

Preface

Over the last two centuries, the role of lipids in the etiology of cardiovascular has garnered significant attention, and in particular, the role of cholesterol on the development of atherosclerosis. The first studies involving cholesterol and cardiovascular disease date back to the early 1900s when Anichkov (an army pathologist) provided rabbits with high cholesterol diets and observed stiffening of their artery walls. In the 1950s, Ancel Keys reported in the Seven Countries study findings relating low fat intake and an association of low mortality from cardiovascular disease. His observations were misinterpreted into high carbohydrate diets that were particularly enriched with simple sugars. Together with sedentary life styles, large portion sizes, these changes contributed in part to the obesity epidemic that peaked toward the end of the twentieth century. The first lipid lowering medication, niacin, was discovered serendipitously after it was tested on a rabbit schizophrenia model. One of the side effects observed was lowering of cholesterol. In the 1960s, the coronary drug project ushered the first clinical trial for lipid lowering therapies featuring niacin use for the prevention of heart disease. Although immediately after the study the two groups did not statistically differ in heart disease rates, 20 years later, the participants assigned to niacin demonstrated a survival advantage. In the late 70s, a Japanese microbiologist Akira Endo first discovered natural products with a powerful inhibitory effect on cholesterol synthesis in a fermentation broth of *Penicillium citrinum*, during his search for antimicrobial agents. Concomitantly, Brown and Goldstein (later earning the Nobel Prize for their work in 1985) showed that HMG-co reductase inhibition represented the rate limiting step in cholesterol synthesis. These exciting basic and translational studies led to the production of statins. The first of many statin trials to come was the 4S study conducted in Scandinavian countries in the late 1980s and showed a significant reduction in cardiovascular events in participants assigned to statin therapy. Importantly, many later trials confirmed the benefits of statins in lowering heart disease risk. On another front, the publication of the Lyon Heart study (Mediterranean diet) in the mid-90s transformed our understandings of the dietary components that protect against heart disease. In that study, participants randomized to good fat (olive oil, nuts) survived longer following coronary bypass surgery than individuals kept on their regular diet. Several Mediterranean dietary studies have been conducted since confirming

a distinct role for fats in the pathogenesis of heart disease, and shedding light into healthy and less healthy fats.

In this book, we attempt to provide both basic concepts and clinical approaches to understanding and managing lipid related disorders that confer increased cardiovascular risk. The first 5 chapters cover basic aspects of lipoprotein metabolism. The remaining chapters focus on management of the patient with lipid disorders. In the first chapter, we go over the basics of lipoprotein metabolism inside the cell and how lipids are packaged in the circulation into lipoproteins. The second chapter focuses on genetic disorders of lipoprotein metabolism with an emphasis on Familial Hyperlipidemia, a common lipid disorder associated with increased heart disease risk. In the third chapter, we discuss the pathophysiology of atherosclerosis, focusing on the roles of lipids and inflammation. Dr. Abela and his colleagues discuss their landmark studies into the role of cholesterol crystals in inducing inflammation in the artery wall. In the third Chapter, Drs. Toledo-Corral, Alderete and Goran report to us important findings from their recent studies on the mechanisms linking obesity to atherosclerosis, particularly in the youth. In the fourth chapter, I discuss recent findings from studies aimed at raising HDL cholesterol but failing to improve outcomes, reviewing basic concepts of HDL metabolism. In the fifth chapter, we provide our approach to managing patients at risk for heart disease incorporating the recent AHA/ACC 2013 guidelines. We then present ten chapters that discuss the management of patients with lipid disorders and at risk for cardiovascular disease. In Chap. 6, Dr. Allevato discusses the latest evidence on dietary intervention trials that confer cardiovascular benefits with a focus on the Mediterranean diet. In Chap. 7, Drs. Abou Assi and Jordanov discuss statins, from trials to side effects and intolerance. Given the importance of statins as cornerstone therapies in the management of hyperlipidemia, Chaps. 9, 10, and 11 review the use of statins in three conditions: chronic kidney disease, non-alcoholic fatty liver and heart failure. In Chap. 12, Dr. Goldberg summarizes the evidence and use of non-statin therapies. In Chap. 13, Dr. Klapper reviews the use LDL apheresis as a modality to treat refractory dyslipidemias or severe familial hypercholesterolemias. Dr. Dube, a leading expert in the treatment of dyslipidemia in HIV presents the latest guidelines and approaches to treatment of dyslipidemia in HIV. Finally, Dr. Wong in Chap. 15 provides a concise summary on the new and emerging therapies for the treatment of hyperlipidemias. This book is intended for the public, scholars and physicians with interest in lipids. We hope that by coupling of basic concepts and management approaches to lipid disorders, we will assist the provider in making the best decisions in diagnosing and treating their patients.



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