

# Contents

Contributors iii

Preface v

## **CHAPTER I Preventive Cardiology: Risk Factors for Coronary Artery Disease and Primary and Secondary Prevention 1**

Christopher P. Cannon, Benjamin A. Steinberg,  
and Alexander C. Fanaroff

### **CHOLESTEROL AND LIPIDS 1**

Epidemiology 1

ACC/AHA Guidelines 3

Drugs 3

Bile Resins (e.g., Cholestyramine, Colestipol) 3

Fibric Acid Derivatives (e.g., Gemfibrozil,  
Fenofibrate) 5

Cholesterol Absorption Inhibitors 5

3-Hydroxy-3-Methylglutaryl-Coenzyme A Reductase  
Inhibitors (Statins) 6

Primary Prevention Trials 7

Secondary Prevention Trials 8

Combined Primary and Secondary Prevention  
Trials 8

Early Statin Initiation Trials 9

Raising HDL Cholesterol 10

Niacin 10

Cholesterol Ester Transfer Protein Inhibitors 11

### **DIET AND VITAMINS 11**

Special Diets 11

Alcohol 13

### **LIFESTYLE FACTORS 13**

Obesity 13

Exercise 14

Smoking 15

### **METABOLIC SYNDROME 15**

**DIABETES 16**

**HYPERTENSION 18**

- Epidemiology 18
- Etiology 18
- Diagnosis 18
- Treatment 20
  - Nonpharmacologic 20
  - Pharmacologic 20
  - Target Blood Pressure 22

**NONMODIFIABLE RISK FACTORS 22**

- Family History 22
- Age 22
- Gender 22
- Genetic Markers 23

**HORMONAL STATUS AND HORMONAL THERAPY 23**

**INFLAMMATION 24**

- C-Reactive Protein 24
- Homocysteine and B Vitamins 25
- Lipoprotein-associated Phospholipase A2 25
- Infections and Cardiovascular Disease 26

**ANTIPLATELET DRUGS FOR PRIMARY AND SECONDARY PREVENTION 27**

- Aspirin 27
  - Primary Prevention Trials 27
  - Secondary Prevention Trials 27
- Clopidogrel 29

**REFERENCES 30**

- General Articles 30
- Lipids and Cholesterol 31
  - Guidelines 31
  - Epidemiology 32
  - Primary Prevention 34
    - Early Trials 34
    - Statins in Primary Prevention 35
    - Combination Therapy in the Statin Era 37
  - Secondary Prevention 38
    - Placebo-controlled Trials 38
    - Intensive- versus Standard-dose Statin Regimens in Stable CAD 41
    - Early Statin Initiation in ACS 42
  - Combined Primary and Secondary Prevention Trials 44

Primary and Secondary Prevention Trials in Patients with Comorbidities	45
Meta-analyses and Noncholesterol Effects of Statins	46
HDL-raising Therapies	48
Niacin	48
CETP Inhibitors	50
Meta-analyses and General Studies	52
Novel Classes of Lipid-lowering Agents	52
Antioxidants, Vitamins, Fish Oil, Chelation, and Hormones	54
Observational Studies	54
Clinical Trials	55
Meta-analyses	60
Diet	61
Observational Studies	61
Clinical Trials	62
Alcohol	64
Lifestyle	64
Guidelines and General Articles	64
Obesity and Weight Loss	67
Exercise	70
Smoking	72
Epidemiology	72
Smoking Cessation	74
Metabolic Syndrome and Diabetes	74
Epidemiology	74
Treatment	76
Hypertension	80
Epidemiology and Risk Factors	82
Studies of Treatment	82
Nonpharmacologic Therapies	82
Medical Therapy	84
Diabetes and Hypertension	92
Invasive Therapies	94
Meta-analyses	95
Nonmodifiable Risk Factors	97
Age and Genetics	97
Inflammation	98
C-Reactive Protein	98
Homocysteine and B Vitamins	100
Observational Studies	100
Trials and Meta-analyses	102

Lipoprotein-associated Phospholipase A <sub>2</sub> (Lp-PLA <sub>2</sub> )	103
Infections and Cardiovascular Disease	104
Antibiotic Trials	104
HIV-related Cardiovascular Risk	104
Miscellaneous	105
Antiplatelet Drugs for Primary and Secondary Prevention	106
Primary Prevention	106
Secondary Prevention	107
General Review Articles and Meta-analyses	108

---

## **CHAPTER 2 Coronary Revascularization and Percutaneous Procedures** 110

**Christopher P. Cannon, Benjamin A. Steinberg, and Justin M. Dunn**

---

### **CORONARY ANGIOGRAPHY** 110

Indications	110
Flow Grade	110
Stenosis Morphology	111

### **PERCUTANEOUS CORONARY INTERVENTION** 111

Uses and Indications	111
Operator and Hospital Volume	112
Procedural Details	113
Access	113
Contrast Agent	113
Lesion Evaluation	113
Balloon Angioplasty	115
Stenting	116
Medications	117
Aspirin	117
Heparin	117
Low Molecular Weight Heparin	117
Direct Thrombin Inhibitors	118
Thienopyridines/ADP Receptor Antagonists	118
Glycoprotein IIB/IIIA Inhibitors	121
Abciximab (ReoPro)	122
Eptifibatid (Integrilin)	122
Tirofiban (Aggrastat)	123
Applications of PCI	123
Stable Angina	123
Unstable Angina/Non-ST Elevation Myocardial Infarction	124
Acute ST Elevation Myocardial Infarction	124
After Thrombolytic Therapy	124

Stenting versus Percutaneous Transluminal Coronary Angioplasty: Major Trials	125
Direct Stenting versus Balloon Predilatation	125
Repeated Intervention	125
Complications	126
Early Complications	126
Later Complications	127
Stent Thrombosis	127
Restenosis	127
Renal Dysfunction	128
Other Postprocedural Complications	128
Treatment and Prevention of Restenosis	129
Drug Studies	129
Radiation Therapy	129
Drug-eluting Stents	129
Directional Atherectomy	131
Rotational Atherectomy	133
Prevention of Distal Embolization	133
Thrombectomy	133
Distal Protection	134
<b>CORONARY ARTERY BYPASS SURGERY</b>	<b>135</b>
Coronary Artery Bypass Surgery versus Medical Therapy	135
Coronary Artery Bypass Surgery versus Percutaneous Coronary Intervention	136
Internal Mammary Artery	138
Saphenous Vein Grafts	138
<b>TRANSCATHETER AORTIC VALVE REPLACEMENT</b>	<b>138</b>
Balloon-expandable TAVR	139
Self-expanding TAVR	139
<b>REFERENCES</b>	<b>140</b>
Guidelines and Classification	140
Operator and Hospital Characteristics	141
Catheterization Technique	143
Contrast Agents	144
Lesion Evaluation (Fractional Flow Reserve, Intravascular Ultrasound)	146
Comparison of Revascularization with Medical Therapy	147
Stent Studies	149
Early Stent Comparisons	149
Provisional Stenting	151
Direct Stenting	153
Drug-eluting Stents	153

Additional Devices/Techniques	159
Cutting Balloon	159
Atherectomy Studies	161
Radiation Therapy	163
Thrombectomy	167
Distal Protection	168
Adjunctive Pharmacologic Therapy	170
Aspirin	170
Heparin	170
Low Molecular Weight Heparin	171
Thienopyridines	172
Glycoprotein IIB/IIIA Inhibitors	178
Thrombin Inhibitors	184
Special Situations	185
Chronic Total Occlusions	185
Bypass Graft Lesions	186
Small Vessels	187
Diabetes	189
Complications	190
Postintervention CK/CK-MB and Troponin Studies	190
Stent Thrombosis	191
Other Complications	192
Coronary Restenosis	194
Repeat Percutaneous Coronary Intervention for Restenosis after Percutaneous Transluminal Coronary Angiography	194
Effect of Stent Design	196
Drug Studies	197
Coronary Artery Bypass Graft Surgery	201
Coronary Artery Bypass Graft Surgery versus Medical Therapy	202
Coronary Artery Bypass Graft Surgery versus Percutaneous Transluminal Coronary Angiography	203
Graft and Patency	210
Transcatheter Aortic Valve Replacement	212

---

**CHAPTER 3 Unstable Angina/Non-ST Elevation MI** 215

Christopher P. Cannon, Benjamin A. Steinberg,  
and Matthew W. Sherwood

---

EPIDEMIOLOGY 215

PATHOPHYSIOLOGY 215

<b>CLASSIFICATION</b>	<b>215</b>
Unstable Angina	215
Non-ST-elevation Myocardial Infarction	217
<b>CLINICAL AND LABORATORY FINDINGS</b>	<b>217</b>
History and Symptoms	217
Electrocardiogram	217
Cardiac Enzymes	217
Creatine Kinase and Creatine Kinase-MB	217
Troponins T and I	218
Myoglobin	218
Estimation of Early Risk at Presentation	218
<b>TREATMENT</b>	<b>220</b>
Aspirin	220
ADP Receptor Antagonists	220
PAR-1 Receptor Antagonists	221
Heparin	221
Low-molecular-weight Heparins	222
Direct Thrombin Inhibitors	223
Factor Xa Inhibitors	224
Glycoprotein IIB/IIIA Inhibitors	224
Intravenous Agents	224
Oral Agents	225
Thrombolytic Therapy	226
Anti-ischemic Medications	226
$\beta$ -Blockers	226
Nitrates	226
Calcium Channel Blockers	227
3-Hydroxy-3-methylglutaryl Coenzyme A Reductase Inhibitors (Statins)	227
Invasive Strategy	227
Coronary Artery Bypass Graft Surgery	229
<b>NONINVASIVE EVALUATION</b>	<b>229</b>
Exercise Treadmill Test	229
Exercise Treadmill Testing with Nuclear Imaging	229
Pharmacologic Stress Testing with Imaging	229
Echocardiography	229
Coronary Computerized Tomography Angiography	230
<b>PROGNOSIS AND BIOMARKERS</b>	<b>230</b>
Unstable Angina	230
Non-ST-elevation Myocardial Infarction	230

Prior Aspirin Use (Aspirin Failures) 230  
Electrocardiography 230  
Troponin Levels 230  
C-Reactive Protein 231  
B-Type Natriuretic Peptide 231

REFERENCES 231

Review Articles and Pathophysiology 231  
Drugs and Studies 232  
    Aspirin 232  
    Thienopyridines 234  
    PAR-1 Receptor Antagonists 236  
    Unfractionated Heparin and Warfarin 237  
    Low-molecular-weight Heparins 239  
    Anti-ischemic Medications 243  
    Direct Thrombin Inhibitors 245  
    Factor Xa Inhibitors 246  
    Glycoprotein IIB/IIIA Inhibitors 247  
    Thrombolytics 253  
Invasive versus Conservative Management 254  
Noninvasive Assessment and Prognosis 258  
    Clinical or General Analyses 259  
Biomarkers 261  
    Review Articles and Multimarker Studies 261  
    Troponins 262  
    High-sensitivity Troponins 263  
    Inflammatory Markers 263  
    B-Type Natriuretic Peptide 264  
    Specific Tests: Angiography, ECG, and Holter 265

---

**CHAPTER 4 ST Elevation Myocardial Infarction 266**

Christopher P. Cannon, Benjamin A. Steinberg,  
and Justin M. Dunn

---

EPIDEMIOLOGY 266

PATHOGENESIS 266

    Diagnosis 267  
    Chest Pain 267  
    Electrocardiography 267  
    Echocardiography 267  
    Biomarkers 267



**TREATMENT 268**

- Aspirin 268
- P2Y<sub>12</sub> Inhibitors 269
- $\beta$ -Blockers 270
- Angiotensin-converting Enzyme Inhibitors 271
- Aldosterone Antagonism 272
- Thrombolytic Therapy 272
  - Indications for Thrombolysis 273
  - Contraindications 274
  - Common Fibrinolytic Agents 274
    - Streptokinase 274
    - Tissue Plasminogen Activator 274
    - Retepase 275
    - Tenecteplase 275
  - Prognostic Indicators 276
- Percutaneous Coronary Intervention 276
  - Primary Angioplasty 276
    - Procedural Volume 277
    - Primary Angioplasty versus Thrombolysis 277
    - Rescue Angioplasty 278
    - Routine PCI (after Thrombolysis) versus Delayed or Conservative Management 278
  - Facilitated Percutaneous Coronary Intervention 279
    - Cardiogenic Shock 280
    - Stenting in STEMI 280
- Antithrombotic Regimens 281
  - Heparin 281
  - Enoxaparin 281
  - Fondaparinux 282
  - Direct Thrombin Inhibitors 282
  - Oral Anticoagulants 283
  - Intravenous Glycoprotein IIB/IIIA Inhibitors 284
    - Use in Primary PCI 284
    - Glycoprotein Iib/Illa Inhibition Plus Reduced-dose Thrombolysis 285
- Other Therapies 285
  - Nitrates 285
  - Calcium Channel Blockers 285
  - Antiarrhythmics 286
  - Magnesium 286
  - Glucose–Insulin–Potassium 286
  - Intra-aortic Balloon Pump 287

<b>RIGHT VENTRICULAR INFARCTION</b>	<b>287</b>
Diagnosis	287
Complications	288
Treatment	288
<b>COMPLICATIONS OF STEMI</b>	<b>288</b>
Early	288
Intermediate	289
Late	289
<b>PROGNOSIS AND RISK STRATIFICATION AFTER MYOCARDIAL INFARCTION</b>	<b>290</b>
Uncomplicated STEMI	290
Complicated Course	291
Specific Tests	292
<b>REFERENCES</b>	<b>293</b>
General Review Articles and Guidelines	293
Epidemiology	293
Pathogenesis	294
Diagnosis	295
Chest Pain and Symptoms	295
Electrocardiography	295
Biomarkers	296
Prehospital and Emergency Department Evaluation	297
Treatment	298
Aspirin	298
P2Y12 Inhibitors	299
$\beta$ -Blockers	301
Angiotensin-converting Enzyme Inhibitors	304
Reviews and Meta-analyses	304
Studies	305
Thrombolytic Therapy	308
Review Articles and Meta-analyses	308
Thrombolytic Comparative Studies	309
Prehospital Thrombolysis Studies	316
Percutaneous Coronary Intervention	318
Reviews	318
Meta-analyses	318
Primary PCI	319
PCI after Thrombolysis	322
Rescue PCI	328
Operator and Hospital Volumes	329
Stenting in STEMI	329

Antithrombotic Regimens	333
Antithrombins	333
Direct Thrombin Inhibitors	336
Oral Anticoagulants	339
Glycoprotein IIb/IIIa Inhibitors	343
Glycoprotein IIb/IIIa Inhibitors and Reduced-dose Thrombolysis	345
Other Therapies	348
Nitrates	348
Calcium Channel Blockers	348
Antiarrhythmics	350
Magnesium	353
Glucose-Insulin-Potassium	354
Infarct Types	355
Left Ventricular Infarctions	355
Right Ventricular Infarction	357
Treatment of Cardiogenic Shock	357
Percutaneous Assist Devices	358
Assessment and Prognosis	360
Reviews and Meta-analyses	360
Electrocardiography, Arrhythmias, and Conduction Disease	361
Exercise Testing	363
Echocardiography and Other Noninvasive Tests	364
Flow, Vessel Patency, and Angiography	364
Other Prognostic Factors	367
Complications of Myocardial Infarction	369
Arrhythmias, Bundle Branch Block	369
Cardiac Rupture	369
Intracranial Hemorrhage in Thrombolysis	370
Reocclusion, Recurrent Ischemia, and Reinfarction	370
Left Ventricular Thrombi	372
Valvular Damage and Septal Defects	372

---

## **CHAPTER 5 Heart Failure** 374

**Benjamin A. Steinberg and Christopher P. Cannon**

---

EPIDEMIOLOGY 374

HISTORY AND PHYSICAL EXAMINATION 376

ETIOLOGY 377

DIAGNOSTIC TESTING 377

**TREATMENT 378**

- Treatment of Acute Heart Failure 378
- Treatment of Chronic Heart Failure 380
  - Angiotensin-converting Enzyme Inhibitors 380
  - Angiotensin II Receptor Antagonists 382
  - Dual Ras Blockade (ACE/ARB) 383
  - $\beta$ -Blockers 384
  - Diuretics 385
  - Aldosterone Blockers 385
  - Digoxin 386
  - Vasodilators 386
    - Hydralazine and Isosorbide Dinitrate 386
    - Calcium Channel Blockers 387
  - Amiodarone 387
  - Emerging Medical Therapies 387
  - Biventricular Pacing 388
  - Surgical Therapies 388
    - Left Ventricular Assist Device 388
    - Coronary Artery Bypass Graft Surgery 389
    - Cardiac Transplantation 390
    - Other Surgical Treatments 390
- Additional Therapeutic Considerations 391
  - Hemodynamic Monitoring 391
  - Exercise Training and Rehabilitation 391
  - Prevention of Sudden Cardiac Death 391

**REFERENCES 392**

- Guidelines and Reviews 392
- Epidemiology 393
- Diagnosis and Prognosis 394
  - Physical Examination 394
  - Diagnostic Testing 395
  - Noninvasive Testing 397
- Treatment 398
  - Angiotensin-converting Enzyme Inhibitors and Angiotensin-II Receptor Blockers 398
    - Meta-analyses 398
    - Studies 398
  - $\beta$ -Blockers 403
    - Review Articles and Meta-analyses 403
    - Carvedilol Studies 403
    - Other Studies 407
  - Diuretics and Aldosterone Antagonists 409

Digoxin	412
Vasodilators	413
Amiodarone	418
Inotropic and Other Agents	419
Mechanical Assist Devices and Surgical Options	421
Invasive Therapy	424
Additional Therapeutic Considerations	425
Anticoagulation	425
Exercise	426

## **CHAPTER 6 Arrhythmias 428**

**Benjamin A. Steinberg and Christopher P. Cannon**

<b>ATRIAL ARRHYTHMIAS</b>	<b>428</b>
Epidemiology	428
Natural History	428
Etiologies and Risk Factors	429
Stroke Risk Factors	430
Treatment	430
Rate versus Rhythm Control	430
Pharmacologic Agents for Control of the Ventricular Rate	432
Pharmacologic Agents for the Acute Conversion of Atrial Fibrillation	433
Intravenous Agents	433
Oral Agents	434
Pharmacologic Agents for Long-term Maintenance of Sinus Rhythm	436
Catheter and Surgical Ablation	438
Catheter Ablation	438
Surgical Ablation	439
Electrical Cardioversion	439
Type and Amount of Energy	439
Anticoagulation before and after Cardioversion	440
Prevention of Thromboembolism	441
Long-term Anticoagulation	441
Non-Vitamin K Oral Anticoagulants	443
Other Strategies to Prevent Thromboembolism	444
Other Treatment Measures	444
Atrial Pacemakers	444
Atrioventricular Junction Ablation with Permanent Pacemaker Implantation	444
Atrial Fibrillation Prevention after Cardiac Surgery	444

<b>VENTRICULAR ARRHYTHMIAS</b>	<b>445</b>
Immediate Therapy: Automated External Defibrillators	445
Immediate Therapy: Intravenous Amiodarone	446
Secondary Prevention Trials: Drugs versus Implantable Cardioverter-Defibrillators	446
Primary Prevention Trials: Antiarrhythmic Drugs	449
Primary Prevention Trials: Drugs versus Implantable Cardioverter-Defibrillators	449
Primary Prevention Trials: Nonischemic Cardiomyopathy Patients	450
Studies of Emerging Tachyarrhythmia Therapies	451
<b>CARDIAC PACING STUDIES</b>	<b>451</b>
Pacemaker Mode Selection Trials	451
Pacing for Vasovagal Syncope	452
Pacing for Prevention of Atrial Fibrillation	452
Resynchronization Therapy for Congestive Heart Failure	453
<b>REFERENCES</b>	<b>454</b>
Atrial Fibrillation	454
Guidelines	454
Epidemiology	454
Risk Stratification	455
Rate versus Rhythm Control	457
Drug Trials for Rate and Rhythm Control in Atrial Fibrillation	458
Catheter and Surgical Ablation	467
Catheter Ablation	467
Surgical Ablation	469
Electrical Cardioversion and Pericardioversion Anticoagulation	470
Long-term Anticoagulation	472
Non-Vitamin K Oral Anticoagulants	477
Nonpharmacologic Stroke Prevention in AF	481
Atrial Fibrillation Prevention after Surgery	481
Ventricular Arrhythmias	482
Guidelines	482
Immediate Therapy: Automated External Defibrillators	482
Immediate Therapy: Intravenous Amiodarone	483
Secondary Prevention Trials: Drugs versus Implantable Cardioverter-Defibrillators	484
Primary Prevention Trials: Antiarrhythmic Drugs	485

Primary Prevention Trials: Drugs versus Implantable  
Cardioverter–Defibrillators 486

Primary Prevention Trials: Nonischemic Cardiomyopathy  
Patients 489

Studies of Emerging Tachyarrhythmia Therapies 490

Cardiac Pacing Studies 491

Guidelines 491

Mode Selection Trials 491

Pacing for Vasovagal Syncope 493

Pacing for Prevention of Atrial Fibrillation 495

Resynchronization Therapy for Congestive Heart  
Failure 495

**Trial Index 501**

**Subject Index 513**