

Contemporary Endocrinology

*Series Editor:* P. Michael Conn

Abhimanyu Garg *Editor*

# Dyslipidemias

Pathophysiology, Evaluation and Management

 Humana Press

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# Contemporary Endocrinology

**Series Editor:**

P. Michael Conn, PhD

Oregon Health & Science University

Beaverton, OR, USA

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Abhimanyu Garg  
Editor

# Dyslipidemias

Pathophysiology, Evaluation  
and Management

 Humana Press

*Editor*

Abhimanyu Garg, M.D.  
Professor of Internal Medicine  
Chief, Division of Nutrition and Metabolic Diseases,  
Distinguished Chair in Human Nutrition Research,  
Director, Lipid Clinics, Parkland Memorial Hospital  
and UT Southwestern  
UT Southwestern Medical Center  
Dallas, TX

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*To*

*My wife, Sandeep, for her enduring encouragement, support and love; to my children, Ooshma and Aashima, for providing sparks in my life; to my parents, Anand Swaroop and Shyam Lata, for their nurturing; and to Scott Grundy, for guiding me through my research in lipids and lipoproteins.*

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## Preface

For the last 20 years, there has been a growing recognition worldwide of the importance of managing dyslipidemia for the primary and secondary prevention of atherosclerotic vascular disease, especially coronary heart disease. This has been mainly due to the publication of the guidelines of National Cholesterol Education Program's Adult Treatment Panel and Pediatric Panel from the USA. These guidelines have stimulated generation of similar recommendations from all over the world, particularly Europe, Canada, Australia and Asia. Thus, it is important for the treating physicians and other providers to understand the pathophysiology, epidemiology, clinical evaluation and management of dyslipidemias. This book entitled, "Dyslipidemias: Pathophysiology, Evaluation and Management" has a clinical focus and is aimed at General Internists, Pediatricians, Cardiologists, Endocrinologists, Lipidologists and Geneticists.

A striking feature of this book is the fact that all the authors are at the forefronts of their disciplines, thereby ensuring inclusion of the latest scientific developments in their chapters. These authors have international reputation in their fields and represent global leadership. The authors were chosen by the Editor in view of their scientific contributions, reputation and most importantly not to have any direct conflicts of interests due to their employment in the pharmaceutical industry. A unique feature of this book is that all chapters have been peer-reviewed by an equally qualified group of experts and have undergone extensive revisions. This process has accomplished at least two goals: (a) improved the scientific quality of the chapters and (b) eliminated the bias of the authors, if any. Thus, I thank all the reviewers who provided constructive critiques but also appreciate the efforts of the authors in revising the chapters according to the comments of the peer reviewers. I hope that this book can provide practical guidance to the clinicians to provide the best care and new opportunities to the patients with dyslipidemias. The online version of the book provides useful links for those who seek an in-depth understanding of a particular topic.

This book could not have been edited without the dedicated administrative help of Erica Sawczuk. I also acknowledge the special contributions made by Michael Griffin at the Springer Science + Business Media.

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## Contributors

**Zahid Ahmad** Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, USA

**Jaime P. Almandoz** Department of Internal Medicine, Division of Nutrition & Metabolic Diseases, University of Texas Southwestern Medical Center, Dallas, TX, USA

**Erdembileg Anuurad** Department of Internal Medicine, UC Davis Medical Center, Sacramento, CA, USA

**Thomas A. Barringer** Novant Heart & Vascular Institute, Charlotte, NC, USA

**Lars Berglund** Department of Internal Medicine, UC Davis Medical Center, Sacramento, CA, USA

**Amanda Brahm** Department of Medicine, LHSC, London, ON, Canada

**John R. Burnett** Department of Clinical Biochemistry, PathWest Laboratory Medicine WA, Royal Perth Hospital, Perth, WA, Australia

Schools of Medicine & Pharmacology and Pathology & Laboratory Medicine, University of Western Australia, Perth, WA, Australia

**Kristen Bova Campbell** Department of Pharmacy, Duke University Hospital, Duke Clinic, Red Zone, Durham, NC, USA

**Andrew Carr** Clinical Research Program, St. Vincent's Centre for Applied Medical Research, St. Vincent's Hospital, Sydney, NSW, Australia

**Henna Cederberg** Department of Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland

**Fernando Civeira** Hospital Universitario Miguel Servet, Department of Internal Medicine, Zaragoza School of Medicine, Zaragoza University, Zaragoza, Spain

**Ravi Dhingra** Division of Cardiovascular Medicine, Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, 600 Highland Avenue, E5/582A; MC 5710WI, USA

**P. Barton Duell** Division of Endocrinology, Diabetes, and Clinical Nutrition, Oregon Health and Science University, Portland, OR, USA

**Robert H. Eckel** Department of Medicine, Charles A. Boettcher Endowed Chair in Atherosclerosis, University of Colorado, Aurora, CO, USA

**Byambaa Enkhmaa** Department of Internal Medicine, UC Davis School of Medicine, 451 East Health Sciences Drive, Genome and Biomedical Sciences Facility (GBSF), Davis, CA, USA

**Sergio Fazio** Center for Preventive Cardiology, Knight Cardiovascular Institute, Oregon Health and Science University, Portland, OR, USA

**Jennifer A. Fleming** Department of Nutritional Sciences, Penn State University, University Park, PA, USA

**Om P. Ganda** Lipid Clinic, Clinical Research section; Joslin Diabetes Center, Boston, USA

Harvard Medical School, Boston, USA

Beth Israel Deaconess Medical Ctr, Department of Medicine, Boston, MA, USA

**Abhimanyu Garg** Division of Nutrition and Metabolic Diseases, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, USA

**Antonio M. Gotto** Weill Cornell Medical College, New York, NY, USA

**Scott M. Grundy** Center for Human Nutrition, Department of Internal Medicine, UT Southwestern Medical Center, Dallas, TX, USA

**John R. Guyton** Department of Medicine, Duke University Medical Center, Durham, NC, USA

**Helena Gylling** Department of Medicine, Division of Internal Medicine, University of Helsinki, Helsinki, Finland

**William S. Harris** Department of Medicine, Health Diagnostic Laboratory, Inc., Sioux Falls, SD, USA

Sanford School of Medicine, University of South Dakota, Sioux Falls, USA

**Robert A. Hegele** Department of Medicine, University of Western Ontario, London, ON, Canada

**Amanda J. Hooper** Department of Clinical Biochemistry, PathWest Laboratory Medicine WA, Royal Perth Hospital, Perth, WA, Australia

School of Medicine & Pharmacology, University of Western Australia, Perth, WA, Australia

Schools of Medicine & Pharmacology and Pathology & Laboratory Medicine, University of Western Australia, Perth, WA, Australia

**Min Jun** Department of Medicine, Division of Nephrology, University of Calgary, Alberta, NW, Canada

**Sumeet A. Khetarpal** Department of Medicine, Genetics, University of Pennsylvania, Philadelphia, PA, USA

**Penny M. Kris-Etherton** Department of Nutritional Sciences, Pennsylvania State University, University Park, PA, USA

**Peter O. Kwiterovich** Johns Hopkins Lipid Clinic, The Johns Hopkins School of Medicine, Baltimore, MD, USA

**Markku Laakso** Department of Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland

**Wanda C. Lakey** Department of Internal Medicine, Duke University Medical Center, Durham, NC, USA

**Frederick J. Lee** Clinical Research Program, St. Vincent's Centre for Applied Medical Research, St. Vincent's Hospital, Sydney, NSW, Australia

**Jessica Sparks Lilley** Department of Pediatrics, Division of Pediatric Endocrinology, University of Mississippi School of Medicine, Nashville, MS, USA

**MacRae F. Linton** Atherosclerosis Research Unit, Vanderbilt University School of Medicine, Cardiovascular Medicine Nashville, TN, USA

**David M. Maahs** Barbara Davis Center for Diabetes, Children's Hospital of Colorado, Aurora, CO, USA

**Sanne M. van der Made** Department of Human Biology, Maastricht University Medical Center, Maastricht, The Netherlands

**Daisaku Masuda** Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

**Akifumi Matsuyama** Platform of Therapeutics for Rare Disease, National Institute of Biomedical Innovation, Ibaraki, Osaka, Japan

**Ronald P. Mensink** Department of Human Biology, Maastricht University Medical Center, Maastricht, The Netherlands

**Jennifer E. Moon** Weill Cornell Medical College, New York, NY, USA

**Kiran Musunuru** Brigham and Women's Hospital, Harvard University, Cambridge, MA, USA

**Markku J. Nissinen** Department of Medicine, Division of Gastroenterology, Helsinki University Central Hospital/Peijas Hospital, Helsinki, Finland

**Shailendra B. Patel** Department of Medicine and Division of Endocrinology, HRC4850, Division of Endocrinology, Clement J Zablocki Veterans Affairs Medical Center, and Medical College of Wisconsin, Milwaukee, WI, USA

**Vlado Perkovic** The George Institute for Global Health, Sydney, NSW, Australia

**Miguel Pocovi** Department of Biochemistry, Molecular and Cellular Biology, Faculty of Sciences, Campus Plaza San Francisco, University of Zaragoza, Zaragoza, Spain

**Daniel J. Rader** Department of Medicine, Genetics, University of Pennsylvania, Philadelphia, PA, USA

**Ernst J. Schaefer** Human Nutrition Research Center on Aging, Friedman School of Nutrition Science and Policy, Lipid Metabolism Laboratory, Tufts University School of Medicine, Boston, MA, USA

**Vinaya Simha** Department of Endocrinology, Mayo Clinic, Rochester, MN, USA

**Mariko Tani** Human Nutrition Research Center on Aging, Lipid Metabolism Laboratory, Tufts University, Boston, MA, USA

**Ramachandran S. Vasan** Section of Preventive Medicine & Epidemiology, Boston University School of Medicine, Boston, MA, USA

**Nosratola D. Vaziri** Division of Nephrology and Hypertension, University of California Irvine Medical Center, Medicine, Orange, CA, USA

**Peter W.F. Wilson** Medicine and Public Health, Emory University, Atlanta, GA, USA

**Shizuya Yamashita** Department of Community Medicine, Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

**Wei Zhang** Department of Internal Medicine, UC Davis School of Medicine, 451 East Health Sciences Drive, Genome and Biomedical Sciences Facility (GBSF), Davis, CA, USA

Daniel J. Rader and Sumeet A. Khetarpal

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## Introduction

Lipoproteins evolved due to the need to transport extracellular hydrophobic lipids within an aqueous environment. The two major lipids they transport are triglycerides (TGs) and cholesterol (both esterified and unesterified). Lipoproteins play an essential role in the absorption of dietary lipids, the transport of TGs from the liver to peripheral tissues, and the transport of cholesterol from peripheral tissues to the liver. Lipoproteins contain a core of hydrophobic lipids (TGs and cholesteryl esters, CEs) surrounded by hydrophilic lipids (phospholipids (PLs), unesterified cholesterol) and proteins that interact with body fluids. The plasma lipoproteins are divided into five major classes based on their relative density (Table 1.1): chylomicrons, very low density lipoproteins (VLDLs), intermediate-density lipoproteins (IDLs), low-density lipoproteins (LDLs), and high-density lipoproteins (HDLs). The proteins associated with lipoproteins are called apolipoproteins (Table 1.2). They serve a number of roles, including the assembly, structure, and function of lipoproteins, the activation of enzymes, and as ligands for cell surface receptors.

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D. J. Rader (✉) · S. A. Khetarpal  
Department of Medicine, Genetics, University of Pennsylvania, 3400 Civic Center Blvd, Smilow Center for Translational Research, 11-125, 19104 Philadelphia, PA, USA  
e-mail: rader@mail.med.upenn.edu

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## Physiology and Metabolism of ApoB-Containing Lipoproteins

Lipoproteins containing apoB exist to transport hydrophobic lipids within the blood. A major role is the transport of energy in the form of TGs, and another key role is the transport of cholesterol largely in the form of CEs. The intestine produces chylomicrons containing apoB-48 and the liver produces VLDL-containing apoB-100. The role of intestinal chylomicrons is the postprandial transport of (exogenous) dietary fatty acids (within TGs) to tissues that use or store them, whereas a key role of hepatic VLDL is the fasting transport of (endogenous) fatty acids to tissues that use them. In each case, the by-product of lipolysis of the TGs is a remnant lipoprotein—chylomicron remnant or VLDL remnant (also known as IDL)—that contains residual TG as well as cholesterol and is removed from plasma by the liver. In the case of IDL, some of the particles are further converted to LDL before removal. These two related pathways are discussed in greater detail below.

First, however, is a discussion of the key structural protein in both chylomicrons and VLDL, namely apoB. ApoB is one of the largest proteins in the human genome and provides the unique structural and functional features of these lipoproteins. Importantly, there is one single molecule of apoB protein per lipoprotein particle. There is a single *APOB* gene that is expressed in both the enterocyte and the hepatocyte. However, whereas the hepatocyte synthesizes a full-length apoB known as apoB-100 (for 100%), the