Subject Index

Abatacept 55
Activity, Graves’ orbitopathy
assessment 7, 11, 12, 106
biomarkers 12
severity comparison 6, 7, 97, 98
Adalimumab, clinical trials 186
Adipogenesis, Graves’ orbitopathy
pathogenesis 43, 47
Age
differences in Graves’ orbitopathy
presentation 4
effect on natural course of Graves’
orbitopathy 101, 102
Graves’ hyperthyroidism versus Graves’
orbitopathy differences 35, 36
risks for Graves’ orbitopathy 37
Alemtuzumab 37
Allopurinol, mild Graves’ orbitopathy
management 135
Amsterdam Declaration
goals met 340
overview 338, 339
purpose 339
signatories 341–343
text 340, 341
Anterior orbit septum (AOS), pathophysiology
of Graves’ orbitopathy 4, 5, 8
Antithyroid drugs (ATDs)
advantages and disadvantages 120
children 306
Graves’ orbitopathy course effects 128
AOS, see Anterior orbit septum
Artificial tears, Graves’ orbitopathy
management 109, 203, 287, 315
ATDs, see Antithyroid drugs
Azathioprine, moderately severe Graves’
orbitopathy management 163, 164
BAFF, therapeutic targeting 56, 178, 187
Binocular single vision (BSV)
assessment 16, 19
eye muscle surgery patients 233, 238, 243,
244
Blepharoplasty, see Eyelid surgery
Botulinum toxin, eyelid retraction
management 204, 248, 249
BSV, see Binocular single vision
Burn-out, Graves’ orbitopathy 100, 101, 132
Caroticocavernous fistula (CCF), differential
diagnosis 85–87
Caruncle, inflammation assessment 9, 10
CAS, see Clinical activity score
Cataract
epidemiology in Graves’ orbitopathy 317,
318
management 318
CCF, see Caroticocavernous fistula
CD3, therapeutic targeting 178
CD20, therapeutic targeting 178
Chemosis
assessment 9, 10
pathogenesis 44
Childhood Graves’ orbitopathy
clinical presentation 302–304
epidemiology 301, 302
management 305, 306
mild course 304, 305
Ciamexone, moderately severe Graves’
orbitopathy management 163, 164
Clinical activity score (CAS)
advantages and disadvantages 11
alternatives 13, 14
derivation 98
disease management utility 106, 107
phase of disease 99
Subject Index

Color vision, Graves’ orbitopathy 2, 16
Computed tomography (CT)
advantages of orbital imaging 61, 62
apical crowding 65–68
diagnosis of Graves’ orbitopathy 83, 84
dysthyroid optic neuropathy 22, 65, 67, 194
orbital tissue volume assessment 65, 67
Conjunctiva
edema assessment 9, 10
redness assessment 9
Corneal breakdown
eyelid surgery patients 249, 250
presentation 199
treatment 200
ulceration in Graves’ orbitopathy 2, 6
Corneal stippling, Graves’ orbitopathy
diagnosis 79, 81
Corticosteroids, see Glucocorticoids
Cosmetic surgery, rehabilitative surgery
comparison 207
CT, see Computed tomography
CTLA4
alleles and Graves’ orbitopathy
susceptibility and course 52, 53
therapeutic targeting 178
Cyclosporine
eye drops 203
moderately severe Graves’ orbitopathy
management 160, 162, 164
protocol 334, 335
Diabetes
diagnosis 309, 310
epidemiology in Graves’ orbitopathy 309
management 309–311
moderately severe Graves’ orbitopathy
management in patients 167, 168
Diagnosis, Graves’ orbitopathy
clinical findings 75–81
DiaGO 75
differential diagnosis 84–90, 291, 292
imaging 83, 84
medical history and clinical picture 81, 82
overview 74, 75, 105
thyroid autoantibody and function tests 82, 83
Diplopia
eye muscle surgery patient management 236
Graves’ orbitopathy association 1, 2
management 205, 287
scoring 15
DON, see Dysthyroid optic neuropathy
Double vision, see Diplopia
Dry eye syndrome
diagnosis 314
epidemiology in Graves’ orbitopathy 313, 314
management 109, 203, 287, 314, 315
Dysthyroid optic neuropathy (DON), Graves’ orbitopathy
assessment 21, 22
blindness 199, 298
criteria 193
imaging 22, 65–68, 194
normal vision 21
ophthalmological signs 196
optic nerve decompression surgery 199, 299
pathophysiology 193, 298
presentation 2, 19–21, 195
progression 197
risk factors 21, 194, 195–197
treatment 197, 198
Economic impact, see Socioeconomic impact, Graves’ orbitopathy
Etanercept
clinical trials 186
moderately severe Graves’ orbitopathy
management 165
Ethnicity, see Race
Euthyroid Graves’ orbitopathy 26–28, 297
Exophthalmos, Graves’ orbitopathy 1, 15, 18
Eye motility
orbital decompression effects 231, 232
restriction in Graves’ orbitopathy 79, 80, 230
surgery, see Eye muscle surgery
Eye muscle surgery
complications 241–243
diagnostic error avoidance 234, 235
diplopia management before surgery 236
muscle identification 232–234
outcomes 243, 244
patient expectations 244
patient selection 237, 238
planning 238–241
pretreatment 236
rectus muscles 230, 231
timing 236

Subject Index 353
Eyelids
  diagnosis of Graves’ orbitopathy
  retraction 77
  swelling 75–77
  erythema assessment 8, 9
  orbital decompression effects 250
  pathogenesis of changes 44
  presentation in Graves’ orbitopathy 1, 5, 6
  retraction management 204, 248, 249
  swelling assessment 7, 8

Eyelid surgery
  blepharoplasty 256, 257
  complications 254, 257
  contour assessment 257
  corneal ulceration patients 249, 250
  horizontal lid tightening 255, 256
  indications 247, 248
  orbital decompression combination 251
  quality of life outcomes 257
  spacers 157, 256
  squint surgery effects on lid configuration 250, 251
  technique
    lower lid retraction 254, 255
    upper lid retraction 252–254

Fast-track clinic 117

GAGs, see Glycosaminoglycans

Glaucoma
  diagnosis 316
  epidemiology in Graves’ orbitopathy 316, 317
  management 317
  pathophysiology 316

Globe subluxation 298

Gluocorticoids
  childhood Graves’ orbitopathy
    management 305
    diabetes induction 309
    dysthyroid optic neuropathy management 198
  eyelid retraction management 204
  intravenous therapy protocol 330–332
  mechanisms of action
    genomic pathway 141–143
    non-genomic pathway 143
  moderately severe Graves’ orbitopathy
    management
    dosing of intravenous steroids 151, 152

failure and retreatment 168
  high-dose pulse therapy morbidity and mortality 153–155
  intravenous 147–151
  oral 144–147
  orbital radiotherapy combination therapy 159–161
  peribulbar injection 155
  oral therapy
    prednisolone for mild disease 134
    protocol 332, 333
  orbital inflammation management 204, 205
  osteoporosis induction 311
  prophylaxis of Graves’ orbitopathy after thyroid radioablation 125, 126, 326
  response rate in Graves’ orbitopathy 177

Glycosaminoglycans (GAGs), Graves’ orbitopathy pathogenesis 43, 48, 49
GO, see Graves’ orbitopathy
GO-QoL, see Quality of life
Graves’ hyperthyroidism, see Hyperthyroidism
Graves’ orbitopathy (GO)
  euthyroid disease 26–28, 297
  nomenclature 26, 27
Guanethidine, eyelid retraction management 204

HIF-1, see Hypoxia-inducible factor-1

Historical perspective, Graves’ orbitopathy
  early accounts 346, 347
  importance of study 345, 348, 349
  milestones 348
  pathophysiology 347, 348

11β-Hydroxysteroid dehydrogenase, Graves’ orbitopathy pathogenesis 47, 48

Hypertension, moderately severe Graves’ orbitopathy management in patients 167, 168

Hyperthyroidism
  childhood Graves’ orbitopathy
    management 305, 306
    eye outcomes with treatment 286
  Graves’ hyperthyroidism management in moderately severe Graves’ orbitopathy 168, 169
  Graves’ orbitopathy relationship 26–29, 324, 325
  management 120–124, 127
natural course for Graves’ orbitopathy 93, 94
total thyroid ablation 127
Hypothyroidism
Graves’ orbitopathy relationship 27, 29, 45, 95
radioiodine induction and Graves’ orbitopathy risks 126
Hypoxia-inducible factor-1 (HIF-1), Graves’ orbitopathy pathogenesis 48

IFN-α, see Interferon-α
IgG4-ROD, see Immunoglobulin G4-related orbital disease
IL-1, see Interleukin-1
IL-1α, see Interleukin-1α
IL-6, see Interleukin-6
Immunoglobulin G4-related orbital disease (IgG4-ROD), differential diagnosis 86, 88, 89
Incidence, Graves’ orbitopathy overview 33
trend over time 34, 35, 110
Inferior rectus muscle, see Eye muscle surgery
Inflammation, early changes in Graves’ orbitopathy 43
Infliximab, clinical trials 186
Insulin-like growth factor-1 receptor autoantibodies in Graves’ orbitopathy 46
therapeutic targeting 178, 185, 187
Interferon-α (IFN-α), Graves’ orbitopathy risks with therapy 37
Interleukin-1 (IL-1), therapeutic targeting 55, 178, 184
Interleukin-1α (IL-1α), alleles and Graves’ orbitopathy susceptibility 53
Interleukin-6 (IL-6), therapeutic targeting 55, 178, 184, 186
Intravenous immunoglobulin (IVIG), moderately severe Graves’ orbitopathy management 163, 164
Iodine, malnutrition and Graves’ orbitopathy 38
IVIG, see Intravenous immunoglobulin
Keratoconjunctivitis, Graves’ orbitopathy 2
Lanreotide, moderately severe Graves’ orbitopathy management 166, 167
Lithium, Graves’ orbitopathy risks 37
Magnetic resonance imaging (MRI)
advantages of orbital imaging 63
apical crowding 65–68
diagnosis of Graves’ orbitopathy 83, 84
dysthyroid optic neuropathy 22
myositis of orbit 65
non-Hodgkin lymphoma of orbit 64, 71
orbital tissue volume assessment 65, 67
Management algorithm, Graves’ orbitopathy 110, 111
Meningioma, orbital 89, 90
Mental disorders
epidemiology in Graves’ orbitopathy 312, 313
management 313
Methimazole 120
Mild Graves’ orbitopathy
criteria 131
management
antioxidants 135–138
oral prednisolone 134
orbital radiotherapy 134
wait-and-see policy 133, 135
progression 131, 132
Moderately severe Graves’ orbitopathy
criteria 140
management
azathioprine 163, 164
ciamexone 163, 164
combination therapy 159–161
cyclosporine 160, 162, 164
diabetic patients 167, 168
etanercept 165
EUGOGO consensus statement 169, 170
EUGOGO guidelines 170, 171
evidence-based medicine 169
hypertensive patients 167, 168
immunosuppression overview 140, 141
intravenous immunoglobulin 163, 164
orbital radiotherapy
clinical trials 155–158
low irradiation dose and protracted protocol 158, 159
safety 159
somatostatin analogs 165–167
steroids
dosing of intravenous steroids 151, 152
failure and retreatment 168

Subject Index 355
high-dose pulse therapy morbidity and mortality 153–155
intravenous 147–151
oral 144–147
peribulbar injection 155
MRI, see Magnetic resonance imaging
Myositis, orbital 85
Myxedema, Graves’ orbitopathy 29–31
NF-κB, see Nuclear factor-κB
NHL, see Non-Hodgkin lymphoma
Nicotinamide, mild Graves’ orbitopathy management 135
Non-Hodgkin lymphoma (NHL), orbit 64, 71, 90
NOSPECS classification 13–19, 22, 133, 158
Nuclear factor-κB (NF-κB), steroid inhibition 142, 143
Octreoscan, orbit 69, 70
Octreotide, moderately severe Graves’ orbitopathy management 165–167
Orbital decompression
aims
functional aims 212–214
overview 211
rehabilitative symptomatic aims 214
childhood Graves’ orbitopathy 306
complications 223–225
conceptual developments 226, 227
eyelid effects 250
eyelid surgery combination 251
innovations 225, 226
ocular motility effects 231, 232
techniques 215–223
Orbital fat, Graves’ orbitopathy effects 96, 97
Orbital radiotherapy
dysthyroid optic neuropathy management 198
mild Graves’ orbitopathy management 134, 135
moderately severe Graves’ orbitopathy management
clinical trials 155–158
low irradiation dose and protracted protocol 158, 159
safety 159
steroid combination therapy 159
pregnancy 290
protocol 333, 334
Osteoporosis
epidemiology in Graves’ orbitopathy 311, 312
management 312
Pediatric Graves’ orbitopathy, see Childhood Graves’ orbitopathy
Pentoxifylline, mild Graves’ orbitopathy management 135
PET, see Positron emission tomography
Photophobia, Graves’ orbitopathy 1
Platelet-derived growth factor receptor, therapeutic targeting 178, 185
Plica, inflammation assessment 9, 10
Positron emission tomography (PET), orbit 71
Prednisolone, see Glucocorticoids
Prevalence, Graves’ orbitopathy 33, 34
Prevention, Graves’ orbitopathy
diet 286
primary and secondary prevention 323–325
risk modification 322, 323
smoking outcomes 327
stages 322
tertiary prevention 325–327
Proptosis
course in Graves’ orbitopathy 5
diagnosis of Graves’ orbitopathy 77–79
differential diagnosis 78
pathogenesis 44
Propylthiouracil 120
Public health, relevance of Graves’ orbitopathy 280–283
Puffiness, management 287
Quality of life (QoL)
eyelid surgery outcomes 257
general health-related quality of life in Graves’ orbitopathy 262, 263
GO-QoL
clinical application 271, 272
overview 131, 257, 263–265
treatment response 266–268
instruments for Graves’ orbitopathy 268–270
MOS-24 263, 264, 271
overview 260
qualitative studies in Graves’ orbitopathy 270
response with treatment 265, 266, 270, 271
utility of measures 260–262
QoL, see Quality of life

Race

differences in Graves’ orbitopathy manifestations 3, 4
Graves’ hyperthyroidism versus Graves’ orbitopathy differences 36
Radiation therapy, see Orbital radiotherapy; Thyroid radioablation
Radioiodine, see Thyroid radioablation
Rectus muscles, see Eye muscle surgery
Recurrence, Graves’ orbitopathy 101
Rehabilitative surgery, see also specific procedures
   cosmetic surgery comparison 207
   patient selection 209, 210
   psychological impact 288
   timing 208, 209
Retinopathy
   epidemiology in Graves’ orbitopathy 318
   management 318
Rituximab
   clinical trials 55, 56, 179–181
dosing 182
   mechanism of action 179
   patient selection 183, 184
   protocol 335
   safety 182, 183
Rundle’s curve, course of Graves’ orbitopathy 6, 95, 96

Selenium
   dosing 330
   malnutrition and Graves’ orbitopathy 38
   mild Graves’ orbitopathy management 135–138
   prevention of Graves’ orbitopathy 326
Severity, Graves’ orbitopathy
   activity comparison 6, 7, 97, 98
   assessment 14–19, 22, 106
   classification 19
   mild disease criteria 131
   moderately severe disease criteria 140
Sex differences
   Graves’ hyperthyroidism versus Graves’ orbitopathy 35, 36
   natural course of Graves’ orbitopathy 101, 102
Smoking
   cessation 108, 109
counseling 327
dysthyroid optic neuropathy risks 21
Graves’ orbitopathy risks and severity impact 38, 45, 53, 54, 101, 107, 108, 289, 323, 324
Socioeconomic impact, Graves’ orbitopathy
   clinical implications 279, 280
cost estimation in Europe 275, 276
   occupational disability 276, 277
   prospective study 277–279
   public health relevance 280–283
SOM230 55
Specialist
   combined thyroid-eye clinics 113, 114, 117
   multidisciplinary approach to Graves’ orbitopathy management 115
   patient characteristics at referral 116
   referral 116, 133
Squint surgery, see Eyelid surgery
Statins, Graves’ orbitopathy prevention 323
Support groups, Graves’ orbitopathy 115, 285, 286, 289
Surgery, see Rehabilitative surgery; specific procedures
TCZ, see Tocilizumab
Tear film, Graves’ orbitopathy features 202
Teprotumumab, clinical trials 187–189
Tg, see Thyroglobulin
T-helper cell, cytokines in Graves’ orbitopathy 48, 50
Thiazolidinediones, Graves’ orbitopathy risks 37
Thyroglobulin (Tg)
   autoantibodies in Graves’ orbitopathy 82
   Graves’ orbitopathy pathophysiology 29
Thyroid acropachy, Graves’ orbitopathy 29–31
Thyroidectomy
   advantages and disadvantages 120
   Graves’ orbitopathy effect studies 38, 39, 94, 95, 122, 123
   hyperthyroidism management 127
Thyroid radioablation
   advantages and disadvantages 120
glucocorticoid prophylaxis of Graves’ orbitopathy 125, 126, 326

Subject Index 357
Graves' orbitopathy effect studies 38, 39, 94, 95, 101, 109, 122, 325
hypo-thyroidism induction and Graves’ orbitopathy risks 126
mechanism of action 121
risk factors for Graves' orbitopathy development 124, 125
Thyroid-stimulating hormone receptor (TSH-R)
activation in Graves' orbitopathy 51, 52
autoantibodies in Graves’ orbitopathy 29, 36, 45–47, 50–52, 83, 106
cloning 348
therapeutic targeting 56, 178, 185
Thyroperoxidase, autoantibodies in Graves’ orbitopathy 82
Tocilizumab (TCZ), clinical trials 186
Triamcinolone, see Glucocorticoids
TSH-R, see Thyroid-stimulating hormone receptor
Twin studies, Graves’ orbitopathy risk and severity 53
UFOFs, see Uniocular fields of fixation
Ultrasound, orbital 68, 70, 71
Unilateral Graves’ orbitopathy
clinical presentation and management 292–295
course 296
prevalence 295, 296
Uniocular fields of fixation (UFOFs), assessment 16, 19
Very severe Graves’ orbitopathy, see Corneal breakdown; Dysthyroid optic neuropathy
VISA system 22
Visual symptoms, Graves’ orbitopathy
acuity loss in diagnosis 81
assessment 16–18
overview 2
pathogenesis 44
treatment 205, 288