The Elixir of Platelet Rich Plasma Therapy in Intervention Dermatology and Regenerative Trichology

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Edited by

Suruchi Garg

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FOREWORD

Dr Suruchi Garg has focused on treating dermatologic and genetic conditions that cause hair loss for many years. Her interest in this field was apparent when she visited my clinic years ago and since then has developed a special interest in regenerative medicine and specifically in the potential that platelet-rich plasma (PRP) has in treating the disorders causing hair loss.

In this book the readers will find the theoretical and practical, the science and the art, all carefully blended for the benefit of the readers. It is clear that Dr Garg is an advocate for using the unique properties of the human biological system to treat various conditions, and this book explains how PRP can be of benefit. When relevant, she provides the studies to support the use of PRP in certain situations and then offers the practical knowledge required to deliver the treatment.

If you treat hair loss and you want to provide PRP to your patients, you will find Dr Garg's book to be thorough and practical and it will allow you to deliver this therapy in a safe and effective manner.

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The passion for regenerative medicine and for the treatment of some pathologies addressed by it, such as alopecia, has led over the years many scientists to better investigate, through rigorous scientific studies, the possible new autologous therapies in the treatment of hair loss.

All the latest knowledge in the treatment of alopecia using platelet-rich plasma reported by all the experts who have decided to contribute to the realization of this work deserves to be read.

Pietro Gentile, MD, PhD
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University of Rome "Tor Vergata"
Regenerative Surgery PhD
Top Italian Scientist (H-Index >31)

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Platelet-rich plasma (PRP) contains several growth factors and cellular adhesion molecules which promote wound healing, angiogenesis and accelerate the rejuvenation of skin and hair follicles. With its proven regenerative and regrowth potential in a plethora of conditions.

Use of PRP alone or in combination with hair transplant in androgenetic alopecia is well-researched indication. It has shown excellent results when utilized in combination with microneedling or ablative lasers in acne scars, post-burn or post-traumatic scars, melasma, striae distensae, chronic ulcers and lichen sclerosis. PRP injections or PRP combined with microneedling are increasingly being utilized for skin rejuvenation and recently have been utilized to provide non-invasive face lifts. Combining non-cultured epidermal cell suspension suspended in PRP results in superior re-pigmentation outcomes in case of vitiligo. PRP has now become an indispensable tool in the dermatology practitioner's armamentarium and a comprehensive text covering all the relevant aspects regarding this therapy was the need of the hour. Though there are a lot of articles available on PRP, each article mentions some different protocol and method creating a great deal of confusion among the readers.

This all-inclusive textbook discusses the various indications, techniques, modifications of PRP as well as its application in various indications in great detail with special mention of the practical aspects.

The book shall be a ready reckoner for the practicing dermatologists, dermatosurgeons, general surgeons, plastic surgeons and other clinicians who are fascinated by this novel technique. It will be a go to book for all your queries regarding PRP.

I wish all the very best to the editor who has great experience in effectively utilizing this "wonder tool" in interventional dermatology as well as trichology. She has previously published several novel research articles and this textbook is an amalgamation of her expertise, knowledge and practical understanding of PRP along with the contributions of leading dermatologists who put in hard work to compile the current knowledge, besides contributing their thoughts and ideas regarding these diverse aspects.

I am sure that this book will be widely received and acclaimed.

Dr Rachita Dhurat
Organizing Chairperson, Trichology Update
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Dermatology is a vast subject which is continuously in a state of evolution. Besides medical dermatology, dermatosurgery and cosmetic dermatology are rapidly growing. Platelet-rich plasma (PRP) therapy is a modality which is being used for several dermatological diseases and the evidence is gradually accumulating. Dr Suruchi Garg is a well-known dermatology practitioner with several publications to her credit and has now produced this multi-authored book on PRP. This book will be a handy reckoner to both early and senior practitioners who use physical modalities in their practice. I would like to congratulate her and all the authors for writing on different aspects of treatment of skin disorders with PRP. I wish the editor luck for her well-intentioned book and happy reading to the interested readers.

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New Delhi, India
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Platelet-rich plasma (PRP) is autologous concentration of platelets contained in small volume of plasma which accelerates the rejuvenation of skin and hair follicles (HFs) due to presence of various growth factors and cellular adhesion molecules. PRP therapy is a relatively new approach to tissue regeneration, which is becoming a valuable adjunct to promote healing and enhance treatment outcomes of various procedures in medical and surgical fields.

Over the last decade, PRP has attained a well-deserved place in the therapeutic armamentarium of dermatologists in variety of indications including hair loss, post-acne scarring, disorders of pigmentation, non-healing ulcers, facial rejuvenation, and regenerative medicine. Apart from dermatology and aesthetic practice, it is increasingly being used in maxillofacial surgery, periodontal and oral medicine, otolaryngology, orthopaedic and trauma, cardiovascular, gastrointestinal, burns, and plastic surgery. While there is growing popularity of PRP among dermatologists and other specialities, a scarcity is felt for textbooks and evidence-based standardized protocols on the science of PRP. Dr Suruchi Garg is one of

the leading experts from India who has extensively used and pioneered art of PRP in dermatology and aesthetic medicine practice. Dr Suruchi Garg and her co-authors have filled this void through their enriching contribution.

This textbook provides an excellent learning and reference material across the whole spectrum of the use of PRP. It is going to be an asset for young dermatologists and postgraduate students who wish to learn and incorporate PRP in their practice. I would highly recommend it for anyone who is interested in obtaining basic knowledge of PRP, research, or updating and perfecting existing knowledge and skills.

I congratulate Dr Suruchi Garg for her vision, conviction, dedication, and all the hard work in bringing out this excellent textbook.

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PREFACE

The insatiable curiosity of the human mind constantly motivates it to improve the existing treatment modalities and has led to path-breaking discoveries and inventions. While many researchers toil hard in labs – discovering and establishing the role of new drugs and formulations; others are fascinated by the body's own healing capacity and ability to regenerate it. This is what essentially lays down the foundation of regenerative medicine.

Regenerative medicine is an upcoming branch where the body's own cells, tissues, or fluids can be regenerated, engineered or replaced to restore and establish normal functions. Platelet-rich plasma is one such promising therapy that is increasingly being utilized as an adjunct to standard medical and surgical therapies and is expected to be the future of various regenerative and restorative therapies.

This book aims at bringing forth the most innovative and minimally invasive techniques, to improve the outcome of existing diseases and to improve the tell-tale signs of burned-out diseases through PRP cocktails. PRP therapy has gained immense popularity in the past decade in the field of intervention dermatology and regenerative trichology, but there are a lot of trials and tribulations making the subject all the more intriguing and difficult to understand. Detailed and organized research work is the need of the hour to bring more clarity to the subject for researchers, clinicians and practitioners working in this field.

This book is written and compiled based on the existing literature on PRP therapy along with excerpts from my own personal experiences and publications in different journals over 10 years.

It will discuss at length the methods of preparation of PRP, single spin versus double spin, role in different types of alopecia, hair transplant and scarring alopecia, scar management, pigmentary disorders, facial rejuvenation and non-healing ulcers. There will also be a mention of the use of novel surgeries like our innovative vitiligo surgery called LA-PEEST (laser ablation of recipient area with PRP-enriched epidermal-dermal suspension transplant) and RA-PEEST (radiofrequency ablation with PRP-enriched epidermal-dermal suspension transplant) aimed at making new skin, which would otherwise heal with secondary intention and possibly scarring.

Towards the end, very passionately and ambitiously we discuss the use of various live cells including hair follicle-derived stem cells which are the future of regenerative therapy, as treatment options for various ailments in intervention dermatology and regenerative trichology.

In various academic forums, one sees a vast majority of clinicians not entirely convinced about the efficacy of platelet-rich plasma in spite of the plethora of literature supporting its mechanism of action and results. Along similar lines, there is another set of clinicians, who believe that nutrition and correction of underlying deficiencies do not offer many roles in modifying a disease process.

In my humble opinion, both regenerative medicine and nutrigenomics lay down the foundation of future medicine, and together they lay down the foundation to a very crucial and synergistic role to be played to facilitate the healing process. It is analogous to supporting the "organic and green approach" instead of "industrialized management of disease pathogenesis" inside the human body. Endorsing the same understanding in my practice, we have very passionately pursued and observed the role of both nutrition and regenerative medicine working hand in glove. At the end of the day, researchers and clinicians need to understand the biology, chemistry and dynamics of the body's signals being generated at the cellular level. The response is based on the type of substrate available; in turn, the response of the tissues, organs and systems is based on circadian rhythm and endocrine, paracrine, autocrine and enzymatic signals dictating the course of action towards healing or inflammation. It is astonishing to observe that the injuries on these sites can be healed and modified with additional growth factors released from platelet-rich plasma and other regenerative tissues, kick-starting an array of chemical reactions and cascade of events to aid the healing process and improve the overall environment. The current work in regenerative medicine is just the beginning of a highly fruitful and fulfilling journey and hopefully, more researchers will be benefited and inspired to explore the vast ocean of knowledge in this direction.

The purpose of bringing out this book is to bridge the gap between existing medical treatments and the body's regenerative capacity through regenerative medicine and to create an understanding of utilizing the body's own immense healing potential. This book provides a concise and result-oriented approach to the field of regenerative medicine and interestingly, some of the major work described is based on cocktail treatments, which hasten the results in fewer sessions without compromising the patient's safety. The work should interest all those physicians and surgeons who believe in providing minimally invasive procedures, which

eventually create a significant difference in their patients' quality of life. The approach has the potential to provide hope to patients suffering from recalcitrant diseases, otherwise not amenable to conventional dermatology treatments.

Dr Suruchi Garg

INTRODUCTION

Dr Suruchi Garg is the Director and Chief Consultant at Aura Skin Institute, Chandigarh, India. She was awarded her MBBS from IGMC Shimla, a premier institute located in the lap of Himalayas and post-graduation in dermatology from one of India's most coveted and prestigious tertiary care institute, the Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh.

Dr Garg has undertaken advanced training in lasers from Cesaria, Israel and hair transplant training from Denver, US. She won a Young Dermatologist Forum Award for her work on cutaneous vasculitis in the most prestigious national conference, Dermacon 2008. She was also honoured with the Distinguished Scholar Award 2020 by the European Journal of Scientific Research for her outstanding contribution for the use of platelet-rich plasma therapy and hair transplant in the field of scarring alopecia. Besides this, she has numerous state and national level awards, and accolades to her credit for bringing in the latest cutting-edge technologies and innovations in the field of intervention dermatology and regenerative trichology.

Dr Garg is the programme director for IADVL (Indian Association of Dermatologists, Venereologists and Leprologists) with a fellowship in lasers and aesthetics, and specializes in training post-dermatology fellows in lasers, vitiligo surgeries, hair transplant, platelet-rich plasma, and various aesthetic procedures. She has innovated a surgical technique in vitiligo patients (LA-PEEST) which delivers faster re-pigmentation and aesthetically more acceptable results, as published in the international journal Dermatologic Surgery. She has performed numerous such surgeries to reduce the psychological impact and the disease burden in scores of vitiligo patients.

She has filed patents in non–surgical facelift through fat repositioning and another on an AI (artificial intelligence) based approach aimed in the same direction, which she genuinely considers "a step towards true anti-ageing". According to her, the approach can minimize the use of external fillers as it utilizes the patient's own facial droopy fat planes. Dr Garg has also proposed and published a global drooping and wrinkle (DW) classification for facial age estimation. She is undergoing pioneering work in regenerative medicine with publications in various national and

international journals and books of high repute, and conducting training courses and workshops at national and international levels.

Dr Garg has been designated the key opinion leader (KOL) by many companies of international repute such as Alma and BTL aesthetics. She is actively contributing to innovation and technology with maximum safety and efficacy for the treatment of Asian skin types. She is also a passionate nutritionist and has various papers on nutrition, skin and hair disorders, and has also conceptualized a protein-based health supplement based on the "principle of circadian rhythm and science of proteins". Currently, she is the section editor for Indian Dermatology Online Journal and a member of editorial team in the journal *Cosmoderma,* and a reviewer for various other prestigious international journals.

CHAPTER 1

THE HISTORY OF BLOOD, BLOOD PRODUCTS AND THEIR USES SINCE ANCIENT TIMES

SURUCHI GARG, KASHVI GARG,
ANUVA BANSAL

"*We are linked by blood, and blood is memory without language*"
—Joyce Carol Oates

Blood is mysteriously being chased in incantations, potions, religious practices, medieval medical treatises and works of fiction. The Ebers papyrus, the ancient Egyptian literature is written in hieratic Egyptian language. It is based on elaborate medical knowledge transferred through pre-existing literature and dates back to 1500 BC.[1] It mentions the heart as the centre of blood supply and various vessels linking the heart to every organ of the body. The prevalent "channel theory" proclaimed unimpeded blood flow to different organs of the body as the essential prerequisite for good health. In the Indian subcontinent, the era of establishing the role of blood and its components goes back to more than 600 BC with the meticulous scrutiny of the available literature. The first manuscripts are written in Sanskrit, the most ancient language of the world often touted as the mother of all languages. These manuscripts are *Sushruta Samhita, Charaka Samhita, Bala Samhita* and so many more written by the eminent Ayurvedic physicians and surgeons in those times. The *Charaka Samhita* deals with medicine, written by famous Ayurvedic physician Charaka and describes in depth the circulatory system (*Rasavaha srotas*) in the body and suggests that the system works like a rotating wheel.[2] Sushruta (around 600 BC) in his primeval compendium *Sushruta Samhita* mentioned that the pattern of blood flow was identical to the velocity of sound, fire and water, which are maximum at the source and gradually diminish away from the source or heart.[3] Sushruta, a renowned plastic surgeon in those times is regarded as the *father of plastic surgery* in the ancient Indian

medical system. He is known to have had excellent knowledge about the circulatory system and it is mentioned in the compendium that his knowledge was principally derived by conducting the post mortems of dead bodies floating in the water, passed on to him by his teachers.[3] As per Ayurvedic literature, there are four components of blood: 1) "Rasa" or plasma, the nutrient fluid that nourishes the rest of the tissues; 2) "Rakta", the red fraction (red blood cells) that is essential for life; 3) "Ojas", a white fraction (white blood cells and platelets), the functions of which are closely associated with immunity; and 4) "Prana", (oxygen) a fraction that is derived through the act of respiration. Therefore, the tissue that is today known as "blood" should include all these components.[4]

Knowledge in the ancient world

In the ancient world, the function of the heart and vessels were a great mystery. Many hundred years BC the Greeks Herophilus of Chalcedon (c. 335 to c. 260 BC) and Alcamaeon of Croton (c. 535 to unknown BC) believed that arteries and veins are dissimilar in animals when compared to those of humans; they believed that arteries are thicker than veins and distribute the blood.[5] There is a possibility of various interactions having taken place between the scholars of ancient Greece and India, especially when Alexander the Great (326 BC) invaded India, specifically the places around Taxila, one of the ancient seats of learning.[6] Eventual outcomes could have been the mixing of information and both sides influencing and contributing to existing knowledge.

The Greeks described the presence of erythrocytes (red blood cells) in blood, giving it the characteristic colour. According to the most widespread ancient Greek scientific views, the blood was believed to be a necessary nutrient of the living body, as are juices for plants.

Hippocrates (450–380 BC) knew that blood moves and performs a periodic or circular movement – *"periodon, cyclon"*.[7] He also believed that blood is produced in the liver and spleen and travels to the heart, and is warmed or cooled in the lungs. There was also existing knowledge that the human body has four types of fluid (blood, phlegm, and black and yellow bile).[8]

Aristotle (384–322 BC) considered blood to be the essence of nutrition and the preserver of body heat, and termed it the ultimate food. Blood is the food in its most perfect form, which creates and preserves the noblest parts of the body – the flesh and other sensory organs.[9]

According to Claudius Galenus of Pergamon (200–130 BC) *hema* is a warm and fluid material that is present in the arteries, from which the

animal is fed.[10] Galenus's words *haema einai ten psychen* meaning blood is the soul were a few of the misleading beliefs in those times. Galenus also believed that life was sustained by food, which turned into blood in the liver, which nourished the lungs, heart, brain and other organs along with the removal of waste products. Thus, blood circulation and metabolism became the significant elements of his philosophical theory, and he was a pioneer in suggesting a relationship between food, blood and air. [10,11]

Later discoveries

Subsequent centuries saw landmark discoveries related to circulatory systems such as the discovery of the existence of heart valves (Iranian Rhazes, AD 865–925) and pulmonary circulation (Syrian Ibn Al-Nafis, AD 1210–1288).[12,13]

The British scientist William Harvey (1627) showed that blood circulated within a closed circuit. He is credited with suggesting a robust mathematical model of the motion of heart and blood in animals, and described the mechanisms of both systemic and pulmonary circulation in humans.[14]

The German (Franz) Ernst Neuman (1866) demonstrated clearly that nucleated erythropoiesis and leukopoiesis formulate in the bone marrow. He also became the first person to postulate the bone marrow as a blood-forming organ with a common stem cell for all haematopoietic cells.[15] The British scientist William Osler (1870) made the first description of *platelets*, explained the formation of blood clots and hinted at possible synthesis in the bone marrow. The British surgeon William Hewson (1869), who noted that the red cells were flat rather than globular and described the leukocytes for the first time, has been referred to as the *father of haematology*.[16]

The first documented blood transfusion to a human from a sheep was administered by the Frenchman Jean-Baptiste Denis (1667) and the first human-to-human transfusion was performed by British obstetrician James Blundell (1818).[4,15,16] The Austrian Karl Landsteiner (1901) documented the three human blood groups (A, B and O) for the first time, and subsequently the American Reuben Ottenberg (1907) is credited for performing the first blood transfusion using blood typing and cross-matching.[12,17,18]

The first report of the application of native blood in wound treatment was recorded in 1876 in Germany, and it was noticed that wounds healed quickly. In 1898 in the USA, autologous blood mixed with normal saline

was used to treat pneumonia and tuberculosis. Reports of accelerated broken bone recovery and consolidation by 30% with the patient's own blood injections in the thigh came from German surgeon August Bier. The method of autohaemotherapy in "nidus of inflammation and infections" such as furuncles and carbuncles in *Purulent surgery assays* was reported in 1934 by Russian surgeon Valentine Voino-Yasenetsky.

Platelet-rich plasma

The terminology, platelet-rich plasma, was used by C. S. Kinsley in 1954[19] to refer to platelet concentrate for transfusion. Subsequently, the various growth factors were detected in platelet-rich plasma aiding the healing process. In the late 1990s Marx et al. pioneered the usage of plasma in the form of gel clots mainly for the repair of bone defects in dental surgeries.[19-21] These case reports were the dawn of the new era of regenerative medicine in the late twentieth and early twenty-first century. Subsequently, the journey of blood embarked upon the healing of wounds, injuries and complicated non-responsive-delayed healing disorders in different streams of orthopaedics, sports medicine, dentistry, dermatology and plastic surgery.

In our humble journey of utilizing platelet-rich plasma in intervention dermatology and regenerative trichology, we observed its great healing potential and termed it an "elixir", provided it is used in the right direction with an adequate supply of nutrition creating the right environment for healing.[22,23] Thus, our approach almost comes full circle with the history of blood, with the Galenus philosophy suggesting a relationship between blood, food and air. It suggests strong interdependence of blood, nutrition and inner well-being to attain the desired results.

> But all these requisites belong of old to Medicine, and an origin and way have been found out, by which many and elegant discoveries have been made, during a length of time, and others will yet be found out, if a person possessed of the proper ability, and knowing those discoveries which have been made, should proceed from them to prosecute his investigations.
> (Hippocrates, *On Ancient Medicine*)

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