. Investigation of lay knowledge of the management of avulsed permanent incisors. Endod Dent Traumatol 1997;13:19–23.
2. Poi WR, Salineiro SL, Miziara FV, Miziara EV. Education as a means of enhancing the prognosis of tooth replantation. Rev Assoc Paul Cir Dent 1999;53:474–9.
3. Panzarini SR, Saad-Neto M, Sonoda CK, Poi WR, Perri De Carvalho AC. Dental avulsion in young and adult patients in the region of Araçatuba. Rev Assoc Paul Cir Dent 2003;57:27–31.
4. Kenny DJ, Barrett EJ. Recent developments in dental traumatology. Pediatric Dent 2001;23:464–68.
5. Andreasen JO, Borum M, Jacobsen HL, Andreasen FM. Replantation of 400 avulsed permanent incisors 4. Factors related to periodontal ligament healing. Endod Dent Traumatol 1995;11:7–89.
6. Lekic P, Mcculloch CAG. Periodontal ligament cell populations: the central role of fibroblasts in creating a unique tissue. Anat Rec 1996;245:327–41.
7. Andreasen JO. Effect of extra-alveolar period and storage media upon periodontal and pulpal healing after replantation of mature permanent incisors in monkeys. Int J Oral Surg 1981;10:43–53.
8. Duggal MS, Toumba KJ, Russell JL, Paterson SA. Replantation of avulsed permanent teeth with avital periodontal ligament: case report. Endod Dent Traumatol 1994;10:282–5.
9. Barbakow FH, Cleaton-Jones PE, Austin JC, Vieira E. Healing of replanted teeth following topical treatment with fluoride solutions and systemic admission of thyrocalcitonin: a histometric analysis. J Endod 1981;7:302–8.
10. Bjorvatn K, Selvig K, Klinge B. Effect of tetracycline and SnF_2 on root resorption in replanted incisors in dogs. Scand J Dent Res 1989;97:477–82.
11. Selvig KA, Bjorvatn K, Claffey N. Effect of stannous fluoride and tetracycline on repair after delayed replantation of root-planed teeth in dogs. Acta Odontol Scand 1990;48:107–12.
12. Hoang AM, Klebe RJ, Steffensen B, Ryu OH, Simmer JP, Cochran DL. Amelogenin is a cell adhesion protein. J Dent Res 2002;81:693–6.
13. Heijl L, Heden G, Svärdström G, Östgren A. Enamel matrix derivative Emdogain® in the treatment of intrabony periodontal defects. J Clin Periodontol 1997;24:705–14.
14. Mellonig JT. Enamel matrix derivative for periodontal reconstructive surgery: technique and clinical and histologic case report. Int J Periodontics Restorative Dent 1999;19:9–19.
15. Pontoriero R, Wennström J, Lindhe J. The use of barrier membranes and enamel matrix proteins in the treatment of angular bone defects. A prospective controlled clinical study. J Clin Periodontol 1999;26:833–40.
16. Rasperini G, Ricci G, Silvestri M. Surgical technique for treatment of infrabony defects with enamel matrix derivative (Emdogain): 3 case reports. Int J Periodontics Restorative Dent 1999;19:579–87.
17. Okamoto T, Okamoto R. Effect of splinting upon healing after immediate replantation of rat upper incisors. Histomorphological study. Rev Odontol UNESP 1995;24:87–97.
18. Panzarini SR, Perri de Carvalho AC, Poi WR, Sonoda CK. Use of vitamin C in delayed tooth replantation. Braz Dent J 2005;16:17–22.
19. Kenny DJ, Barrett EJ, Johnston DH, Sigal MJ, Tenenbaum HC. Clinical management of avulsed permanent incisors using Emdogain: initial report of an investigation. J Can Dent Assoc 2000;66:21–29.
20. Blomlöf L, Andersson L, Lindskog S, Hedstrom KG, Hammarström L. Periodontal healing of replanted monkey teeth prevent from drying. Acta Odontol Scand 1983;41:117–23.
21. Kanno CM, Saad Neto M, Oliveira JA, Escobar CAB, Saito CTMH. Efeito do hipoclorito de sódio sobre o ligamento periodontal de incisivos de ratos. Arq Odontol 2001;37:35–43.
22. Sonoda CK, Poi WR, Okamoto T, Toyota E, Takeda RH. Mediate teeth reimplantation after root treatment with 1%, 2,5%, 5% and 10% sodium hypoclorite solution. Rev Bras Odontol 2000;57:293–6.
23. Hammarström L, Pierce A, Blomlöf L, Feiglin B, Lindskog S. Tooth avulsion and replantation–a review. Endod Dent Traumatol 1986;2:1–8.
24. Flores MT, Andreasen JO, Bakland LK. Guidelines for the evaluation and management of traumatic dental injuries. Dent Traumatol 2001;17:193–6.
25. Hammarström L, Alatli I, Fong CD. Origins of cementum. Oral Dis 1996;2:63–9.
26. Lindskog S, Blomlöf L, Hammarström L. Repair of periodontal tissues in vivo and in vitro. J Clin Periodontol 1983;10:188–205.
27. Hammarström L, Heijl L, Gestrelius S. Periodontal regeneration in a buccal dehiscence model in monkeys after application of enamel matrix proteins. J Clin Periodontol 1997;24:669–77.
28. Heden G, Wennström J, Lindhe J. Periodontal tissue alterations following Emdogain® treatment of periodontal sites with angular bone defects. A series of case reports. J Clin Periodontol 1999;26:855–60.
29. Sculean A, Reich E, Chiantella GC, Brecx M. Treatment of intrabony periodontal defects with an enamel matrix derivative (Emdogain): a report of 32 cases. Int J Periodontics Restorative Dent 1999;19:157–63.
30. Sculean A, Donod N, Windsch P, Brecx M, Gera I, Reich E et al. Healing of human intrabony defects following treatment with enamel matrix proteins or guided tissue regeneration. J Periodontal Res 1999;34:310–22.
31. Silvestri M, Rasperini G, Euwe E. Enamel matrix derivative in treatment of infrabony defects. Pract Periodontics Aesthet Dent 1999;11:615–8.
32. Yukna RA, Mellonig JT. Histologic evaluation of periodontal healing in humans following regenerative therapy

with enamel matrix derivative. A 10-case series. J Periodontol 2000;71:752–9.
33. Iqbal MK, Bamaas NS. Effect of enamel matrix derivative (Emdogain®) upon periodontal healing after replantation of permanent incisors in beagle dogs. Dent Traumatol 2001;17:36–45.
34. Araújo M, Hayacibara R, Sonohara M, Cardaropoli G, Lindhe J. Effect of enamel matrix proteins (Emdogain) on healing after re-implantation of periodontally compromised roots. An experimental study in the dog. J Clin Periodontol 2003;30:855–61.
35. Lam K, Sae-Lim V. The effect of Emdogain gel on periodontal healing in replanted monkeys' teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2004;97:100–7.
36. Filippi A, Pohl Y, Von Arx T. Treatment of replacement resorption with Emdogain® – preliminary results after 10 months. Dent Traumatol 2001;17:134–8.
37. Filippi A, Pohl Y, Von Arx T. Treatment of replacement resorption with Emdogain® – a prospective clinical study. Dent Traumatol 2002;18:138–43.
38. Schjøtt M, Andreasen JO. Emdogain does not prevent progressive root resorption after replantation of avulsed teeth: a clinical study. Dent Traumatol 2005;21:46–50.
39. Barrett EJ, Kenny DJ, Tenenbaum HC, Sigal MJ, Johnston DH. Replantation of permanent incisors in children using Emdogain? Dent Traumatol 2005;21:269–75.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.