Contents

Foreword xiii
Preface xv
Acknowledgements xix

Chapter 1
Epidemiology of Lipids, Lipid Management and Risk for Coronary Heart Disease: An Overview

1.1 Early History of Cardiovascular Epidemiology 2
1.2 Lipid Risk Factors are Central to Efforts at CHD Prevention 3
1.3 LDL-C and CHD Risk 4
1.4 LDL-C Lowering and CHD Risk Reduction 6
1.5 Other Atherogenic Lipoproteins: Atherogenic Remnants 7
1.6 HDL-C and CHD Risk 9
1.7 Trends in Lipids and Lipid Management in the USA 10
1.8 The National Cholesterol Education Program Evaluation Project Using Novel E-Technology (NEPTUNE) II Survey Controversy: Should a Measure of Atherogenic Lipoprotein Particle Number be used in Risk Assessment And/Or to Evaluate the Response to Lipid Therapy? 12

Chapter 2
Vascular Biology and Atherogenesis 19

2.1 Introduction 20
2.2 Arterial Structure 20
2.3 Endothelial Cell Function and Dysfunction 21
2.4 The Role of Monocytes and Lymphocytes 24
2.5 Atheromatous Plaques 25
## CONTENTS

### Chapter 3

**Detection, Evaluation, and Treatment Goals for Lipid Disorders in Adults**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Matching Aggressiveness of Treatment to Absolute Risk</td>
<td>32</td>
</tr>
<tr>
<td>3.2 Screening for Dyslipidemias</td>
<td>32</td>
</tr>
<tr>
<td>3.3 Risk Stratification</td>
<td>34</td>
</tr>
<tr>
<td>3.4 Steps in the Risk Stratification Process – Major Risk Categories</td>
<td>35</td>
</tr>
<tr>
<td>3.5 Tips for Calculating the Framingham Risk Score</td>
<td>36</td>
</tr>
<tr>
<td>3.6 Subcategories for Consideration of More Aggressive Optional Treatment Goals</td>
<td>39</td>
</tr>
<tr>
<td>3.7 Very High Risk Patients, Optional LDL-C Goal &lt;70 mg dl⁻¹</td>
<td>40</td>
</tr>
<tr>
<td>3.8 Moderately High Risk Patients, OPTIONAL LDL-C Goal &lt;100 mg dl⁻¹</td>
<td>40</td>
</tr>
<tr>
<td>3.9 Treatment Goals for Patients with Elevated Triglycerides</td>
<td>40</td>
</tr>
<tr>
<td>3.10 Triglycerides and HDL-C as Targets for Therapy</td>
<td>41</td>
</tr>
<tr>
<td>Controversy: Should Treatment Guidelines Include Targets for the Total/HDL Cholesterol Ratio?</td>
<td>41</td>
</tr>
</tbody>
</table>

### Chapter 4

**Therapeutic Lifestyle Changes in the Management of Lipid Disorders and the Metabolic Syndrome**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1 Nature and Nurture in the Development of CHD Risk Factors</td>
<td>52</td>
</tr>
<tr>
<td>4.2 Lifestyle Factors as Determinants of CHD Risk in Populations</td>
<td>53</td>
</tr>
<tr>
<td>4.3 Within Country Variations in Lifestyle and CHD Risk</td>
<td>53</td>
</tr>
<tr>
<td>4.4 The Metabolic Syndrome</td>
<td>54</td>
</tr>
<tr>
<td>4.5 Therapeutic Lifestyle Changes</td>
<td>55</td>
</tr>
<tr>
<td>4.6 The TLC Diet</td>
<td>56</td>
</tr>
<tr>
<td>4.7 Dietary Adjuncts: Viscous Fibers and Plant Sterol/Stanol Products</td>
<td>58</td>
</tr>
<tr>
<td>4.8 Physical Activity and Weight Reduction</td>
<td>59</td>
</tr>
<tr>
<td>4.9 Smoking Cessation</td>
<td>59</td>
</tr>
<tr>
<td>4.10 Importance of Allied Health Professionals</td>
<td>59</td>
</tr>
</tbody>
</table>
Chapter 5
Management of Elevated Low-Density Lipoprotein Cholesterol
5.1 Relationship between LDL-C and Risk for Cardiovascular Events 64
5.2 Clinical Trial Support for Very Aggressive LDL-C Reduction for Those at Highest Risk 66
5.3 Genetic Disorders Associated with Elevated LDL-C 73
5.4 Atherogenic Impact of LDL-C 73
5.5 Management of Elevated LDL-C 74
5.6 Summary 82
Controversy: How Low Should We Go? 82
Controversy: Risks and Benefits of High-Dose Statin Therapy Versus Combination Lipid Drug Therapy 87
Controversy: Do the Benefits of Low-Density Lipoprotein Cholesterol Reduction Depend Strictly on “How Low You Go” or also on “How You Get There”? 90

Chapter 6
Management of Elevated Triglycerides and Non-High-Density Lipoprotein Cholesterol 105
6.1 Clinical Factors Associated with Elevated TG and Non-HDL-C Levels 106
6.2 Disorders of TG-Rich Lipoprotein Clearance 107
6.3 Insulin Resistance and Hypertriglyceridemia 108
6.4 Excessive Production of VLDL: The Primary Lipid Abnormality in the Insulin-Resistant State 108
6.5 Reasons for Elevated Free Fatty Acid Levels in Insulin-Resistant States 109
6.6 Body Fat Distribution and Insulin Resistance 109
6.7 Insulin Resistance in the Nonobese Patient 109
6.8 Hypertriglyceridemia and the Development of Atherogenic Dyslipidemia 110
6.9 Lifestyle Management for the Metabolic Syndrome and Atherogenic Dyslipidemia 111
6.10 Drug Therapies 112
6.11 Intensification of Efforts to Lower LDL-C as a Means of Achieving the Non-HDL-C Goal 112
6.12 Targeting Triglyceride-Rich Lipoprotein Reduction as a Means of Achieving Non-HDL-C Goal 113
6.13 Fibrates 113
6.14 Niacin 114
CONTENTS

6.15 Omega-3 Fatty Acids  115
6.16 Management of Diabetic Dyslipidemia  115
  Controversy: Do we Need a Triglyceride Treatment Target
to Insure a Predominance of Larger, More Buoyant LDL
Particles?  116

Chapter 7
Management of Depressed High-Density Lipoprotein
Cholesterol  127
7.1 The Relationship between HDL and Risk For CVD  128
7.2 Prevalence of Low HDL-C  130
7.3 Goals for HDL Treatment  131
7.4 Antiatherogenic Effects of HDL  132
7.5 HDL and Insulin Resistance  137
7.6 Effects of Lifestyle Modification on Serum HDL  137
7.7 Pharmacologic Management of Low HDL  139
  Controversy: Do we Need HDL Treatment Goals?  143

Chapter 8
Lipid Management in Population Subsets: Women, the
Elderly, Ethnic Minorities, Children, and Adolescents  155
8.1 Women  156
8.2 Lipids in Women  157
8.3 Treatment of Dyslipidemia in Women  157
8.4 Sex Hormone Therapy, Lipids, and Cardiovascular Risk in
Menopausal Women  159
8.5 The Elderly  159
8.6 Special Considerations for Lipid Management in the Elderly  160
8.7 Ethnic Minorities  160
8.8 Risk Factor Incidence and Prevalence in Ethnic Minority
Groups  162
8.9 Children and Adolescents  162

Chapter 9
Emerging Risk Factors and Biomarkers of Cardiovascular
Disease  167
9.1 Role of Inflammation in the Pathogenesis of Atherosclerosis  168
9.2 Biomarkers of Cardiovascular Disease  168
Chapter 10

A Primer on Clinical Trials and Critical Review of Clinical Trial Reports for the Clinician

10.1 Design Issues Affecting the Validity and Generalizability of Clinical Trial Results

10.2 Chance, Bias, and Confounding as Potential Explanations for Trial Results

10.3 Efficacy versus Effectiveness

10.4 Useful Questions to ask when Evaluating a Published Clinical Trial Report

Controversy: Should Lipid Drugs be Approved without Clinical Event Data?

Chapter 11

Case Studies

Case One: CAD with Recent Acute Coronary Syndrome
Case Two: Peripheral Arterial Disease (PAD)
Case Three: Patient with Heterozygous Familial Hypercholesterolemia
Case Four: Severe Hypertriglyceridemia
Case Five: Metabolic Syndrome
Case Six: Intolerance of Intermediate-Dose Statin Therapy
Case Seven: Patient with Ischemic Stroke
Case Eight: Patient with Chest Pain on Gemfibrozil
Case Nine: Low HDL-C in a Patient with Stable CHD and Early Carotid Disease
Case Ten: Statin Drug Interaction With Hepatotoxicity
Case Eleven: Patient with Dyslipidemia and History of Rhabdomyolysis
Case Twelve: Statin-Induced Myalgia without Myopathy

Index