

Contents

Preface	xiii
Contributors	xvii
 Chapter 1: Thyroid Hormone Metabolism	 1
<i>Stephen A. Huang and Luciana A. de Castro Neves</i>	
1.1 Introduction	1
1.2 Thyroid Hormone Synthesis and Plasma Transport	2
1.3 Thyroid Hormone Action	5
1.4 Thyroid Hormone Metabolism	5
1.5 Alternative Pathways of Thyroid Hormone Metabolism	5
1.5.1 Conjugation	5
1.5.2 Alanine Side-Chain Modification	6
1.6 Thyroid Hormone Deiodination	7
1.7 The Iodothyronine Deiodinase Enzyme Family	8
1.7.1 Type 1 Deiodinase (D1)	9
1.7.2 Type 2 Deiodinase (D2)	9
1.7.3 Type 3 Deiodinase (D3)	10
1.8 Thyroid Hormone Metabolism and T3 Homeostasis	10
1.8.1 Iodine Deficiency	10
1.8.2 Hypothyroidism	11
1.8.3 Hyperthyroidism	12
1.9 Altered Thyroid Hormone Metabolism as a Cause of Abnormal Thyroid Function Testing	12
1.9.1 Low-T3 Syndrome	13
1.9.2 Medications that Alter Thyroid Hormone Metabolism	14
1.9.3 Tumoral D3 and Consumptive Hypothyroidism	15
1.9.4 Tumoral D2 in Metastatic Follicular Thyroid Carcinoma	15
1.9.5 Selenium Deficiency and Inborn Errors in Selenoprotein Synthesis	16
References	16

Chapter 2: Genetic Influences on Thyroid Function Tests	21
<i>Wendy M. van der Deure, Marco Medici, Robin P. Peeters and Theo J. Visser</i>	
2.1 The Hypothalamus-Pituitary-Thyroid Axis	21
2.2 Influence of Genetic Variation on Thyroid Function Tests	23
2.3 Genetic Variation in Thyroid-Regulating Genes: TRH, TRHR, TSH, TSHR	25
2.4 Genetic Variation in Thyroid Transcription Factors: PAX8, TTF1, TTF2	26
2.5 Genetic Variation in Thyroid Hormone Synthesis Genes: NIS, Pendrin, Tg, TPO, DUOX2, DEHAL	27
2.6 Genetic Variation in Thyroid Hormone Receptor Genes: TR α , TR β	29
2.7 Genetic Variation in Serum TH Transport Proteins: TBG, TTR, and Albumin	30
2.8 Genetic Variation in TH Transporters: MCT8, MCT10, OATPs	31
2.8.1 MCT8 and MCT10	31
2.8.2 OATP1A2, 1B1, 1B3, and 1C1	32
2.9 Genetic Variation in Deiodinases: D1, D2, D3	35
2.10 Genome-Wide Association (GWA) Studies	36
2.11 Concluding Remarks	36
References	37
Chapter 3: Influence of Iodine Deficiency and Excess on Thyroid Function Tests	45
<i>Maria Andersson and Michael B. Zimmermann</i>	
3.1 Introduction	45
3.2 Iodine Metabolism and Thyroid Function	47
3.3 Thyroid Adaptation to Iodine Deficiency	47
3.4 Epidemiology of Thyroid Function in Areas of Low Iodine Intake	49
3.4.1 Adults	49
3.4.2 Pregnancy	50
3.4.3 Newborns	52
3.4.4 Children	54
3.5 Introducing/Increasing Iodine Intakes and/or Iodine Excess: Effects on Thyroid Function in Populations	56
3.5.1 Cross-Sectional Studies: The Epidemiology of Thyroid Function in Areas of Low and High Iodine Intakes	57
3.5.2 High Iodine Intake Produces Thyroid Dysfunction in Children	58
3.5.3 Longitudinal Studies: The Effects of Increasing Iodine Intakes in Populations on Thyroid Function	59
3.6 Conclusions	61
References	61

Chapter 4: Regulation of Thyroid Hormone Production and Measurement of Thyrotropin	71
<i>Jerome M. Hershman</i>	
4.1 Introduction	71
4.2 Production of Thyroid Hormone	71
4.2.1 Sodium/Iodide Symporter	71
4.2.2 Dietary Iodine Requirements	72
4.2.3 Thyroid Peroxidase	73
4.2.4 Hydrogen Peroxide Generation	73
4.2.5 Apical Iodide Transport	73
4.2.6 Thyroglobulin	74
4.3 TSH Biochemistry and Physiology	74
4.3.1 T3 Negative Regulation of TSH	75
4.4 Thyrotropin-Releasing Hormone	75
4.5 Diurnal Rhythmicity of TSH	76
4.6 Other Factors that Regulate TSH Secretion	77
4.7 Clinical Effects of TRH	78
4.8 Measurement of TSH	79
4.9 Normal Serum TSH Levels	80
4.10 Factors Affecting TSH Clinically	81
References	82
 Chapter 5: Measurements of Thyroxine and Triiodothyronine	85
<i>Jim R. Stockigt</i>	
5.1 Introduction	85
5.2 The Trophic–Target Gland Relationship	85
5.3 The Basis of Total and Free Thyroid Hormone Methodology	86
5.4 Total T4 and T3 Methods	88
5.5 Principles of Free T4 Methods	88
5.6 Factors that Limit the Validity of Free T4 Methods	90
5.7 Evaluation of Serum Free T4 Methods	95
5.8 Free T4 in Special Situations	96
5.8.1 Pregnancy	96
5.8.2 Thyrotoxicosis and Hypothyroidism	97
5.8.3 Thyroxine Replacement	98
5.8.4 Critical Illness	98
5.8.5 Premature Infants	100
5.9 Total T4 Measurement	101
5.10 Indications for Measurement of Serum T3	101

5.11	Approach to Anomalous Results	102
5.12	Conclusion	103
	References	104
Chapter 6: Thyroid Autoantibody Measurement		109
<i>R. A. Ajjan and A. P. Weetman</i>		
6.1	Introduction	109
6.2	Humoral Immunity in Autoimmune Thyroid Disease	110
6.2.1	Thyroid Autoantigens	110
6.2.2	The Role of Thyroid Autoantibodies in Disease Pathogenesis	111
6.3	Assays for Thyroid Antibodies	113
6.3.1	Thyroid Stimulating Hormone Receptor	113
6.3.2	Thyroid Peroxidase	114
6.3.3	Thyroglobulin	114
6.3.4	Sodium/Iodide Symporter	115
6.4	Clinical Applications of Antibody Measurement	115
6.4.1	Graves' Disease	115
6.4.2	Graves' Ophthalmopathy	116
6.4.3	Autoimmune Hypothyroidism	116
6.4.4	Pregnancy and Postpartum Thyroiditis	117
6.4.5	Differentiated Thyroid Cancer	118
6.5	Recommendation for the Use of Thyroid Autoantibodies in Clinical Practice	118
6.6	Conclusion	119
	References	120
Chapter 7: Thyroglobulin Measurement		125
<i>Carole Spencer and Ivana Petrovic</i>		
7.1	Tg Biosynthesis and Metabolic Clearance	125
7.2	Tg Assay Methodology: Technical Issues	126
7.2.1	Standardization/Specificity	127
7.2.2	Methodologic Sensitivity	129
7.2.3	Interferences	130
7.3	TgAb Measurements Used as a Surrogate Tumor Marker	132
7.4	Tg mRNA as a Tumor Marker	133
7.5	The Clinical Utility of Tg Measurement when TgAb Is Present	133
7.6	The Clinical Utility of Tg Measurement when TgAb Is Absent	135
7.6.1	Factors Influencing Circulating Tg Concentrations	135
7.6.2	Serum Tg Reference Range	136
7.6.3	Serum Tg Measurements for Nonmalignant Thyroid Conditions	137
7.6.4	Tg Measurement for Differentiated Thyroid Cancer	139
	References	142

Chapter 8: Thyroid Function Testing in Ambulatory Practice	155
<i>Angela M. Leung and Alan P. Farwell</i>	
8.1 Choice of Tests in Thyroid Function Testing	156
8.2 Evaluation of the Symptomatic Patient	157
8.2.1 Suspected Thyrotoxicosis	158
8.2.2 Suspected Hypothyroidism	159
8.2.3 Nodular Goiter	160
8.3 Use of Thyroid Function Tests to Monitor Treated Thyroid Dysfunction	161
8.3.1 Monitoring Hypothyroidism	161
8.3.2 Monitoring Hyperthyroidism	162
8.4 Screening of the General Population for Thyroid Dysfunction	163
8.5 Screening of Targeted Populations	164
8.5.1 Women of Childbearing Age, Pregnant Women, and Lactating Women	164
8.5.2 Elderly	165
8.5.3 Patients with Specific Comorbidities	166
8.6 Conclusions	167
References	167
 Chapter 9: Assessing Thyroid Function in Infants and Children	 173
<i>Alicia G. Marks and Stephen H. LaFranchi</i>	
9.1 Introduction	173
9.2 Infants	174
9.2.1 Hypothyroidism	174
9.2.2 Hypothyroxinemia in the Preterm Infant	178
9.2.3 Hyperthyroidism	179
9.3 Children	180
9.3.1 Hypothyroidism	180
9.3.2 Hyperthyroidism	182
References	184
 Chapter 10: Assessing Thyroid Function in Hospitalized Patients	 187
<i>Jonathan S. LoPresti and Komal S. Patil</i>	
10.1 Introduction	187
10.2 Low T3 State	189
10.3 Low T3/T4 State	192
10.4 Measurement of Thyroid Hormones in Illness	193
10.5 TSH Regulation in the Low T3 and Low T3/T4 States	194
10.6 Interpretation of Thyroid Tests in the Hospitalized Patient	195
10.7 Drugs that Affect Thyroid Function Tests	198
10.7.1 Glucocorticoids	198
10.7.2 Dopamine	198

10.7.3	Amiodarone	200
10.7.4	Heparin and Low Molecular Weight Heparins	200
10.7.5	Diphenylhydantoin	201
10.8	Variants of Nonthyroidal Illness	201
10.8.1	HIV and Thyroid Function	201
10.8.2	Liver Disease and Thyroid Function	202
10.8.3	Hyperemesis Gravidarum	202
10.8.4	Psychiatric Illness and Thyroid Function	203
10.9	Concluding Remarks	203
	References	204

Chapter 11: Assessing Thyroid Function in Pregnancy 209

John H. Lazarus, Offie P. Soldin and Carol Evans

11.1	Importance of Thyroid Status in Pregnancy	209
11.1.1	Thyroid Physiology in Pregnancy	209
11.2	Human Chorionic Gonadotrophin	211
11.3	Clinical Relevance of Assessing Thyroid Function in Pregnancy	213
11.3.1	Hyperthyroidism	213
11.3.2	Hypothyroidism	214
11.4	Maternal Thyroid Disease in Pregnancy: Effect on Child Development	214
11.5	Clinical Implications of Thyroid Antibodies in Gestation	215
11.6	Methods for Measuring Thyroid Function in Pregnancy	215
11.6.1	Total and Free Thyroid Hormone Measurements in Pregnancy	216
11.6.2	TSH Tests in Pregnancy	217
11.6.3	Free Thyroid Hormone Testing in Pregnancy	223
11.7	Development of Reference Intervals for Thyroid Hormones in Pregnancy	223
11.7.1	Trimester-Specific Method-Specific Reference Intervals	224
11.7.2	Trimester-Specific Thyroid Function Tests	224
11.8	Screening for Thyroid Function in Pregnancy	226
11.9	Conclusions	228
	References	228

Chapter 12: Assessing Thyroid Function in the Elderly 235

Mary H. Samuels

12.1	Changes in Normal Thyroid Function with Aging	235
12.2	Hypothyroidism in the Elderly	236
12.2.1	Prevalence	236
12.2.2	Etiology	237
12.2.3	Clinical Manifestations	237
12.2.4	Diagnosis	239
12.2.5	Treatment	239

12.3	Hyperthyroidism in the Elderly	240
12.3.1	Prevalence	240
12.3.2	Etiology	241
12.3.3	Clinical Manifestations	241
12.3.4	Diagnosis	243
12.3.5	Treatment	243
12.4	Thyroid Nodules and Cancer	245
12.5	Challenges in Assessing Thyroid Function in the Elderly	245
12.5.1	What is the Normal TSH Range in the Elderly?	245
12.5.2	Altered Presentation of Thyroid Disease in the Elderly	247
12.5.3	The Effects of Comorbid Conditions and Drugs on Thyroid Function in the Elderly	247
12.5.4	Risks of Treatment in the Elderly	247
	References	248
	 Chapter 13: Influence of Drugs on Thyroid Function Tests	 251
	<i>Sonia Ananthakrishnan and Elizabeth N. Pearce</i>	
13.1	Introduction	251
13.2	Alterations of Thyroid Hormone Secretion	251
13.2.1	Thionamides	251
13.2.2	Lithium	253
13.2.3	Iodides	253
13.2.4	Other Medications that Decrease Thyroid Hormone Secretion	255
13.3	Changes in T4 and T3 Serum Transport Proteins	255
13.3.1	Medications that Increase TBG	256
13.3.2	Medications that Decrease TBG	257
13.3.3	Competition with T4 and T3 Binding Sites on Thyroid Hormone Binding Proteins	258
13.4	Metabolism of Thyroid Hormones	259
13.4.1	Hepatic Metabolism	259
13.4.2	Deiodination	260
13.5	Central TSH Suppression	261
13.6	Medications with Multiple Effects	262
13.6.1	Glucocorticoids	262
13.6.2	Amiodarone	263
13.6.3	Bexarotene	265
13.6.4	Cytokines	265
13.6.5	Other Medications with Effects on Thyroid Function Tests	266
13.7	Levothyroxine Absorption	267
13.8	Conclusions	268
	References	268
	 Index	 279

Thyroid Function Testing

Brent, G.A. (Ed.)

2010, X, 392 p. 5 illus. in color., Hardcover

ISBN: 978-1-4419-1484-2