Subject Index

ACTH, see Adrenocorticotrophin

Adiposity, see Body mass index

Adolescent friendly health care
adaptation to patient developmental stage 248
adult care transition 251
ethics 251
overview 245–247
prospects for study 251, 242
self image exploration 248
sexuality exploration 249, 250
team approach 250
therapeutic education and adherence 248, 249

Adrenocorticotrophin (ACTH), anorexia nervosa disturbances 158, 159

AN, see Anorexia nervosa

Anastrozole
familial male-limited precocious puberty management 237
McCune-Albright syndrome management boys 235
girls 233
ANE syndrome, genetics 80
Animal models, puberty
early life influences
clinical relevance 111–114
kisspeptin system in convergent mechanisms 101–109
nutritional manipulation
overnutrition 99, 100
overview 96, 97
undernutrition 97–99
overview 89–91
prospects for study 109–111
sex steroid manipulation through environmental exposures

bisphenol A 94, 95
diethylstilbesterol 96
estradiol benzoate 96
pesticide 94
phthalates 95
phytoestrogens 92, 93
polychlorinated biphenyls 93, 94
hypothalamic-pituitary-gonadal axis
maturation 87–89

Anorexia nervosa (AN)
bone health
bone mineral density 159, 160
IGF-1 role 160, 161
leptin role 160, 161
miscellaneous hormone function 161
nutrition effects 160
sex hormone studies 160
diagnostic criteria 154, 155
endocrine disturbances
hypothalamic-pituitary-adrenal axis 158, 159
hypothalamic-pituitary-gonadal axis 155, 156
hypothalamic-pituitary-growth hormone axis 157, 158
hypothalamic-pituitary-thyroid axis 158
treatment
bisphosphonates 163
IGF-1 replacement 163
nutrition 162
physical activity 163
sex steroid replacement 162, 163

ARC, see Arcuate nucleus
Arcuate nucleus (ARC), gonadotropin-releasing hormone release regulation 2, 3, 7, 8–11, 88

Athletes, see Female athlete triad
Bicalutamide
- familial male-limited precocious puberty management 237
- McCune-Albright syndrome management in boys 235

Biopsychosocial development
- brain 242
- puberty timing effects 243–245
- stages in adolescence 241, 242

Bisphenol A (BPA), animal models of early exposure effects on puberty 94, 95

Bisphosphonates, anorexia nervosa management 163

BMD, see Bone mineral density

BMI, see Body mass index

Body mass index (BMI)
- alternative hormonal activity and obesity 127
- cancer survivor obesity 71
- early nutritional manipulation of puberty in animal models
  - overnutrition 99, 100
  - overview 96, 97
  - undernutrition 97–99
- gonadotropin-releasing hormone agonist therapy
  - monitoring 218, 219
  - outcomes 222–224
- puberty timing effects
  - childhood obesity studies 163–165
  - clinical relevance 28, 29
  - females 21–24, 123, 124
  - males 24, 25, 124, 125

Bone mineral density (BMD)
- anorexia nervosa 159, 160
- female athlete triad 167, 168

BPA, see Bisphenol A

Breast cancer, risks with gonadotropin-releasing hormone agonist therapy 226

Cancer survivors
- gonadal dysfunction 169–171
  - management 171
  - obesity 171
  - pubertal alterations 169
- CBX7, female puberty epigenetic regulation 10

CDPG, see Constitutional delay in growth and puberty

Central precocious puberty (CPP)
- chromosomal abnormalities 58–60
  - epidemiology 50, 51
- genetics
  - candidate gene studies 60–62
  - KISS1 18, 51–54
  - KISS1R 18, 51–54
  - MKRN3 18, 54–58
  - GNAS somatic activating mutations 63–65
  - gonadotropin-releasing hormone agonist therapy 215, 216
  - LHCG and autonomous gonadal activation 62, 63
  - management 65

CHD7, Kallmann syndrome genetics 39

Congenital hypogonadotropic hypogonadism
- (CHH), see also specific syndromes
  - ANE syndrome 80, 81
  - associated syndromes 75
  - autosomal-recessive hereditary cerebellar ataxias 76, 77
  - gonadotropin axis activation 72–75
  - leukodystrophies 79, 80
  - management 83
  - molecular mechanism overview 81–83
  - novel syndrome with peripheral neuropathy 77–79
  - peripheral demyelinating neuropathy 77

Constitutional delay in growth and puberty (CDPG)
- males
  - diagnosis 185–187
  - treatment 188–190
  - overview 36, 37

Consultation, see Adolescent friendly health care

Convention of the Rights of the Child (CRC) 251

Corticotrophin-releasing hormone (CRH), anorexia nervosa disturbances 158, 159

CPA, see Cyproterone acetate

CPP, see Central precocious puberty

CRC, see Convention of the Rights of the Child

CRH, see Corticotrophin-releasing hormone

Cyproterone acetate (CPA)
- familial male-limited precocious puberty management 236
- McCune-Albright syndrome management in girls 232

DAXI, normosmic idiopathic hypogonadotropic hypogonadism genetics 41
DCAF17, Woodhouse-Sakati syndrome genetics 80, 81, 83
DDT, puberty timing effects 178, 179
Dehydroepiandrosterone (DHEA), female hypogonadism and hormone replacement therapy 209, 210
Delayed puberty, see also Constitutional delay in growth and puberty
hypogonadotropic hypogonadism, see Congenital hypogonadotropic hypogonadism; Idiopathic hypogonadotropic hypogonadism
male delayed puberty
diagnosis 185–187
prospects for study 193
treatment
constitutional delay in growth and puberty 188–190
hypergonadotropic hypogonadism 192, 193
idiopathic hypogonadotropic hypogonadism 189–192
rationale 187, 188
DES, see Diethylstilbestrol
DHEA, see Dehydroepiandrosterone
Diethylstilbestrol (DES), animal models of early exposure effects on puberty 96
DMXL2, congenital hypogonadotropic hypogonadism genetics 78, 79
EAP1, central precocious puberty studies 62
EB, see Estradiol benzoate
EDCs, see Endocrine-disrupting chemicals
EED, female puberty epigenetic regulation 10, 11
Endocrine-disrupting chemicals (EDCs), see also specific chemicals
animal model studies of early exposures on puberty 102–106
clinical relevance 180–182
Epigenetics
clinical evidence in pubertal outcome
birthweight studies 136, 138
environmental exposures 146, 147
gestational diabetes 147
gestational weight gain effects 140, 141
infancy weight gain studies 137, 138, 140, 141
overview 135, 137
polycystic ovary syndrome 142
prematurity effects 139, 141
small for gestational age 138–140, 144, 146, 147
early life events and puberty timing 25–27
female puberty regulation
clinical relevance 12, 13
gonadotropin-releasing hormone expression activation during neuronal maturation 7
Kiss1 expression activation
preovulatory gonadotropin surge 7
puberty initiation 7, 8–11
posttranscriptional regulation 11, 12
gene regulation in puberty 145, 146
heredity of changes 147, 148
mechanisms of regulation
DNA methylation 4
histone modification 4
noncoding RNA 4, 5
overview 3
metabolic programming factors 142–144
Polycomb group and Trithorax group in chromatin posttranslational modification 6
Estradiol benzoate (EB), animal models of early exposure effects on puberty 96
Estrogen
anorexia nervosa
bone health 160
replacement therapy 162, 163
female hypogonadism and estrogen replacement therapy
administration route 200, 201
adolescence guidelines 206, 207
androgen replacement studies 207–210
dosing 201, 202
estrogen formulations 199, 200
initiation 202–205
mid-puberty guidelines 205, 206
rationale 198, 199
Fadrozole, McCune-Albright syndrome management in girls 233
Familial male-limited precocious puberty (FMPP), clinical features and management 235–238
Female athlete triad
bone health 167, 168
eating disorders 166
gonadal axis effects 166, 167
overview 166
treatment 168

FEZF1, Kallmann syndrome genetics 40, 41
Fibroblast growth factor (FGF), Kallmann syndrome genetics 38, 39
FKTN, puberty timing 19
FMPP, see Familial male-limited precocious puberty
Follicle-stimulating hormone (FSH)	anorexia nervosa disturbances 155
gonadotropic axis activation 72–75
4H syndrome, genetics 44, 79, 80, 82
FSD1L, puberty timing 19
FSH, see Follicle-stimulating hormone
Fulvestrant, McCune-Albright syndrome management in girls 234

GABRA1, central precocious puberty studies 60
GH, see Growth hormone
Ghrelin
anorexia nervosa bone health 161
eyearly life events and puberty timing 27
GHS, see Gordon Holmes syndrome
GNAS, somatic activating mutations 63–65
GnRH, see Gonadotropin-releasing hormone
Gonadotropin-releasing hormone (GnRH) agonist therapy in sexual precocity adverse events 219
breast cancer risks 226
cessation 219, 220
doses and formulations 217, 218
indications
central precocious puberty 215, 216
children after radiation therapy 216
McCune-Albright syndrome management in girls 232
monitoring 218, 219
outcomes
body mass index 222–224
first menstruation 220
first spermarche 220, 221
height 221, 222
metabolic syndrome 225
polycystic ovary syndrome 224, 225
pregnancy studies 225, 226
principles 214, 215
analogs for early puberty treatment 29
female puberty regulation 1–3
gonadotropic axis activation 72–75

normosmic idiopathic hypogonadotropic hypogonadism genetics 41, 42, 44
release regulation 2, 3, 43, 88
Gordon Holmes syndrome (GHS), genetics 43, 44, 76, 77, 81, 82
Growth hormone (GH)	anorexia nervosa disturbances 155, 157
early life events and puberty timing 25, 26

HS6ST1, Kallmann syndrome genetics 40
Hypergonadotropic hypogonadism, treatment 19, 192
Hypogonadotropic hypogonadism, see Congenital hypogonadotropic hypogonadism; Idiopathic hypogonadotropic hypogonadism

Idiopathic hypogonadotropic hypogonadism (IHH), see also Kallmann syndrome; specific syndromes
diagnosis 185–187
 genetics overview 37
gonadotropin-releasing hormone agonist therapy, see Gonadotropin-releasing hormone
normosmic idiopathic hypogonadotropic hypogonadism genetics DAX1 41
gonadotropin-releasing hormone 41, 42
kisspeptin 42
leptin 41
TAC3 42, 43

Idiopathic hypogonadotropic hypogonadism, treatment 189–192
IGF-1, see Insulin-like growth factor-1
IHH, see Idiopathic hypogonadotropic hypogonadism
Insulin, anorexia nervosa bone health 161
Insulin-like growth factor-1 (IGF-1) anorexia nervosa
bone health 160
disturbances 155, 157, 158
replacement therapy 163
early life events and puberty timing 25, 26
nutritional response 125, 143

KAL1 38
Kallmann syndrome (KS) epidemiology 38
Subject Index

Ketoconazole
- familial male-limited precocious puberty management 236, 237
- McCune-Albright syndrome management in girls 232, 233

Kisspeptin
- animal model studies of early interventions
  - endocrine-disrupting chemicals 102–106
  - nutrition studies 106–109
- overview 101, 102
- central precocious puberty genetics
  - KISS1 18, 51–54
  - KISS1R 18, 51–54
- epigenetic regulation 145, 146
- gonadotropin-releasing hormone release regulation 2, 3, 43, 88
- Kiss1 expression activation in female puberty
  - preovulatory gonadotropin surge 7
  - puberty initiation 7–11
- normosomic idiopathic hypogonadotropic hypogonadism genetics 42

KS, see Kallmann syndrome

Leptin
- anorexia nervosa
  - bone health 160, 161
  - disturbances 155, 156
- central precocious puberty studies 60, 61
- early life events and puberty timing 27
- normosomic idiopathic hypogonadotropic hypogonadism genetics 41
- puberty timing effects 179, 180

Letrozole, McCune-Albright syndrome management in girls 233, 234

LH, see Luteinizing hormone

LHCGR, autonomous gonadal activation 62, 63

LIN28B
- central precocious puberty studies 61
- female puberty epigenetic regulation 11
- puberty timing 19, 128

Luteinizing hormone (LH)
- anorexia nervosa disturbances 155
- female puberty regulation 2
- gonadotropin axis activation 72–75

Martsolf syndrome, genetics 44

MAS, see McCune-Albright syndrome

McCune-Albright syndrome (MAS)
- clinical features and management
  - boys 235
  - girls 231–235
  - GNAS somatic activating mutations 63–65
- Metabolic syndrome, gonadotropin-releasing hormone agonist therapy outcomes 225

MKRN3, central precocious puberty genetics 18, 54–58, 128

NELF, Kallmann syndrome genetics 40

Neurokinin B (NKB)
- central precocious puberty studies 61
- gonadotropin-releasing hormone release regulation 43, 88

NKB, see Neurokinin B

Obesity, see Body mass index

Oliver-McFarlane syndrome, genetics 77

OTUD1, Gordon Holmes syndrome genetics 76

Oxandrolone, female hypogonadism and hormone replacement therapy 207–209

PCBs, see Polychlorinated biphenyls

PcG, see Polycomb group

PCOS, see Polycystic ovary syndrome

Peptide YY (PYY), anorexia nervosa bone health 161

Peripheral precocious puberty (PPP), see also

McCune-Albright syndrome
differential diagnosis 230, 231
familial male-limited precocious puberty 235–238

Pesticides, animal models of early exposure effects on puberty 94

Phthalates, animal models of early exposure effects on puberty 95

Phytoestrogens, animal models of early exposure effects on puberty 92, 93
**PNPLA6**, Gordon Holmes syndrome genetics 76, 77, 82

**POLR3A**, 4H syndrome genetics 79, 80, 82

**POLR3B**, 4H syndrome genetics 79, 80, 82

Polychlorinated biphenyls (PCBs), animal models of early exposure effects on puberty 93, 94

Polycomb group (PcG) chromatin posttranslational modification 6

time effect on female puberty epigenetic regulation 9, 10, 13

gene transcription repression 5, 6

Polycystic ovary syndrome (PCOS) epigenetics 142

gonadotropin-releasing hormone agonist therapy outcomes 224, 225

PPP, see Peripheral precocious puberty

Precocious puberty, see Central precocious puberty; Peripheral precocious puberty

**PROK2**, Kallmann syndrome genetics 39

Puberty animal models, see Animal models, puberty

epigentic regulation, see Epigenetics

timing, see Timing, puberty

PYY, see Peptide YY

**RAB18**, Warburg micro syndrome genetics 77

**RAB3a**, congenital hypogonadotropic hypogonadism genetics 78

**RAB3GAP1**, Warburg micro syndrome genetics 77, 78

**RAB3GAP2**, Warburg micro syndrome genetics 77, 78

Rbcn-3α, congenital hypogonadotropic hypogonadism genetics 78, 79

**RBM28**, ANE syndrome genetics 80, 83

**RNF216**, Gordon Holmes syndrome genetics 76, 81

Self image exploration in adolescent friendly health care 248

puberty timing effects 243–245

**SEMA3**, Kallmann syndrome genetics 39

**SOX10**, Kallmann syndrome genetics 40

Spironolactone, familial male-limited precocious puberty management 237

**STUB1**, Gordon Holmes syndrome genetics 76, 81

**TAC3** central precocious puberty studies 61, 62

normosmic idiopathic hypogonadotropic hypogonadism genetics 42–44

**TACR3** central precocious puberty studies 61, 62

normosmic idiopathic hypogonadotropic hypogonadism genetics 42–44

**TAL2**, puberty timing 19

Tamoxifen, McCune-Albright syndrome management in girls 234

**TBC1D20**, Warburg micro syndrome genetics 77

Testolactone familial male-limited precocious puberty management 237

McCune-Albright syndrome management in girls 233

Testotoxicosis, see Familial male-limited precocious puberty

Thyroid hormone, anorexia nervosa disturbances 158

Thyroid-stimulating hormone (TSH), anorexia nervosa disturbances 158

Timing, puberty animal models, see Animal models, puberty

body size effects females 21–24, 123, 124

males 24, 25, 124, 125

time changes over time indicators 175, 176

mechanisms 176–180

early life events and epigenetics 25–27

genic influences 127, 128

genetics

**FKTN** 19

**FSD1L** 19

genome-wide association studies 19–21

**LIN28** 19

**TAL2** 19

**TMEM38B** 19

**ZNF462** 19

heritability 18

impact on psychosocial development, self image, and sexuality 243–245

obesity effects in childhood 163–165

precocious puberty, see Central precocious puberty

trends 18, 122–124, 175

variability 17

**TMEM38B**, puberty timing 19
Triflumizole, obesogenic activity 126, 127
Trithorax group (TrxG)
  chromatin posttranslational modification 6
  female puberty epigenetic regulation 9, 10
  Polycomb group antagonism 6
TrxG, see Trithorax group
TSH, see Thyroid-stimulating hormone
TTF1, central precocious puberty studies 62
Turner’s syndrome, oxandrolone therapy 209
Warburg micro syndrome, genetics 44, 77
WDRI1, Kallmann syndrome genetics 39
Woodhouse-Sakati syndrome (WSS), genetics 80, 81, 83
ZNF462, puberty timing 19