Vital Pulp Treatment

Vital Pulp Treatment

Edited by

Henry F. Duncan
Professor and Consultant in Endodontics
Division of Restorative Dentistry and Periodontology, Dublin Dental University Hospital
Trinity College Dublin, Lincoln Place, Dublin 2, Ireland

Ikhlas A. El-Karim
Clinical Professor and Consultant in Restorative Dentistry
School of Medicine, Dentistry and Biomedical Sciences, Queen's University
Belfast, Northern Ireland, UK

WILEY Blackwell

This edition first published 2024

Registered Offices
John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030, USA
John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

For details of our global editorial offices, customer services, and more information about Wiley products visit us at www.wiley.com.

Wiley also publishes its books in a variety of electronic formats and by print-on-demand. Some content that appears in standard print versions of this book may not be available in other formats.

Limit of Liability/Disclaimer of Warranty
The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting scientific method, diagnosis, or treatment by physicians for any particular patient. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. While the publisher and authors have used their best efforts in preparing this work, they make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of merchantability or fitness for a particular purpose. No warranty may be created or extended by sales representatives, written sales materials or promotional statements for this work. The fact that an organization, website, or product is referred to in this work as a citation and/or potential source of further information does not mean that the publisher and authors endorse the information or services the organization, website, or product may provide or recommendations it may make. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for your situation. You should consult with a specialist where appropriate. Further, readers should be aware that websites listed in this work may have changed or disappeared between when this work was written and when it is read. Neither the publisher nor authors shall be liable for any loss of profit or any other commercial damages, including but not limited to special, incidental, consequential, or other damages.

Library of Congress Cataloging-in-Publication Data
Names: Duncan, Henry, 1971- editor. | El-Karim, Ikhlas A., editor.
Title: Vital pulp treatment / edited by Henry F. Duncan, Ikhlas A. El-Karim.
Description: Hoboken, NJ : Wiley-Blackwell, 2024. | Includes index.
Identifiers: LCCN 2023043780 (print) | LCCN 2023043781 (ebook) | ISBN 9781119930389 (hardback) | ISBN 9781119930396 (adobe pdf) | ISBN 9781119930402 (epub)
Subjects: MESH: Dental Pulp Diseases–therapy
Classification: LCC RK351 (print) | LCC RK351 (ebook) | NLM WU 230 | DDC 617.6/342–dc23/eng/20231107
LC record available at https://lccn.loc.gov/2023043780
LC ebook record available at https://lccn.loc.gov/2023043781

Cover Design: Wiley
Cover Images: © Henry Duncan

Set in 9.5/12.5pt STIXTwoText by Straive, Pondicherry, India

Contents

List of Contributors

Isaac J. de Souza Araújo
Department of Cariology, Restorative Sciences, and Endodontics
University of Michigan School of Dentistry
Ann Arbor, MI, USA

Department of Bioscience Research, College of Dentistry
University of Tennessee Health Science Center
Memphis, TN, USA

Lars Bjørndal
Cariology and Endodontics, Section of Clinical Oral Microbiology, Department of Odontology, Faculty of Health and Medical Sciences
University of Copenhagen
Copenhagen, Denmark

Marco C. Bottino
Department of Cariology, Restorative Sciences, and Endodontics
University of Michigan School of Dentistry
Ann Arbor, MI, USA

Department of Biomedical Engineering, College of Engineering
University of Michigan
Ann Arbor, MI, USA

Roberto Careddu
Division of Restorative Dentistry and Periodontology
Dublin Dental University Hospital, Trinity College Dublin
Dublin, Ireland

Bruno Cavalcanti
Department of Cariology, Restorative Sciences and Endodontics
University of Michigan School of Dentistry
Ann Arbor, MI, USA

Daniel Chiego, Jr.
Department of Cariology, Restorative Sciences and Endodontics
University of Michigan School of Dentistry
Ann Arbor, MI, USA

Paul R. Cooper
Faculty of Dentistry, Sir John Walsh Research Institute
University of Otago
Dunedin, New Zealand

Siobhan Cushley
Centre for Dentistry, School of Medicine Dentistry and Biomedical Sciences
Queen's University Belfast
Belfast, Northern Ireland, UK

Renan Dal-Fabbro
Department of Cariology, Restorative Sciences, and Endodontics
University of Michigan School of Dentistry
Ann Arbor, MI, USA

Till Dammaschke
Department of Periodontology and Operative Dentistry
University of Münster
Münster, Germany

Henry F. Duncan
Division of Restorative Dentistry and Periodontology
Dublin Dental University Hospital, Trinity College Dublin
Dublin, Ireland

Ikhlas A. El-Karim
Department of Restorative Dentistry, School of Medicine, Dentistry and Biomedical Sciences
Queen's University Belfast
Belfast, Northern Ireland, UK

Helena Fransson
Department of Endodontics, Faculty of Odontology
Malmö University
Malmö, Sweden

Lara T. Friedlander
Faculty of Dentistry, Sir John Walsh Research Institute
University of Otago
Dunedin, New Zealand

Johnah C. Galicia
College of Dentistry, Manila Central University
EDSA-Monumento
Caloocan City, Philippines

Kerstin M. Galler
Department of Operative Dentistry and Periodontology
Friedrich-Alexander-University
Erlangen, Germany

Bill Kahler
Faculty of Medicine and Health, Department of Restorative and Reconstructive Dentistry, Sydney Dental School
The University of Sydney
Surry Hills, NSW, Australia

Asma A. Khan
Department of Endodontics, School of Dentistry
UT Health San Antonio
San Antonio, TX, USA

Yoshifumi Kobayashi
Department of Oral Biology
Rutgers School of Dental Medicine
Newark, NJ, USA

Mark Lappin
Department of Restorative Dentistry, School of Medicine, Dentistry and Biomedical Sciences
Queen's University Belfast
Belfast, Northern Ireland, UK

Fionnuala T. Lundy
The Wellcome-Wolfson Institute for Experimental Medicine
School of Medicine, Dentistry and Biomedical Sciences
Queen's University Belfast
Belfast, Northern Ireland, UK

Venkateshbabu Nagendrababu
Department of Preventive and Restorative Dentistry
College of Dental Medicine, University of Sharjah
Sharjah, UAE

Giampiero Rossi-Fedele
Adelaide Dental School, The University of Adelaide
Adelaide, SA, Australia

Emi Shimizu
Department of Oral Biology, Rutgers School of Dental Medicine
Newark, NJ, USA

Matthias Widbiller
Department of Conservative Dentistry and Periodontology
University Hospital Regensburg
Regensburg, Germany

Foreword

In this era of sustainability, the need for minimally invasive, conservative and biologically based treatment approaches has never been more compelling. The patient-centred benefits of such strategies have been clearly illustrated in the success of selective removal of deep caries in operative dentistry, and this approach is now attracting significant interest in the field of vital pulp treatment (VPT). VPT offers a suite of minimally invasive therapies that have the potential to make treatment less invasive, simpler and biologically based while replacing more complex and invasive traditional root canal therapies.

Although not a new concept, the last two decades witnessed a remarkable interest in VPT. Advances in pulp biology research and an improved understanding of the nature of the reparative and regenerative processes in dental pulp, coupled with the continued development of biomaterials, have contributed to the trend. Many published clinical studies have recently demonstrated success for VPT over conventional root canal treatment. It is evident that there are advantages in preserving pulp vitality, highlighted by the simplicity of the techniques and potential cost savings and to that end, VPT has now been endorsed by major professional bodies including the European Society of Endodontology and the American Association of Endodontists. However, many dentists point out that they do not feel well-trained in the area. As the area evolves and the quality of the research supporting VPT continues to improve, it is important that current evidence is summarized and explained systematically in order to improve the understanding of the dental practitioner interested in carrying out VPT. To date, VPT techniques are usually reduced to one chapter in an operative dentistry or endodontic textbook, so we thought it imperative that the breath of VPT, from reasons to keep the pulp, through diagnosis, to management and outcome, were detailed in one user-friendly text.

Furthermore, at present, controversial practices and lack of consensus among clinicians on the best approach to manage deep caries and exposed pulp remain, and there is a need for more education and training to increase awareness and improve the clinical decision-making process and appropriate case selection for VPT. The aim of this book is to provide contemporary, evidence-based and scientific reference to the clinical development and application of VPT in permanent teeth. For this, an international group of experts in pulp biology, cariology, dental trauma, VPT, dental materials and regenerative endodontics contributed chapters highlighting their state-of-the-art skills and knowledge in their respective fields. The result is a book that provides an in-depth knowledge and understanding of the scientific basis for pulp preservation therapies and the importance of maintaining pulp vitality. Secondly, clear clinical guidance with evidence-based clinical protocols is provided for all VPT procedures such as direct pulp capping and partial and complete pulpotomy for both the cariously and traumatically exposed pulps. Accurate diagnosis is

a prerequisite for successful VPT; therefore, pulpal diagnosis is considered as a standalone chapter, but the subject is covered throughout the book, reflecting the importance and also the limitations of our current practice in this area. The development in applied biomaterials, revitalization and regenerative endodontic treatment as well as expected outcomes and follow-up, are covered in the later chapters of the book.

The book combines cutting-edge information with protocols and an array of illustrations, making it suitable for a wide range of clinicians including undergraduate students, postgraduate clinical trainees and researchers, endodontists and general dental practitioners. The book aims to provide a contemporary evidence-based reference in the first book dedicated to VPT, providing answers to existing controversies and considering future perfectives and development in the field. VPT is no doubt evolving, and the hope is that future editions of this book will keep with the momentum. We hope you enjoy the text.

Ikhlas A. El-Karim, Belfast, Northern Ireland, UK
Henry F. Duncan, Dublin, Ireland

Preface

Vital pulp treatment in its various forms has been a subject discussed in dentistry courses for decades. However, it is only recently, in the last five years or so, that converging developments in dental material science, pulp biology and dental have made this treatment a valid, predictable and evidence-based strategy.

It is not even 25 years ago that the long-term success rate of direct pulp capping was estimated as well below 50%, or a flip of coin; this poor outcome understandably has led many clinicians to view vital pulp treatment as somewhat of a second-class treatment, more like an attempt rather than as a bone fide definitive treatment. This perception is changing due to clear and compelling evidence from clinical trials supporting vital pulp therapy and it is rather exciting to see a case made for its application made in this book.

Reasons to maintain a functional pulp-dentine complex are numerous and can be summarized broadly into categories: adding positive features and avoiding potentially negative elements inherent to the main comparator, i.e. root canal treatment (RCT). Vital pulp treatment or VPT retains immunocompetent tissues that effectively provide microbial clearance and protection from apical periodontitis. Moreover, in teeth with incomplete root formation, VPT promotes further dentine apposition and apical maturation. Conversely, RCT is associated with a larger damage to structural integrity, higher cost and specifically for molars with significantly higher clinical complexity.

Indeed, many patients may benefit from VPT in their desire to retain the natural dentition for the long term. It is therefore very fitting and timely that Ikhlas El-Karim and Henry (Hal) Duncan, two clinicians with a strong biomedical understanding, have edited this book; it offers a compelling and comprehensive update on all aspects of VPT, from the case for the selection of the procedure, over material choices to related biology and outcomes.

A balanced group of international authors has contributed to this volume, providing a broad and well-reasoned approach. First the case for treating, rather than removing, the pulp is made by Daniel Chiego and Bruno Cavalcanti succinctly from a functional and a biologic approach. The next chapter authored Paul Cooper, Lara Friedlander and Fionnuala Lundy draws from the vast experience of these authors in pulp biology to strengthen the rationale even more.

This book is directed towards clinicians with a scientific mindset and the following chapters provide contemporary viewpoints on practical aspects of vital pulp therapy. First Asma Khan and Johnah Galicia describe various aspects of pulp diagnostics, an essential step in predicable VPT. With the understanding that VPT is often prescribed in treatment of deep caries, Lars Bjørndal and Helena Fransson provide relevant information from the viewpoint of caries removal strategies.

Moving forward to VPT procedures that are more extensive Till Dammaschke in his chapter looks at direct pulp capping, a procedure that has received much attention with the development

of silicate-based biomaterials. Pulpotomy, an approach that aims to physically remove all coronal pulp with little or no capacity to heal is then discussed by the editors themselves, supported by Roberto Careddu and Mark Lapin.

Chapters 7–10 provide important information for other areas that are critical to the current understanding, including materials (Renan Dal Fabbro, Isaac De Souza Araujo and Marco Bottino), treatment of traumatic injuries (Giampiero Rossi Fedele and Bill Kahler) and regenerative procedures (Matthias Widbiller and Kerstin Galler).

The last chapter on epidemiology and outcomes (Siobhan Cushley, Venkatesh Nagendrababu and Emi Shimizu), again written by authorities in the field, completes this volume.

The enthusiasm of the editors and authors for the topic is palpable and fits where the field is moving internationally, that is towards a much broader acceptance of vital pulp therapy. Providing current and directly applicable information that underpins this therapy is a crucial step in this direction. I am convinced that this book will enjoy a wide readership, equally for seasoned clinicians those at the beginning of their careers.

Ove A. Peters, Professor of Endodontics,
School of Dentistry, The University of Queensland,
Brisbane, QLD, Australia

1

The Importance of Maintaining Pulp Vitality

Bruno Cavalcanti and Daniel Chiego, Jr.

Department of Cariology, Restorative Sciences and Endodontics, University of Michigan School of Dentistry, Ann Arbor, MI, USA

Introduction

When the pulp is inflamed, either reversibly or irreversibly, it is important for clinicians to question the success rates, possible outcomes and patient satisfaction associated with each treatment option. This is also true when considering using more conservative options like vital pulp treatment (VPT) or traditional therapies such as root canal treatment. As highlighted elsewhere in this book, both have a good success rate and can be used as reliable options for the management of pulpal disease.

In this context, one question commonly asked by clinicians is 'what are the real benefits of maintaining the pulp?' It is well-known that immature teeth benefit considerably from VPT. However, clinicians may not see the importance of keeping the pulp tissue for other cases, as the only perceived benefit would be the maintenance of tooth sensitivity. While this benefit is correct, the pulp plays other important roles within the tooth, most notably with the molecular mechanisms to defend the body from bacterial challenge. Furthermore, with the fast development of regenerative therapies, the pulp will be essential to rebuild lost tooth structures and improve the tooth's prognosis. This book chapter will show a number of molecular mechanisms that are involved in this regenerative process, how the pulp physiology contributes to clinical practice and, most important, show the importance of the pulp tissue in the maintenance of tooth homeostasis.

Dental Pulp Development

To appreciate the importance that the pulp plays on tooth homeostasis, it is necessary to appreciate how the dentine-pulp complex develops. The developmental stages bring a number of insights into the participation of different cell types and the subsequent organization of dental tissues, which can also be recapitulated into the desired repair and regeneration processes after dental procedures.

Tooth development is a process that involves a well-coordinated effort between cells from different origins, leading to the formation of a complex organ (detailed in Chapter 2). Unfortunately, when analysing pulp repair/regeneration processes, the clinician is not able to mimic whole tooth formation. This is complicated further by the cells present in the pulp tissue that may not have the

Vital Pulp Treatment, First Edition. Edited by Henry F. Duncan and Ikhlas A. El-Karim.

same potential as the original cells during tooth development. Nonetheless, the translation of the process at the molecular level to the clinical activity can be of great importance to direct future studies and biomaterial development.

In this context, the participation of stem cells in the development process is important. It is now well established that the pulp tissue has its own reserve of multipotent cells, capable of differentiating into the necessary tissues and/or replacing cells that were damaged or simply completed their function and enter into senescence (1). In fact, most dental tissues have their own mesenchymal stem cells; the enamel, for obvious reasons, is deprived of any cells after tooth eruption and, thus, does not have the same regenerative potential as other tissues. The discovery of dental pulp stem cells (DPSCs) brought many possibilities, more specifically in the understanding of the success of VPT and regenerative endodontics. DPSCs are capable of differentiation into a myriad of cells and tissues, including odontoblasts, fibroblasts, endothelial cells and neurons (2–4), being capable of regenerating all cell types necessary to form a new pulp tissue. This potential appears superior to responses observed with other stem cell populations (3). In addition, the literature shows, in animal models, that the neoformed pulp tissue in complete root models is very similar to the original pulp tissue (5, 6) (Figure 1.1). Moreover, these new pulp tissues were induced only in the presence of the host vasculature and DPSCs, suggesting that the potential is there for complete regeneration or at least functional repair.

Cell Signalling and Dental Pulp Development

Most studies using DPSCs have focused on the potential of these cells to differentiate into odontoblasts (7–9). This is understandable as, in the reparative process, clinicians want the neoformed pulp tissue to produce dentine in order for this barrier to serve as protection to the tissue. Understanding odontoblast differentiation is a difficult process: some studies have shown that the reparative dentine, particularly when induced by certain materials, can be tubular (10–12); other studies have shown that, most of the time, the barrier does not have the tubular aspect, meaning that the formed tissue is more akin to 'osteodentine' than to actual dentine (13, 14). This brings uncertainty, as there is no specific odontoblast marker(s) to confirm that the differentiated stem cell is a real odontoblast. Studies have looked into dentin-matrix-acidic-phoshoprotein 1 (DMP-1), dentin-sialophosphoprotein (DSPP), matrix extracellular phosphoglycoprotein (MEPE), nestin and others, generally trying to observe their presence in combination with each other (2, 7, 15–17). However, it is important to emphasize that some of these genes can be expressed by osteoblasts and other cell types, meaning that the differentiated cells observed in molecular analysis may not be a typical odontoblast cell.

With this, it is possible to separate the two concepts of regeneration and repair: from a clinical standpoint, having an adequate regeneration/repair with a solid dentine (or osteodentine) barrier, pulp vitality and functional tooth is good enough for patient satisfaction. On the other hand, from a research standpoint, it can be frustrating that with all the potential observed from the stem cells, we are still not able to regenerate the tissues as they are, complete with an odontoblast pseudostratified layer, cell junctions and tubular dentine.

Some answers for this dichotomy may be due to a shortage of information on molecular signalling. As discussed above, during tooth development, there is a very well-coordinated effort and interaction between different cell types and layers to induce tissue formation and even tooth shape (18, 19). For example, it is known that the signalling between the ameloblasts and mesenchymal cells in the dental papilla induces the initial cell differentiation towards odontoblasts, which consequently directs the deposition of an initially 'disorganized' layer (the mantle dentine) and then starts the construction of the typical tubular pattern of orthodentine, by a centripetal

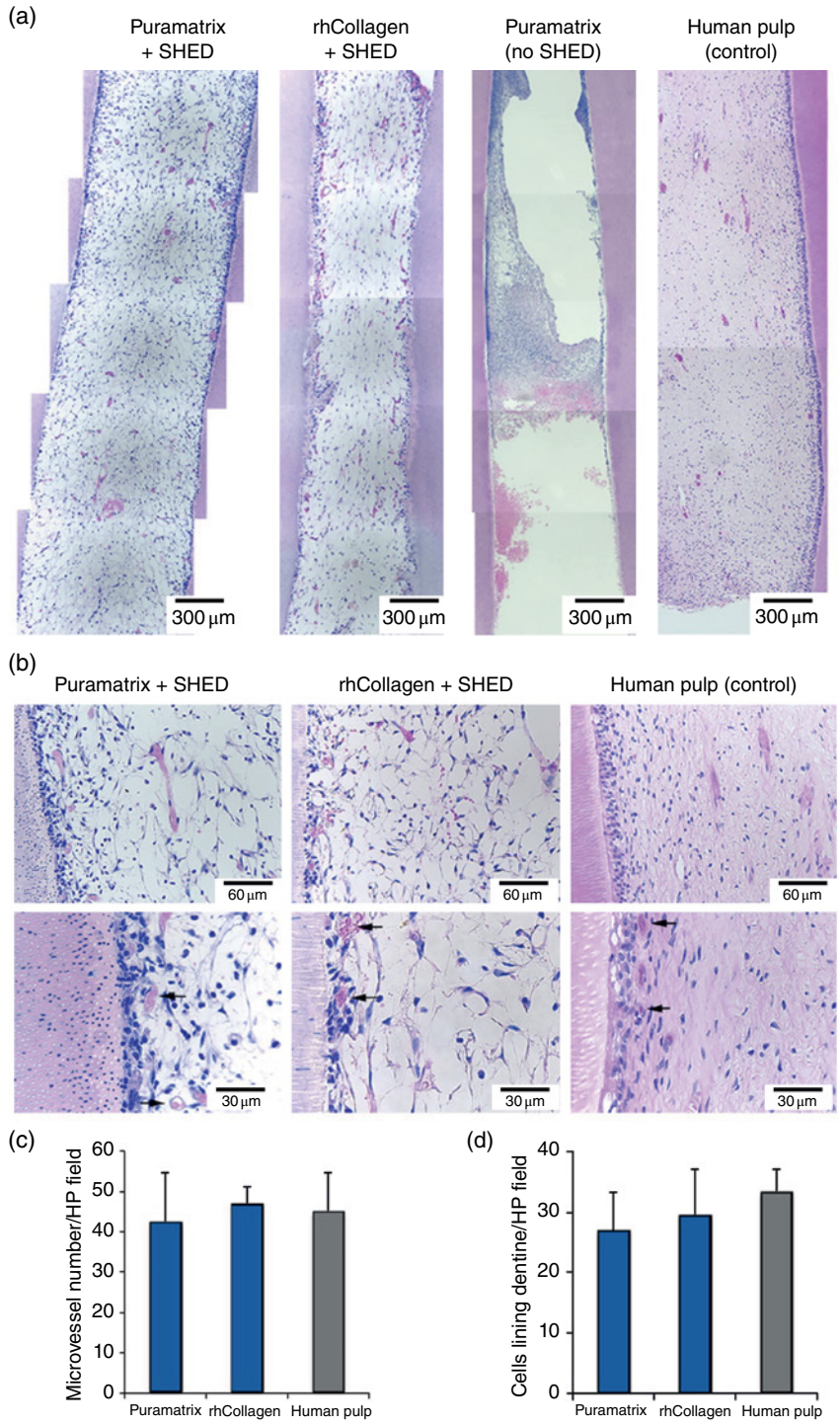

Figure 1.1 Dental pulp tissue engineering with SHED injected into human root canals and transplanted into immunodeficient mice. (a) Low-magnification and (b) high-magnification images of tissues formed when SHED mixed with scaffolds (Puramatrix™, rhCollagen type I groups) were injected into full-length root canals of human premolars. A vascularized connective tissue occupied the full extension of the root canal. Cell densification and many blood vessels were observed along dentin walls. Scaffolds (Puramatrix™) injected into the root canals without cells were used as controls for SHED. Freshly extracted human premolars were used as tissue controls. Black arrows point to blood vessels close to the odontoblastic layer. (c) Graph depicting microvessel density and (d) cellular density of dental pulp tissues engineered with SHED injected into full human root canals. Microvessel density and cellular density were similar in both

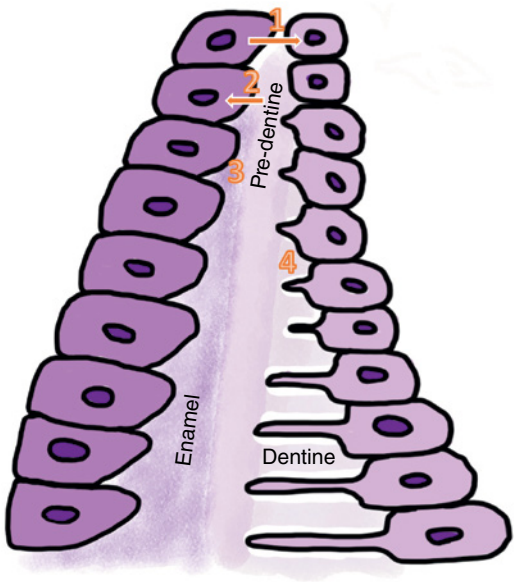

Figure 1.2 Sequence of dentine formation – (1) signalling from pre-ameloblasts to pre-odontoblasts (DSPP, enamelysin and ameloblastin) and deposition of a baseline collagen matrix; (2) deposition of pre-dentine by the immature odontoblasts, leading to signalling to ameloblasts; (3) enamel deposition; (4) dentin (tubular deposition). Both ameloblasts and odontoblasts mature throughout the process.

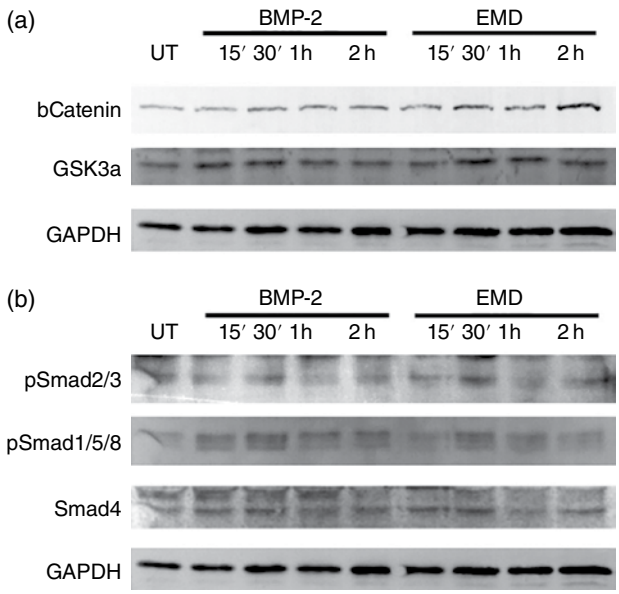

Figure 1.3 Western blotting analysis of pathways affected by BMP-2 (a known dentine inducer) and EMD (enamel matrix derivatives) on dental pulp stem cells. Differences can be seen by the increase of expressed Wnt pathway proteins for EMD (a) and the increase of Smad 4 for BMP-2 in the canonical BMP pathway (b). Unpublished data.

direction of movement of the odontoblast layer (Figure 1.2). This signalling is comprised principally of DSPP, enamelysin and ameloblastin (20). However, it is evident that the Wnt and Sonic hedgehog (SHH) pathways and the deposition of a baseline collagen matrix are also essential for the correct cell lining (18, 21). With this, attempts were made to use enamel derivative proteins to induce pulp repair. However, there are differences between the differentiation induced by enamel matrix derivatives (EMD) and mineral trioxide aggregate (MTA), for example, even if the gene expression changes are similar (Figure 1.3). Clinically, none of the materials used for pulp capping and/or regenerative procedures is capable of synthesizing and secreting the original signalling molecules

layered by ameloblasts. This does not mean that the regeneration process is impossible. The literature has shown examples that the dentine itself is a major reservoir of multiple growth factors that can activate multiple signalling pathways into DPSCs (22). More importantly, these growth factors can be mobilized by current materials used for pulp capping (e.g. calcium hydroxide and MTA), which can be of great importance in chemotaxis prior to inducing cell differentiation and production of the dentine barrier (23–25).

The Role of the Apical Papilla

Last, but not least in tooth development, is the role of the apical papilla. While considered an embryonic tissue, the apical papilla is a mesenchymal tissue that remains active until the complete maturation of the tooth (Figure 1.4). After the deposition of the first layers of dentine at the crown level and subsequent formation of the primitive pulp tissue, the remnants of the dental papilla continue to work with the Hertwig's epithelial root sheath in order to guide the development of the cementum, alveolar bone, radicular dentine and periodontal ligament (26, 27). As with the crown, the signalling between epithelial and mesenchymal cells is responsible for tissue differentiation of the stem cells present in this tissue and consequent dentinogenesis. Even after the tooth eruption, the root(s) will continue to develop and, until the development is complete, the apical papilla will remain. As the original dental papilla, the apical papilla is rich in undifferentiated cells with multipotent capacity, which makes it a great source of stem cells for revitalization or revascularization procedures (28).

This understanding of the tooth development process brings insight into the repair process induced by VPTs. The first associated with the presence of undifferentiated cells and its potential to differentiate into odontoblasts and other cell types necessary for repair and regeneration. Second, it is expected that an effective material will closely mimic the interactions between these mesenchymal stem cells and the epithelial cells that formerly underlined the primitive pulp tissue. Third, molecules that participate not only in the differentiation process but also in the cell recruiting events may be of interest for using dental materials. This can happen directly or indirectly as dentine serves as a reservoir for many of these factors, and materials can be affected by extracting them from the tissue and mobilizing them for cell intake.

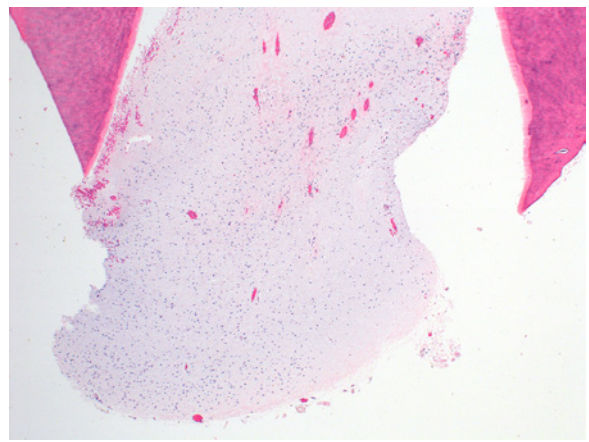

Figure 1.4 Histologic image from the apical papilla, detaching from the root apex of an immature third molar. Observe the high cellularity and vascularization of the tissue, which can be preserved partially and used for endodontic regenerative purposes (HE, 40×).