Primary Immune Deficiencies

Made Simple

is a compilation of real-life cases and the book makes an attempt to bring the science of immunology and primary immune deficiencies from 'bench to bedside'.

Case-based learning, clinical algorithms, age-norms for immunoglobulins and lymphocyte subsets, and description of common immune deficiencies in an easy to understand format are the unique features of this book.

Written by a young and dynamic pediatric immunologist, this book will serve as a ready reckoner for the pediatric trainees, internists and physicians across the country.

Simplicity of concept and presentation and clarity of thought are the hallmarks of this book.

Sagar Bhattad MD, DM

is the first DM superspecialist in the field of pediatric clinical immunology and rheumatology in India. He received his training under the mentorship of Dr Surjit Singh, Professor and Head, Department of Pediatrics, and Chief, Allergy Immunology Unit, Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research, Chandigarh. He has been awarded Silver Medal for MD (Pediatrics) and Major Gen Amir Chand Gold Medal for his research on complement deficiency in pediatric lupus.

He has a vast experience in the diagnosis and treatment of primary immune deficiency disorders. Having received extensive training in clinical and laboratory immunology, he has been instrumental in setting up the center of excellence in Immunology at Aster CMI Hospital, Bangalore. Foundation for Primary Immune Deficiency (FPID), an international organization based in the US, has recognized the Department of Pediatric Immunology and Bone Marrow Transplant at Aster CMI as the centre of excellence for the diagnosis and management of primary immune deficiencies. He has written over 25 articles for national and international peer-reviewed journals and has made several presentations at professional conferences and symposia. Raising awareness regarding primary immune deficiencies in the medical fraternity and the community is his passion and this book is a reflection of the same.

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Primary Immune Deficiencies Made Simple Bhattad

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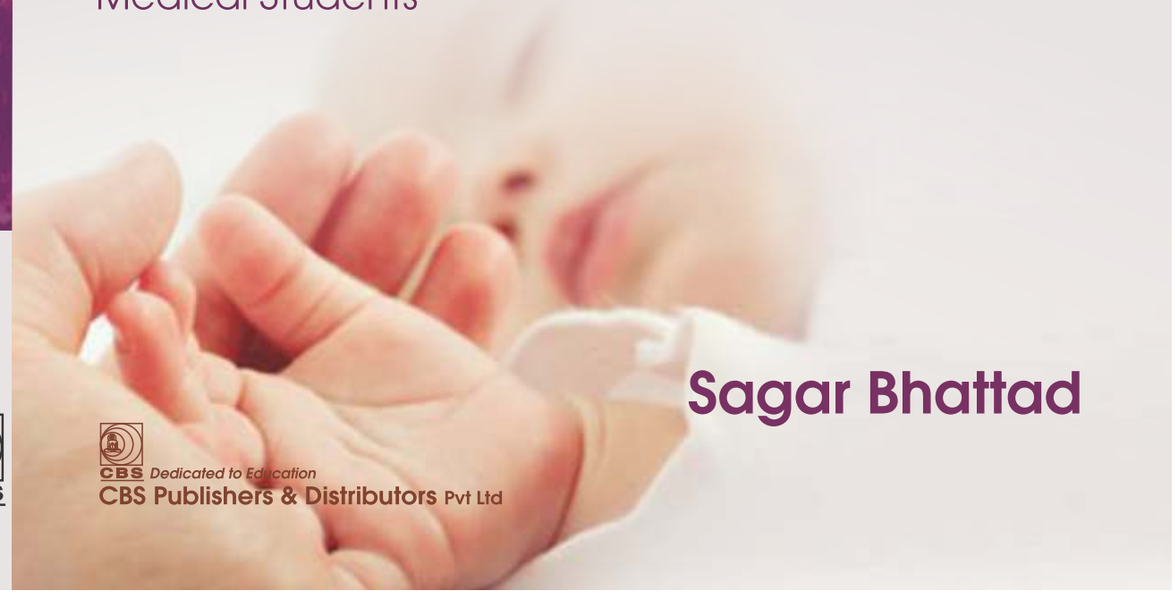
Primary Immune Deficiencies

Made Simple

Handbook for Practicing Pediatricians, Physicians and Medical Students



Sagar Bhattad

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Primary Immune Deficiencies Made Simple

Handbook for Practicing Pediatricians, Physicians, and Medical Students

Primary Immune Deficiencies Made Simple

Handbook for Practicing Pediatricians, Physicians, and Medical Students

Sagar Bhattad
MBBS, MD (Pediatrics), DM (Pediatric Clinical Immunology and Rheumatology) (PGI Chd)
Consultant, Pediatric Immunologist and Rheumatologist
Aster CMI Hospital, New Airport Road
Sahakara Nagar, Hebbal, Bengaluru-560092, Karnataka

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Ph: 011-23289259, 23266861, 23266867 Fax: 011-23243014
Website: www.cbspd.com e-mail: delhi@cbspd.com; cbspubs@airtelmail.in

Corporate Office: 204 FIE, Industrial Area, Patparganj, Delhi 110 092, India
Ph: 011-49344934 Fax: 011-49344935 e-mail: publishing@cbspd.com; publicity@cbspd.com

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Foreword

I consider it a unique honour, and a singular privilege, to be asked to write this note of introduction for our erstwhile student and now a dear colleague Dr Sagar Badrinarayan Bhattad.

Sagar completed his residency in pediatrics in our department in December 2013. He topped his batch and was awarded the coveted Silver Medal for excellence in the subject. His MD thesis paper on childhood lupus (under guidance of Prof Amit Rawat) was selected for Maj. Gen. Amir Chand Gold Medal as the best published paper amongst all MD/MS students in the institute for that year. This prize is one of the most prestigious awards in our institute.

Sagar had the courage (and the foresight) to apply for the first batch of DM in Pediatric Clinical Immunology and Rheumatology that had been initiated at our institute in January 2014. And this at a time when there were several other well-established DM programmes running in our department. He completed the course with flying colors in December 2016 and, in the process, set-up standards of training and patient care that we still follow. Having completed his training, he chose to move on nearer home and set-up a first-rate service in Pediatric Immunology and Rheumatology at Bengaluru. This service is now widely perceived to be one of the finest such efforts in South India.

'Primary Immune Deficiencies Made Simple' is a compendium of short essays on common primary immunodeficiency disorders that we encounter (and often miss) in our clinical practice. I have no hesitation in stating that this would soon become a 'ready reckoner' for all pediatricians and physicians in our country. The book reflects Sagar's own insight, experience and perspective on diagnosis and management of such patients who, unfortunately, often have to struggle for long periods before even getting to know what is wrong with them. Simplicity of concept and clarity of thought are the hallmarks of this book.

'Primary Immune Deficiencies Made Simple' is a very welcome initiative by one of our brightest students. I wish him all success!

Prof Surjit Singh
MD; DCH (Lon.); FRCP (Lon.); FRCPCH (Lon.); FAMS
Head, Department of Pediatrics and
Chief, Allergy Immunology Unit
Advanced Pediatrics Centre
Post Graduate Institute of Medical Education and Research
Chandigarh, India-160012

President
Asia Pacific Society for Immunodeficiencies (2020–2024)

Principal Investigator
Indian Council of Medical Research Centre
for Advanced Research in Primary Immunodeficiency Diseases
(2015–2020)

Vice-President
Indian Rheumatology Association (2017–2019)

Message...

Immunodeficiency disorders are a group of conditions that are not uncommon in pediatric practice. They often present with either severe, persistent, unusual or recurrent infections. Manifestations can be dramatic and early or subtle and delayed. While the awareness of these disorders is increasingly recognised in practice, advances in clinical training, laboratory sophistication and genetic analytic capabilities have helped clinicians define these conditions precisely. Once the diagnosis is clearly defined, therapeutic options have kept a rapid pace.

To partner with clinicians and to offer the best options of care, specialised immunologists are the need of the hour.

Dr Sagar Bhattad who has trained under the world renowned rheumatologist/immunologist Dr Surjit Singh from the Post Graduate Institute, Chandigarh, has written a synopsis of immunodeficiency disorders seen in practice. This is peek into the immunologist's mind and the way he thinks through problems in practice. It will be of immense value to all pediatric clinicians.

With best wishes

Dr Jagdish Chinnappa
Cluster Head
Bangalore region, Manipal Hospitals
March 2020

Message...

This concise yet informative book on primary immune deficiency diseases authored by Dr Sagar Bhattad makes interesting reading to practicing pediatricians as well as postgraduates. It aptly fills in the long-felt gap in this area of clinical pediatrics. Suspecting PID is a job half completed. This book provides easy to follow, case-scenario based stepwise approach to the problem. Suspecting and initial screening for PID with available resources and timely referral as necessary will now happen and our children will benefit at large.

Dr Shashidhararao Nagabhushana
Visiting Professor, Rainbow Children Hospital, Bangalore
National Convener, Asthma Training Module of IAP

Message...

The foundation of Immunology were laid by Nobel Laureates Elie Metchnikoff (Father of Immunology—discovery of phagocytes and phagocytosis—1882), von Behring (serum therapy with neutralizing antibodies diphtheria and tetanus—1890) and Paul Ehrlich (blood smear staining for identifying different types of leucocytes, antiserum treatment for diphtheria and salvarsan for treatment of syphilis).

Immunology, as a pediatric subspeciality, has made great strides and progressed to unravel the mysteries of a plethora of inherited and acquired immunodeficiency states at all sites of immunoprotective and defensive mechanisms deciphered at cellular and humoral components of T and B lymphocytes and macrophages.

Quoting the British novelist and poet David Herbert Lawrence (1885–1930) "What the eye doesn't see and the mind doesn't know, doesn't exist". Pediatricians of my generation, though they thought of the possibility of an underlying PID in children presenting as generalised molluscum contagiosum in a young child, in others with recurrent pyoderma, eczema, mucosal infections with rare organisms, disseminated tuberculosis caused by BCG bacilli in live vaccine, they reached a dead end. Many such children with recurrent infections had finally succumbed to their fate termed genetics for want of diagnostic facilities and adequately trained subspecialists.

Primary Immunodeficiency Disorders (PIDs) in children, once considered rare, are no longer considered rare. Rightly, Dr Sagar Bhattad, Pediatric Immunologist, trained by Prof. (Dr) Surjit Singh of Advanced Pediatric Center, PGIMER, Chandigarh, India has begun his basic treatise–"*Handbook on Primary Immune Deficiencies–Made Simple*" with a positive approach and statement—"Eyes see only what mind knows", thus making the primary objective crystal clear. He has made a very important statement that pediatric residents in PGIMER, Chandigarh, would suspect and go on to diagnose these "no longer rare" entities on a day-to-day basis due to the important thrust given in training by one of the foremost and internationally known pediatric immunologists, Dr Surjit Singh.

All medical trainees and practitioners are told to keep 'open' mind, ears (history taking) and eyes (observation) whenever infants and children present with infections fulfilling the acronym 'SPUR' (S-Serious/Severe; P-Prolonged and/or Persistent in spite of appropriate treatment; U-Unusual agents; R-Recurrent) to suspect an underlying PID state. Though this is extremely relevant, it is also to be appreciated that PIDs can be suspected and diagnosed in the presence of a family history of deaths following infections in family members and siblings and in looking for a few specific "noninfectious signs" like unexplained persistent lymphadenopathy, eczema, etc., and thus need to be referred for specialist evaluation.

All current well-trained pediatric immunologists like Dr Sagar Bhattad have now a significant number of referred PID states from pediatric centers which could have been diagnosed earlier, if the importance of the above-mentioned noninfectious signs were given due consideration in the referring centers. Hence, Dr Sagar Bhattad, from his vast clinical experience from a large number of Childhood PIDs, has realized that it is high time to give adequate emphasis in training of pediatric trainees as well as practicing pediatricians by bringing out a tailor made, comprehensive, easily readable and uncomplicated handbook with the following objectives:

1. Elicit appropriate history of infections with 'SPUR' characteristics and deaths due to infections in the child, siblings and family members.
2. Understand and recognize the vital 'signs and symptoms' of infections pointing to the presence of a possible underlying 'PID' state.
3. Understand and recognize vital and specific "noninfectious signs and symptoms" distinctive of different inherited PID states.
4. Consult in house immunologist early to plan and investigate for PID without delay or refer to such a consultant nearby.
5. Counsel parents regarding the condition, need for special investigations to diagnose and the importance of early institution of appropriate treatment measures.
6. Recognize secondary causes of acquired secondary causes of deranged immunological function either due to infections or drugs or both.

I am privileged to know Dr Sagar Bhattad's expertise and work in this area and listen to his lucid and illustrative case presentations of PID conditions in infants and children since mid 2000. I am glad that he has taken up this commendable job to give new life to these unfortunate children with

PID states and hope to their parents. I am sure his primary objectives will bring in the desired orientation of the pediatric trainees and practitioners. I congratulate him for embarking on this ambitious project solely for early referral and work-up of these children to be cured of their PID and his mentor Dr Surjit singh for having trained such a competent and ideal pediatric immunologist.

Dr S Srinivasan
MD, DCH
Director, Professor and Head (Retd)
Department of Pediatrics, JIPMER, Pondicherry
Adjunct Professor
Department of Pediatrics
Mehta Multispeciality Hospital, Chennai

Message...

The book written by Dr Sagar Bhattad on primary immune deficiencies is a simple, informative, educative and easy to understand book. This book contains mainly basics of primary immune deficiencies and as many case scenarios which we come across our practice. These are often missed because of lack of orientation towards primary immunodeficiencies. This book would help to sensitize medical students, postgraduates and practicing pediatricians for early recognition and confirmation by basic tests and early referral, which will go a long way in improving the quality of life and longevity of these unfortunate children.

I congratulate Dr Sagar Bhattad for this innovative book.

Dr Bhaskar Shenoy
Head, Department of Paediatrics
Manipal Hospital
Bangalore

Preface

I was trained in the field of pediatric immunology and the science of primary immune deficiency diseases at the prestigious Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh. "Eyes see only what mind knows"—pediatric residents at PGIMER would diagnose immune deficiencies on a day-to-day basis; thanks to the department of immunology, excellent laboratory facilities and the phenomenal mentorship of Prof Surjit Singh.

As I began my career in Bangalore, I quickly realized the challenges faced by practicing pediatricians and residents in medical colleges. They were keen on diagnosing immune deficiencies and would love to help children suffering from these diseases, but had unique challenges: (a) Lack of trained immunologist who could guide them, (b) lack of laboratory facilities. But the most important issue was the lack of availability of a handbook on immune deficiency. A handbook which described these diseases in a simple language, provided clinical insights and clinically relevant algorithms for diagnosis, avoiding all the jargon of complex terminology and molecular immunology.

This handbook is a sincere effort in this regard. It aims to provide a clinical insight to practicing pediatricians, physicians and especially to medical students who often are thrilled to diagnose these conditions. Case-based learning is one of the best ways to understand a difficult subject and this book describes several real-life cases and would make you say, "I have seen such a case/many such cases". This, however, by no means is a complete textbook of immunology and a list of such textbooks would be provided in the handbook for the interested readers.

I hope you enjoy reading this book and in the process help children and adults suffering from primary immune deficiency diseases.

Sagar Bhattad

Acknowledgments

I would like to thank Almighty and my parents for showering their blessings on me; my wife Prerna and daughter Prisha for their love and constant support.

I would like to dedicate this book to my mentor Prof Surjit Singh (Head, Department of Pediatrics, PGIMER, Chandigarh) and my alma mater PGIMER, Chandigarh. It was only because of his guidance and the training at this prestigious institute, I am in a position to write this book today.

I would like to thank Dr Chetan Ginigeri, Dr Harish Kumar, Dr Sudheer, Dr Ravi Kumar, Dr Stalin Ramprakash, and Dr Raghuram, my colleagues at Aster CMI Hospital for inspiring me to take up this task. Dr Chetan has been the driving force behind my YouTube videos on immune deficiency.

I would also like to thank Dr Avinash Sharma (Assistant Professor, Pediatric Immunology and Rheumatology, Rajendra Prasad Government Medical College, Tanda, Himachal Pradesh), my friend and colleague; and Dr Amit Rawat (Professor, Department of Pediatrics, PGIMER, Chandigarh) for proofreading the book and providing valuable inputs for the final and improved version of this book.

My special thanks to the medical residents whose eagerness to learn the science of immune deficiency provided me the energy to pen this book.

Most important of all, I would like to thank my patients, who have taught me and continue to teach me, the fascinating science of immunology. I sincerely hope this small contribution of mine, would lead to timely diagnosis and therapy in patients with primary immune deficiency.

Sagar Bhattad

Abbreviations

PID	: Primary immune deficiency
IEI	: Inborn errors of immunity
HIV	: Human immune deficiency virus
AIDS	: Acquired immune deficiency syndrome
NADPH oxidase	: Nicotinamide adenine dinucleotide phosphate hydrogen oxidase
CGD	: Chronic granulomatous disease
LAD	: Leukocyte adhesion defect
SCID	: Severe combined immune deficiency
MSMD	: Mendelian susceptibility to mycobacterial disease
XLA	: X-linked agammaglobulinemia
CVID	: Common variable immune deficiency
WAS	: Wiskott-Aldrich syndrome
IBD	: Inflammatory bowel disease
IVIg	: Intravenous immunogloblin
CBC	: Complete blood count
Hb	: Hemoglobin
TC	: Total white cell count
DC	: Differential white cell count
PC	: Platelet count
ANC	: Absolute neutrophil count
ALC	: Absolute lymphocyte count
MPV	: Mean platelet volume
LFT	: Liver function test
RFT	: Renal function test
NBT	: Nitroblue tetrazolium test
DHR	: Dihydrorhodamine test
NGS	: Next-generation sequencing
JMF	: Jeffrey Modell Foundation
IUIS	: International Union of Immunological Societies

Contents