

Contents

Preface	xv
Contributors	xix
Chapter 1: Neuroendocrine Control of Food Intake	
<i>Andrew A. Butler, James L. Trevaskis and Christopher D. Morrison</i>	1
1. Introduction	1
2. Central Nervous System Regulation of Feeding Behavior	2
3. Neuroendocrine Factors Secreted from the Gut	2
3.1. Cholecystokinin	3
3.2. Peptide YY	5
3.3. Ghrelin	6
3.4. Amylin	7
3.5. Enterostatin	7
3.6. Glucagon-like Peptide	8
3.7. Bombesin Family: Bombesin, Gastrin-releasing Peptide and Neuromedin B	8
3.8. Oxyntomodulin	9
3.9. Leptin	10
4. Neuroendocrine Indicators of Long-term Energy Balance: Leptin and Insulin	10
4.1. Leptin and Insulin Signaling in Diet-induced Obesity	12
5. Summary	13
References	13
Chapter 2: Body Composition Assessment of Obesity	
<i>Wm. Cameron Chumlea</i>	23
1. Introduction	23
2. Overview of Body Composition Methods	24
2.1. Anthropometry	24
2.2. Weight and Stature	24
2.3. Body Mass Index	25
2.4. Abdominal Circumference	26
2.5. Skinfolds	27
2.6. Bioelectric Impedance Analysis	28

2.7. Body Density	29
2.8. Total Body Water	29
2.9. Dual-energy x-ray Absorptiometry	29
3. Ethnic Differences in Body Composition	30
4. Available Reference Data	30
5. Recommendations	31
6. Conclusion	31
Acknowledgments	32
References	32
Chapter 3: Prevalence of Obesity and the Metabolic Syndrome	
<i>Ali H. Mokdad and Earl S. Ford</i>	37
1. Overweight and Obesity	37
2. Prevention and Control Programs	44
3. THE Metabolic Syndrome	45
4. Preventive and Control Strategies	47
5. Future Perspectives	48
References	49
Chapter 4: The Genetic Contribution to Obesity	
<i>Raul A. Bastarrachea, Jack W. Kent Jr., Jeff T. Williams, Guowen Cai, Shelley A. Cole and Anthony G. Comuzzie</i>	55
1. Introduction	55
2. Obesity as a Common Complex Phenotype	56
3. Ancient Genes in a Modern World: An Evolutionary Genetic Perspective on Obesity	57
4. Approaches to Obesity Gene Discovery	58
4.1. Candidate Gene Association Study	59
4.2. Genome Scan	59
4.3. mRNA	60
5. Evidence from Animal Models for the Genetic Contribution to Obesity	60
5.1. Monogenic Obesity	60
5.2. Oligogenic Obesity	62
6. Evidence for the Genetic Contribution to Obesity in Humans	63
6.1. The Genetic Contribution to Rare Forms of Human Obesity	63
6.2. Genetic Contribution to Common Human Obesity	66
7. Conclusion	72
Acknowledgments	73
References	73

Chapter 5: Etiology of Obesity: The Problem of Maintaining Energy Balance

Barry E. Levin and Deborah J. Clegg 83

1. Introduction: Obesity and the Concept of Defended Body Weight 83
2. Neural Control of the Defended Body Weight 85
3. Obesity and the Problem of Maintaining Body Weight 88
4. How Is Body Weight Really Regulated? 90
5. Factors That Lower the Defended Body Weight 91
6. Implications for Future Research 91
- References 92

Chapter 6: Current Views of the Fat Cell as an Endocrine Cell: Lipotoxicity

Tamara Tchkonina, Barbara E. Corkey and James L. Kirkland 105

1. Introduction 105
2. Functions of Fat Tissue 105
3. Conditions Associated with Lipotoxicity 106
4. Mechanisms of Lipotoxicity 108
5. Inherent Properties of Cells Contribute to Susceptibility to Lipotoxicity 111
6. Association between Lipids and Inflammatory Responses 111
7. Mechanisms of Defense against Lipotoxicity 112
8. Preadipocytes and Fat Cells Are more Resistant than Other Cell Types to FA 114
9. Summary 116
10. Conclusions 117
- Acknowledgments 118
- References 118

Chapter 7: Ectopic Fat and the Metabolic Syndrome

Frederico G.S. Toledo and David E. Kelley 125

1. Introduction 125
2. Consequences of Excess Adiposity to Whole-body Glucose Homeostasis 126
3. FFA-induced Insulin Resistance 127
4. Ectopic Fat in Skeletal Muscle and Insulin Resistance 128
5. Relationships between Ectopic Fat in Liver and Insulin Resistance 129
6. Human Lipodystrophic Syndromes 130
7. Concluding Remarks 131
- References 132

Chapter 8: Abdominal Obesity and the Metabolic Syndrome

Jean-Pierre Després, Isabelle Lemieux and Natalie Alméras 137

1. Introduction 137
2. Metabolic Syndrome without Hyperglycemia Predicts an Increased CHD Risk 140

3.	Why Measure Waist Circumference as well and not just BMI?	141
4.	Abdominal Obesity: The Driving Force behind the Metabolic Syndrome?	143
5.	The Metabolic Syndrome: Is Waist Girth Sufficient?	143
6.	Are NCEP-ATP III Criteria Valid in All Populations?	144
7.	Managing CHD Risk in Patients with the Metabolic Syndrome: What Should Be Our Goal?	145
8.	Summary	146
	Acknowledgments	148
	References	148

Chapter 9: The Problems of Childhood Obesity and the Metabolic Syndrome

Sonia Caprio and Ram Weiss 153

1.	Introduction	153
2.	Prevalence of the Metabolic Syndrome in Children and Adolescents: Impact of Obesity	154
3.	Effects of Insulin Resistance (HOMA-IR) on the Prevalence of the Metabolic Syndrome	155
4.	Proinflammatory and Antiinflammatory Markers and Insulin Resistance	158
5.	Pathophysiological Studies of the Prediabetic Phenotype in Youth	159
6.	Relationship between Insulin Resistance and Tissue Lipid Partitioning	160
7.	Early Reduction of β -cell Sensitivity to Glucose in Obese Youth with Impaired Glucose Tolerance	162
8.	Longitudinal Study of Changes in Glucose Tolerance Status in Obese Youth	164
	Acknowledgments	165
	References	165

Chapter 10: Evaluation of the Overweight and Obese Patient

George A. Bray and Donna H. Ryan 169

1.	Introduction	169
2.	Definitions	170
3.	Anthropometric Measures	170
	3.1. Height and Weight	170
	3.2. Waist Circumference	170
4.	Instrumental Methods for Measuring Body Fat	171
	4.1. Dual X-ray Absorptiometry	172
	4.2. Density	172
	4.3. Isotope Dilution	173
	4.4. Bioelectric Impedance	173
5.	Imaging Techniques for Body Composition	173
6.	Summary of Clinical Recommendations for Measurement of Body Composition	173
7.	Body Fat through the Life Span	173
8.	Prevalence of Overweight	174

9.	Clinical Evaluation of Overweight Patients	176
9.1.	Body Mass Index	176
9.2.	Waist Circumference	178
9.3.	Weight Gain	178
9.4.	Sedentary Lifestyle	178
9.5.	Laboratory and Other Measures	179
10.	The Metabolic Syndrome	179
11.	Etiologic Factors Underlying Obesity	180
12.	Introduction to Treatment: Risk–Benefit Assessment	183
13.	Conclusion	183
	References	184

Chapter 11: Dietary Approaches to Obesity and the Metabolic Syndrome

	<i>Gary D. Foster and Angela P. Makris</i>	187
1.	Introduction	187
2.	Low-fat Diets	188
2.1.	Efficacy of Low-fat Diets on Weight Loss, Hypertension, and Diabetes	188
3.	Very-low-fat Diets	191
3.1.	Efficacy of Very-low-fat Diets on Weight Loss and Cardiovascular Disease	191
4.	Moderate-fat Diets	192
4.1.	Efficacy of Moderate-fat Diets on Weight Loss, Cardiovascular Disease, and Diabetes	193
5.	The High-protein Diet	195
5.1.	Efficacy of High-protein Diets on Weight Loss	196
6.	Low-carbohydrate Diets	198
6.1.	Efficacy of Low-carbohydrate Diets on Weight Loss, Insulin Sensitivity, and Lipids	198
7.	Low Glycemic Index Diet	202
7.1.	Effects of Low Glycemic Index Diets on Hunger and Weight Loss and Insulin Sensitivity	202
8.	Clinical Implications and Future Directions for Research	205
	References	205

Chapter 12: Exercise as an Approach to Obesity and the Metabolic Syndrome

	<i>John M. Jakicic and Amy D. Otto</i>	211
1.	Introduction	211
2.	Effect of Exercise on Health-related Parameters	211
3.	Impact of Exercise on Weight Loss	213
4.	Exercise Prescription Considerations for Long-term Weight Control	214
5.	Summary	216

Acknowledgments	216
References	216
Chapter 13: Behavioral Strategies for Controlling Obesity	
<i>Donald A. Williamson, Corby K. Martin and Tiffany M. Stewart</i>	219
1. Introduction	219
2. History of Behavioral Strategies for Controlling Obesity	220
2.1. Philosophy of Treatment	220
3. Behavioral Treatment for Adults	221
3.1. Approach and Outcomes	221
3.2. Duration of Treatment	221
3.3. Targets and Tools	221
3.4. Weight Maintenance Strategies	225
3.5. Special Considerations	226
4. Behavioral Treatment for Children and Adolescents	227
4.1. Approaches, Tools, and Outcomes	227
4.2. Reinforcement, Adherence, and Behavior Change	227
4.3. Social Support and Parent Training	228
4.4. Problem-solving	228
4.5. Meal Planning	228
4.6. Physical Activity	229
4.7. Special Considerations	229
5. Conclusions	230
6. Summary	230
References	231
Chapter 14: Obesity Prevention	
<i>Shiriki K. Kumanyika and Stephen R. Daniels</i>	233
1. Introduction	233
2. Defining the Task	234
2.1. Individual Level Perspective	234
2.2. Population Perspective	235
2.3. Goals and Priorities	235
3. Population-wide Approaches	237
3.1. Initiatives Related to Food	238
3.2. Initiatives Related to Physical Activity	238
3.3. Social Marketing	239
4. Prevention Targeted to Selected Population Groups	239
4.1. Adults	240
4.2. Children	243
5. Individually Targeted Approaches	247
6. Multilevel Approaches	247

7.	Methodological Considerations	248
8.	Conclusion	249
	Note	249
	References	249

Chapter 15: Orlistat and Sibutramine in the Management of Obesity *Holly Wyatt* 255

1.	Introduction	255
2.	Who Is Appropriate? Criteria for Use of Weight Loss Medications	255
3.	Why Do Health Care Providers Choose not to Use Weight Loss Medications?	257
4.	What Weight Loss Drugs Are Available?	258
5.	How Should Weight Loss in Medication Clinical Trials Be Evaluated?	259
6.	Sibutramine	260
	6.1. Mechanism of Action	261
	6.2. Therapeutic Potential for Obesity	261
	6.3. Efficacy in Weight Loss Maintenance	262
	6.4. Efficacy in Managing Obesity-related Risk Factors	264
	6.5. Tolerability and Safety	265
	6.6. Special Considerations when Prescribing Sibutramine	266
7.	Orlistat	266
	7.1. Mechanism of Action	267
	7.2. Therapeutic Potential for Obesity	267
	7.3. Efficacy in Weight Loss Maintenance	270
	7.4. Efficacy in Managing Obesity-related Risk Factors	270
	7.5. Tolerability and Safety	271
	7.6. Special Considerations when Prescribing Orlistat	272
8.	The Future of Weight Loss Medications	272
	8.1. Sibutramine and Orlistat Usage in Adolescents	272
	8.2. Combination Therapy	273
	8.3. Continuous vs. Episodic Medication Usage	273
9.	Summary	274
	References	274

Chapter 16: A Status of Drugs on the Horizon for Obesity and the Metabolic Syndrome—a Comprehensive Review 2005 *Frank Greenway and George Bray* 281

1.	Introduction	281
2.	Drugs Approved for Indications Other than Obesity and That Cause Weight Loss	282
	2.1. Bupropion	282
	2.2. Fluoxetine/Sertraline	283
	2.3. Zonisamide	284
	2.4. Topiramate	284

2.5. Metformin	285
2.6. Somatostatin	286
2.7. Pramlintide	287
2.8. Exenatide	287
3. Drugs in Phase III Clinical Trials with no Approval	288
3.1. Rimonabant	288
3.2. Axokine	289
3.3. Leptin	289
4. Drugs in the Early Phases of Development	290
4.1. Growth Hormone Fragment	290
4.2. Cholecystokinin	290
4.3. PYY 3-36	290
4.4. Oleoylestrone	291
4.5. Serotonin 2C Receptor Agonist	291
4.6. Neuropeptide Y Receptor Antagonists	291
4.7. Melanin Concentrating Hormone Receptor-1 Antagonist	292
4.8. Pancreatic Lipase Inhibitor	292
4.9. Glucagon-like Peptide-1 Agonists and Dipeptidyl Peptidase-4 Inhibitors	292
5. Drugs no Longer under Investigation or Withdrawn	293
5.1. β 3-adrenergic Agonists	293
5.2. Ephedra	293
5.3. Phenylpropanolamine	294
5.4. Bromocriptine	294
5.5. Ecopipam	295
6. New Areas where Drugs Are Being Developed	295
6.1. Histamine-3 Receptor Antagonists	295
6.2. Ghrelin Antagonist	295
6.3. 11β -hydroxysteroid Dehydrogenase Type I Inhibitor	295
6.4. Modulators of Energy Sensing in the Brain (Acetyl Co-A Carboxylase 2 Inhibitor; Fatty Acid Synthase; Carnitine Palmitoyltransferase-3)	296
6.5. Adiponectin	296
6.6. Melanocortin-4 Receptor (MC4R) Agonists	296
7. Natural Products (over-the-counter Preparations)	297
7.1. Chromium	297
7.2. <i>Garcinia cambogia</i>	297
7.3. Chitosan	298
7.4. <i>Hoodia</i>	298
7.5. <i>Stevia</i>	298
7.6. <i>Citrus aurantium</i>	299
8. Summary and Conclusions	299
References	300

Chapter 17: Surgical Treatment of the Overweight Patient	
<i>George A. Bray</i>	307
1. Introduction	307
2. Surgical Approaches to Obesity and Their Historical Context	309
3. Indications and Contraindications	310
3.1. Indications in Adults	310
3.2. Contraindications for Adults	310
3.3. Bariatric Surgery for the Pediatric Age Group	311
4. Effectiveness of Surgical Procedures	312
5. Mechanisms for Weight Loss	315
6. Benefits from Bariatric Surgery	316
7. Complications Associated with Bariatric Surgery	318
7.1. Complications Following Lap-band Bariatric Surgery	318
7.2. Complications Following Restrictive Bariatric Surgery	318
7.3. Complications with Malabsorptive Operations	319
8. Other Operative Procedures for the Overweight Patient	321
8.1. Intra-gastric Balloon	321
8.2. Gastric Stimulation or Gastric Pacing	321
8.3. Liposuction and Omentectomy	321
9. Summary	322
References	323
Index	329