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Understanding **Platelet-Rich Fibrin**

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Understanding Platelet-Rich Fibrin

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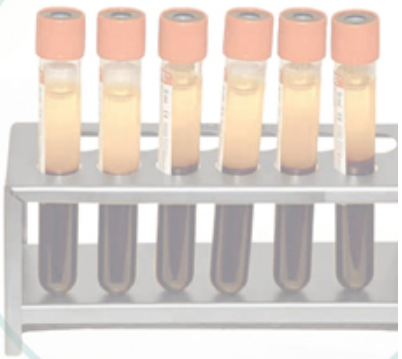

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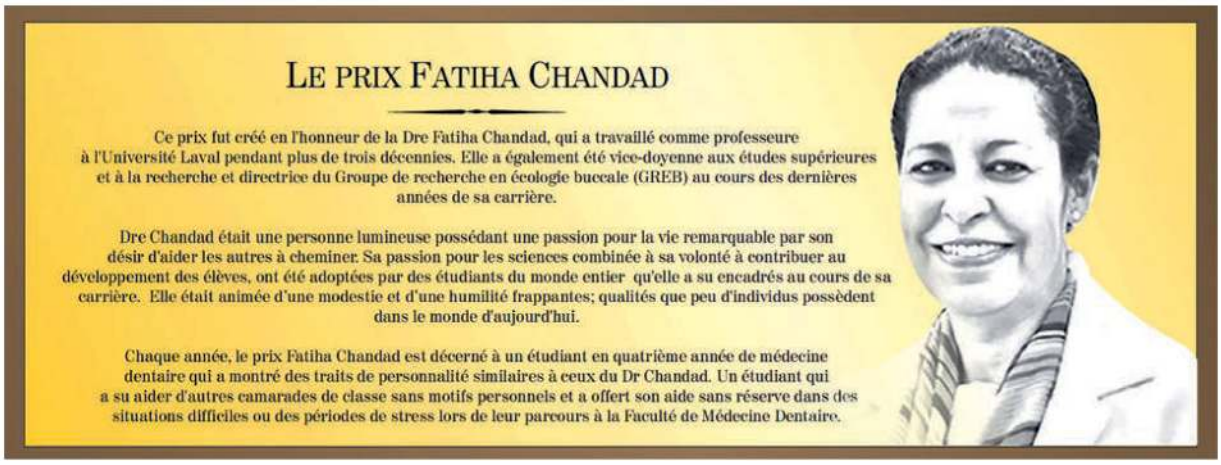
Dedication



I would like to dedicate this textbook specifically to Dr Fatiha Chandad and the Dental Faculty at the University of Laval in Quebec, Canada, who devoted countless hours to training students like me in dentistry.

Dr Chandad, Dean of Dental Research, was someone who motivated me and more importantly made it possible for students to work within her laboratory on research projects during their 4 years of dental studies. It was here that I first started my research activities on PRP/PRF and became fascinated with research as a whole. Dr Chandad is one of the only people I have ever met never wanting to be recognized for her achievements, instead insisting that her students be recognized and at the forefront of their own success. It was during these times that I was awarded the prestigious Hatton Award in Canada and was later named the IADR Young Investigator of the Year in Implant Dentistry.

In appreciation of her contributions to my career, 100% of the royalties from this textbook will be donated to create a scholarship named after her for new dental graduates at the University of Laval. *Milles fois merci pour tout tes efforts!*

Foreword

Many important medical/dental discoveries were stumbled upon by pure chance. An example of this is osseointegration, which launched the modern era of dental implants and orthopedic-embedded prostheses. It occurred when orthopedic researcher Per-Ingvar Brånemark found that his titanium research cages in sheep were so completely ingrown with bone that he couldn't remove them. Similarly, platelet-rich plasma (PRP)/platelet-rich fibrin (PRF) was discovered by the serendipity of observing accelerated and more complete healing in patients who developed hematomas. From that simple observation in the 1980s, the components of the blood clot responsible for the advanced healing have since been determined to be the complete and active growth factors in the alpha granules of viable platelets and several cell adhesion molecules and homing signals in the fibrin clot.

From the early pioneering work in the 1990s to the present, the benchmark of platelet numbers and the functional characteristics of the growth factors, cell adhesion molecules, and homing signals of PRP/PRF have progressed to a mature science and easy-to-use point-of-care devices.

Today, PRP/PRF devices are able to predictably concentrate platelets to known therapeutic levels by a variety of technologic means and to include or exclude leukocytes as per the needs of the wound. PRP/PRF has become a mainstay in bone regeneration in dental implantology and jaw reconstruction, for tendon and joint repair in orthopedics, for soft tissue healing in wound care centers, and in plastic surgery; it has thus benefited hundreds of thousands of patients worldwide.

As one of several individuals who were there at the beginning of the PRP/PRF discovery and who helped to move it along the way somewhat, I am delighted to see that the next generation of clinical researchers as published in *Understanding Platelet-Rich Fibrin* have brought it to the next level.

This text is written for the clinician to understand how and why PRF promotes healing of both bone and soft tissue as well as how to apply it to improve their own results. Written with a balanced blend of science and clinical applications by the most experienced and accomplished PRP/PRF scientists and clinicians of the day, and beautifully illustrated, *Understanding Platelet-Rich Fibrin* is a book for this decade that transcends all specialties of dentistry and many of medicine.

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Preface

Over 20 years ago, platelet concentrates entered into the medical field as a means to deliver autologous growth factors responsible for favoring wound healing. During this time span, it has gained widespread acceptance in many fields of medicine due to its more natural delivery system.

Most notably, the past 5 years have seen a tremendous increase in publications on PRF, with over 200 scientific peer-reviewed papers being published each and every year. During this span, a marked increase in our understanding of PRF therapy has been made with respect to selection of appropriate centrifugation devices, impact of tube chemistry on clotting, the optimization of protocols to better concentrate PRF, and even the ability to extend the working properties of PRF from 2–3 weeks toward 4–6 months using a simple heating process. Collectively, we continue to gather new knowledge, and as a result, PRF therapy has become one of the fastest-growing therapeutic options in dentistry. Thousands of users have now benefited from this technology, and this number is only expected to continue to increase.

This book is very different from others in its concept design. More than a dozen expert researchers and clinicians alike were gathered as editors across their different fields of expertise. As section editors, these true experts of their respective disciplines were able to produce a much higher overall quality of this textbook. I am grateful for their encouraging team spirit, their effort in bringing this book to an entirely new level, and their level of professionalism and mindset that ultimately led to this comprehensive textbook. I am also grateful to the numerous clinicians who have provided videos to better educate/demonstrate surgical

techniques and concepts with PRF, which will greatly enhance the learning experience of the reader.

The book is divided into four primary sections, including *(1)* biology of PRF, *(2)* periodontology, *(3)* implant dentistry, and *(4)* additional dental and medical applications. The book aims to take the reader from a basic biologic understanding of PRF through explanations of the various protocols utilized followed by application of these concepts in numerous clinical scenarios.

I therefore am thrilled to introduce our textbook titled *Understanding Platelet-Rich Fibrin*. I hope you enjoy learning the many aspects centered around the use of PRF in regenerative dentistry.

Acknowledgments

To my parents, family, and friends who have all sacrificed far too often in my pursuit of a career in academic dentistry.

To my classmates, colleagues, and mentors who constantly raised the bar and strived for better.

To Quintessence Publishing for your thorough input in the editing, illustrations, and design of this textbook.

To my family at Lakewood Ranch Dental in Florida who have made clinical practice as enjoyable an experience as can be on a *daily* basis.

To all leaders and researchers alike who have contributed enormously to the field of PRP/PRF and laid the foundation for this textbook to be written.

To the faculty in the Department of Biomedical Sciences and Cell Biology at the University of Western Ontario (London, Canada; BMSc, MSc), the Dental School at the University of Laval (Quebec; DDS), the Department of Music at Berklee College (Boston; MMus), the Department of Periodontology at the University of Bern (PhD, Dr med dent), the Department of Oral Implantology at Wuhan University

(China; postdoctoral research fellow), the Plastic Surgery Department at Queen Mary University (London; clinical masters in facial esthetics), and the Department of Periodontology at the University of Illinois at Chicago (clinical masters in periodontology). Your education and mentorship has provided endless opportunities.

And lastly, to the team at Advanced PRF Education (www.prfedu.com) for making excellence in teaching a top priority.

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Abbreviations

The abbreviations listed here are used throughout the book and are NOT always spelled out in the chapters for ease of reading.

ALP	alkaline phosphatase
AM	amniotic membrane
A-PRF	advanced PRF
BoP	bleeding on probing
BMP	bone morphogenetic protein
CAF	coronally advanced flap
CAL	clinical attachment level
CBC	complete blood count
CEJ	cementoenamel junction
C-PRF	concentrated-PRF
CTG	connective tissue graft
DBBM	deproteinized bovine bone mineral
DFDBA	demineralized freeze-dried bone allograft
ECM	extracellular matrix
EDTA	ethylenediaminetetraacetic acid
EGF	epidermal growth factor
EMD	enamel matrix derivative

e-PRF	extended-PRF
ePTFE	expanded polytetrafluoroethylene
FDA	US Food and Drug Administration
FDBA	freeze-dried bone allograft
GBR	guided bone regeneration
GF	growth factor
H&E	hematoxylin-eosin stain
hPDLC	human periodontal ligament cell
H-PRF	PRF obtained through horizontal centrifugation
IGF	insulinlike growth factor
IL	interleukin
i-PRF	injectable-PRF
ISQ	implant stability quotient
KTW	keratinized tissue width
L-PRF	leukocyte PRF
LPS	lipopolysaccharide
LSCC	low-speed centrifugation concept
mRNA	messenger RNA
MRONJ	medication-related osteonecrosis of the jaw
MSC	mesenchymal stem cell
OFD	open flap debridement
ONJ	osteonecrosis of the jaw

PD	probing depth
PDGF	platelet-derived growth factor
PPE	personal protective equipment
PPP	platelet-poor plasma
PRF	platelet-rich fibrin
PRGF	plasma rich in growth factors
PRP	platelet-rich plasma
PTFE	polytetrafluoroethylene
RBC	red blood cell
RBH	residual bone height
RCF	relative centrifugal force
RCT	randomized controlled trial
rpm	revolutions per minute
RT-PCR	real-time polymerase chain reaction
SD	standard deviation
SE	standard error
SEM	scanning electron microscopy
TGF-β	transforming growth factor β
TMJ	temporomandibular joint
TNF-α	tumor necrosis factor α
T-PRF	titanium-prepared PRF

VEGF	vascular endothelial growth factor
WBC	white blood cell

Evolution of Platelet Concentrates

Contributors

Richard J. Miron

Chapter Highlights

- *Evolution of PRF and the reasons for its discovery*
- *Discussion of PRP vs PRGF vs PRF vs L-PRF, A-PRF, etc*
- *Biologic background of key steps involved during wound healing*

Video 1-1

Platelet concentrates were derived more than 20 years ago following the discovery that platelets themselves act as key regulators during the wound healing process. Initial attempts were first made to concentrate these cells using anticoagulants and a centrifugation device; the resulting biomaterial was called *platelet-rich plasma*

(PRP). Shortly thereafter, protocols were developed with the aim of avoiding the use of anticoagulants altogether, because clotting is a pivotal step during the wound healing cascade; the resulting biomaterial was called *platelet-rich fibrin* (PRF). Today, platelet concentrates have become incredibly relevant worldwide, with their use spanning across nearly every field of regenerative medicine. Furthermore, one of the main growth factors (GFs) found in platelets—platelet-derived growth factor (PDGF)—has been commercialized as a ready-made laboratory recombinant protein under the trade name GEM 21S (Lynch Biologics). Thus, as medicine has continued to evolve and progress, an obvious and clear trend favoring GF use has been established. Furthermore, by modifying centrifugation devices and spin protocols of PRP/PRF, a greater ability to concentrate not only platelets but also leukocytes became possible, further favoring tissue regeneration. This chapter takes a deep look at the years of research leading to the significant advancement that has been made in this field. The evolution from PRP to PRF, including pioneering concepts such as the low-speed centrifugation concept and horizontal centrifugation, are discussed in terms of their ability to favor higher cell content, GF concentration, and ultimately better wound healing.

Platelet concentrates have been utilized in medicine for over two decades because of their ability to rapidly secrete autologous GFs and ultimately speed wound healing. They have gained tremendous momentum as a regenerative agent derived from autologous sources capable of stimulating tissue regeneration in a number of medical fields.[1,2] Many years ago, it was proposed that by concentrating platelets using a centrifugation device, GFs

derived from blood could be collected from a platelet-rich plasma layer and later utilized in surgical sites to promote local wound healing.[1,2] Today, it has been well established that platelet concentrates act as a potent mitogen capable of the following (Fig 1-1):

- Speeding the revascularization of tissues (angiogenesis)
- Recruiting various cells including stem cells
- Inducing the prompt multiplication of various cell types found in the human body (proliferation)

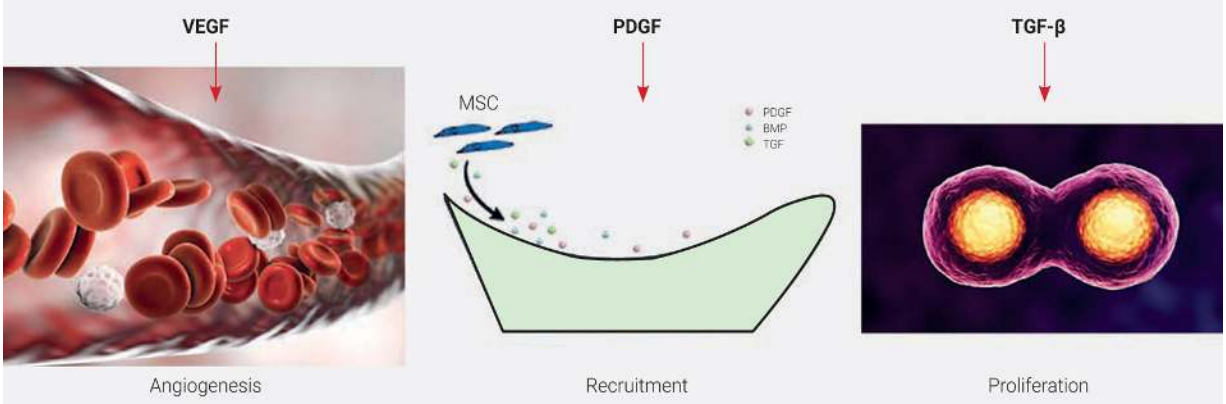

Fig 1-1 The three main GFs that are released from PRF include VEGF, a known inducer of angiogenesis; PDGF, a known inducer of cell recruitment; and TGF-β1, a known stimulator of cell proliferation. MSC, mesenchymal stem cell.

Wound healing is a complex biologic process whereby many cell types interact with one another as well as their local extracellular matrix (ECM) in order to repair and regenerate damaged tissues.[3–6] While many regenerative agents currently exist on the market to help speed tissue regeneration, it is important to note that the majority are derived from other human sources (allografts) and animal byproducts. These naturally create a foreign body reaction when implanted into host tissues. While the majority of such biomaterials do certainly favor improved healing, it has