

Index

- 46,XX disorders of sexual development, 36
- Abaelard, Peter, 4
- abdominal aortic aneurism, 342
- abiraterone, 285
- acetylation of histones, 26
- acetyl-coenzyme A, 16
- acne
in women, 101
- acne conglobata, 537
- acne vulgaris, 536–7
- acromegaly, 62, 166
- activational effects of hormones, 88
- activational effects of testosterone (men), 90–8
aggression, 93–6
comparison with women, 110–14
depression, 93
effects on sleep, 96–7
impact of aging, 90
mood effects, 93
relevant information, 90
sexual desire and response, 90–3
summary of evidence, 97–8
testosterone replacement in hypogonadism, 90–2
- activational effects of testosterone (women), 98–110
aggression and assertiveness, 108–9
circulating androgens and sexuality, 98–100
comparison with men, 110–14
complexity of influences on sexuality, 110
effects of aging, 100
effects of iatrogenic lowering of testosterone, 100–3
effects on sexual problems in women, 103–6
exogenous testosterone administration and sexuality, 103–6
extent of conversion to estrogen, 110
individual variability of response, 109–10
menopause, 100
mood effects, 106–8
sexual desire and response, 98–106
summary of evidence, 109–10
- activin, 127
- acute coronary syndromes, 217
- acute non-lymphocytic leukemia, 389
- Addison's disease, 443, 444
- adipocytes
fat deposition, 238–40
influence of DHT, 199
- adipocytokines, 238–9
- adipogenic lineage, 254
- adipose tissue
hormones produced by, 238–9
interactions with the HPT axis, 238–40
- adrenal androgens
age-related decline in women, 100
- adrenal cortex
fetal zone, 438
- adrenal glands
effects of over-stimulation, 107
- adrenal insufficiency, 440, 447
DHEA treatment, 442–4
- adrenal steroidogenesis, 16
- adrenalectomy, 254
- adrenarche, 37, 89, 438
- adrenopause, 438
- adult Leydig cells, 35
- adverse effects of testosterone
strategies to avoid, 197–200
- adverse events
testosterone therapy in older men, 195–6
- age-related differences
response to testosterone treatment, 193
- aggression
effects of testosterone in men, 93–6
effects of testosterone in women, 108–9
gender differences, 94
- aggressive personality and testosterone, 93
- Aggressive Provocation Questionnaire (APQ), 96
- aging
altered neuroendocrine regulation, 344–5
and bioavailable testosterone levels, 338–9
and ejaculate volume, 336
and erectile dysfunction, 251–2
and fertility, 336–7
and hypogonadism, 323
and percentage spermatozoa with normal morphology, 336
and sperm motility, 336
and total sperm output, 336
androgen receptors, 339
androgen supplementation debate, 337
andropause, 336
aromatase activity, 340
aromatization of testosterone, 339–40
biotransformation in the tissues, 339–40
changes in coronary vasodilatation, 214
effects in generally healthy men, 336–7
effects of co-morbidity on testosterone levels, 338
effects of decline in testosterone levels, 323
effects of increasing fat mass, 340
effects of obesity on testosterone levels, 338
effects of testosterone, 97
free testosterone levels, 338–9
GnRH secretion, 344–5
gonadotropin levels, 343–4
impact on effects of testosterone, 90
increase in SHBG binding capacity, 345
increase of serum SHBG, 345
interindividual variability in effects, 337–8
Leydig cell function, 337
metabolic clearance rate for testosterone, 337, 339
metabolism of androgens, 339–40
pathophysiology of declining testosterone levels, 343–5
primary testicular changes, 343–4
production of DHT, 339–40
5 α -reductase activity, 339–40

Index

- aging (*cont.*)
 reduction in mean testicular volume, 343
 regulation of LH secretion, 344–5
 Sertoli cell function, 336–7
 serum testosterone levels, 337–8
 SHBG levels, 338–9
 SHBG-bound testosterone, 339
 spermatogenesis, 336–7
 testosterone conversion to estradiol, 340
 testosterone production, 337–8
 tissue levels of androgens, 339–40
see also androgen therapy in elderly men.
- aging and hypoandrogenism
 and depression, 351–2
 and quality of life, 352
 androgen status measurement, 352
 body composition, 348–9
 bone mineral density, 350–1
 cardiovascular risk profile, 347–8
 clinical relevance, 345–52
 cognitive function, 351
 effects on fat mass, 348
 effects on mood, 351–2
 effects on muscle function, 348–9
 effects on muscle mass, 348–9
 erectile function, 346–7
 erythropoiesis, 351
 hemoglobin levels, 351
 long-term effects of androgen therapy, 348
 nocturnal penile tumescence (NPT), 346
 risk of falls, 349
 risk of fractures, 349–51
 sarcopenia, 348–9
 senile osteoporosis, 349–51
 sexual function, 346–7
 signs and symptoms of androgen deficiency, 345–6
 skeletal effects of testosterone, 349–51
- aging and testosterone levels, 340–3
 and androgen receptor polymorphisms, 341
 birth cohort effect, 341
 body composition and adiposity, 341
 drug side-effects, 343
 effects of alcohol, 342
 effects of diet, 342
 effects of medications, 343
 effects of smoking, 342
 effects of stress, 342
 effects of thyroid hormone changes, 342
 ethnic differences, 341
- genetic influences, 340–1
 influence of insulin levels, 341
 interindividual variations, 340
 lifestyle factors, 342
 metabolic factors, 341
 physiological factors, 340–2
 serum testosterone levels in disease, 342–3
 SHBG levels, 341–2
- Aging Male Symptom Score, 46
- Albertus Magnus, 6
- albumin, 21, 60, 61, 273, 423
- alcohol
 effects on testosterone level, 342
- aldo-keto reductase (AKR), 24
- aldosterone, 442
- aldosterone antagonists, 219
- alendronate, 183
- Alzheimer's disease, 351
- American Association of Clinical Endocrinologists, 413
- American Society of Reproductive Medicine, 413
- amygdala, 89
- amygdaloid nuclei, 89
- anabolic androgenic steroids, 9, 191–2, 373, 461
 and cardiac disease, 208
 and liver disease, 208
 and sudden cardiac death, 208
 anti-doping fight in sport, 530–1
 athlete doping program in the GDR, 518, 536
 black-market products, 520–1
 designer steroids, 519, 522–3
 development of synthetic steroids, 517–20
 discovery of, 191–2
 doping with Oral-Turinabol, 536
 extent of the doping problem, 535–6
 findings from anti-doping testing, 520
 frequency of steroid misuse, 520–1
 history of misuse in sports, 517–20
 illegal use and abuse, 9
 misuse in bodybuilding, 520
 misuse in controlled competition sports, 520
 misuse in fitness studios, 520
 misuse in non-controlled sports, 520–1
 prohibition by sports organizations, 517–20
 prohormones, 519
 prohormones of androgens, 521–2
 prohormones of dihydrotestosterone, 521
- prohormones of nortestosterone, 521
- prohormones of testosterone, 521
- supplements contaminated with prohormones, 523
- testosterone-to-epitestosterone ratio, 519
- tetrahydrogestrinone (THG), 522
- use in sports, 191–2, 221
- anabolic androgenic steroids side-effects
 acne conglobata, 537
 acne vulgaris, 536–7
 amenorrhea in women, 541
 anovulation in women, 541
 atherosclerosis risk, 538
 athletes' attitudes towards misuse, 542
- azoospermia, 540
- behavioral disturbances, 539
- blood effects, 537
- bones, 538–9
- breast cancer risk, 541–2
- cardiac arrhythmias, 537
- cardiac death risk in young athletes, 538
- causes of sudden death, 539–40
- deepening of voice in women, 541
- depressive mood, 539
- difficulty in establishing the cause, 535–6
- dilatative cardiomyopathy (DCM), 538
- dysmenorrhea in women, 541
- gynecomastia, 540
- heart and vessels, 537–8
- hepatocellular carcinoma, 538, 539
- hirsutism, 536–7, 541
- hypertension, 538
- hypogonadotropic hypogonadism, 540
- increase in erythrocytes, 537
- increase in hematocrit, 537
- increase in hemoglobin concentration, 537
- increased fibrinolysis, 537
- intrahepatic cholestasis, 538
- intratesticular leiomyosarcoma, 540
- kidneys, 539
- liver, 538
- muscles, 538–9
- need for more public education, 542
- pathological myocardial hypertrophy, 537–8
- peliosis hepatis, 538
- rhabdomyolysis, 539
- seborrhea, 536–7
- skin effects, 536–7
- specific effects in men, 540

- specific effects in women, 540–2
 striae distensae, 536–7
 suppression of spermatogenesis, 540
 tumors, 539
- anabolic androgenic steroids testing
 A and B sample testing, 523–4
 derivatization, 526
 detection of endogenous anabolic androgenic steroids, 528–9
 detection of synthetic anabolic androgenic steroids, 526–8
 development of testing methodology, 524
 DHT doping, 528
 gas chromatography–mass spectrometry (GC-MS) method, 524–5
 high-resolution mass spectrometry (HRMS), 528
 isotope ratio mass spectrometry (IRMS), 528–9
 metabolism and excretion, 525
 organization of doping tests, 523–4
 pharmacokinetics, 525
 sample preparation, 525–6
 sample taking and transportation, 523–4
 stages of analysis, 524–5
 testosterone-to-epitestosterone ratio, 528–9
 WADA-approved laboratories, 524
- anabolic hormones, 220
- Anabolic Steroid Control Act, 522
- anastrozole, 183, 211
- ancient Egypt, 2, 3
- androgen ablation therapy
 for metastatic prostate cancer, 284–5
- androgen binding protein (ABP), 15, 21, 130
- androgen-dependent reporter genes, 41–2
- androgen deprivation therapy, 10
 cardiovascular risk, 209
 for prostate cancer, 209, 236, 238, 240
 risk factor for metabolic syndrome, 238
 risk factor for type 2 diabetes, 238
- androgen functions
 development of external genitalia, 36–7
 fetal prostate development, 35–6
 male puberty and adulthood, 37–8
 masculinization of the fetus, 37
 sexual differentiation of embryo and fetus, 35–7
 target genes in fetal prostate development, 36
- androgen-induced hepatotoxicity, 374
- androgen-induced polycythemia, 375
- androgen insensitivity syndrome (AIS), 38–42
 androgen receptor gene mutations, 41
 androgen-regulated genes, 42
 clinical findings, 38–9
 functional characteristics of mutations, 41–2
 genetics, 40–1
 laboratory assessment, 39–40
 somatic mosaicism, 41
- androgen insufficiency syndrome (AIS)
 effects on hair growth, 161
- androgen receptor (AR), 10, 15, 24, 88, 123, 215
 alternative (non-nuclear) receptors, 27–8
 androgen-binding domain, 26
 cellular membrane receptors, 27–8
 defects, 27
 distribution in the brain, 89–90
 DNA-binding domain, 26
 effects of aging, 339
 effects of androgen administration, 27
 evolution of, 271
 expression on adipocytes, 240
 genomic pathway of action, 135–6
 hinge region, 26
 interaction with DNA, 26
 mechanism of androgen action, 24–7
 mediation of androgen action on bone cells, 184
 methylation/demethylation enzymes, 26
 modulation of transcription activity, 33–4
 non-genomic pathways of action, 136
 N-terminal domain, 25
 phosphorylation, 26
 regulation of action, 26
 role in hair growth, 161
 selective androgen receptor modulators (SARMs), 27
 testicular androgen receptors, 132–5
 transcriptional regulation, 40
- androgen receptor CAG repeat polymorphisms, 25, 42–8, 240, 341
 and benign prostatic hyperplasia (BPH), 44
 cardiovascular risk factors, 45–6
 effects of, 33–4
 effects on bone tissue, 45
- effects on reproductive function, 44–5
- ethnic differences, 43–4
- gender differences in effects, 111–12
- hypotheses, 47–8
- influence on body tissues, 45
- influence on hair growth, 47
- influence on sperm concentration, 45
- influence on spermatogenesis, 44–5
- influence on testosterone therapy, 47–8
- Kennedy syndrome (XSBMA), 42–3
- mouse model of human sequence, 43
- pharmacogenetics, 47–8
- prostate development and malignancy, 43–4
- psychological effects, 46–7
- androgen receptor gene, 25
 CAG repeat polymorphisms, 89
 location, 40
 location and structure, 33
 mutations, 41
 role in androgenetic alopecia in men, 165
 role in organizational effects of testosterone, 89
 somatic mosaicism, 41
 structure and function, 40–38
- androgen receptor GGC repeat polymorphisms, 25
- androgen receptor knock-out mice, 35, 36, 184, 212
- androgen receptor modulators, 191
- androgen receptor mutations, 10
- androgen receptor pathophysiology
 androgen insensitivity in humans, 38–42
 effects of CAG repeat polymorphisms, 42–8
 Kennedy syndrome (XSBMA), 42–3
 outlook, 48–9
 prostate development and malignancy, 43–4
- androgen receptor polymorphisms, 309
 and testosterone levels in elderly men, 341
 and type 2 diabetes, 240
see also androgen receptor CAG repeat polymorphisms.
- androgen receptor TGG repeat polymorphisms, 25
- androgen-regulated genes, 42
- androgen response elements (AREs), 26, 40, 135–6, 163
- androgen sensitivity
 and type 2 diabetes, 240
- androgen sensitivity test, 40
- androgen status measurement, 352

Index

- androgen suppression
and spermiation failure, 134
- androgen therapy in elderly men,
352–8
diagnosing androgen deficiency,
352–5
effects on the prostate, 356–7
goals of androgen therapy, 352–5
gynecomastia, 356
increase in hematocrit, 355–6
increase in hemoglobin levels,
355–6
indications for treatment, 352–5
long-term benefit–risk ratio, 353
modalities of androgen substitution,
357
potential benefits, 355
potential risks, 355–7
sleep apnea, 356
use of screening questionnaires,
354
- androgen therapy in non-gonadal
disease
approaches to androgen therapy,
372–3
body weight problems, 394–5
bone disease, 383–4
critical illness, 384–6
effects of androgen therapy, 373
goals of androgen therapy, 373
hematological disorders, 375–7
immune disease, 386–8
liver disease, 374–5
malignant disease, 388–9
muscular disorders, 380–1
neurological disease, 391–3
renal disease, 377–80
respiratory disease, 389–91
rheumatological disorders, 381–3
steroid-induced osteoporosis, 384
surgery rehabilitation, 384–6
trauma, 384–6
vascular disease, 393–4
- androgenetic alopecia, 158, 163–4
androgenetic alopecia in men, 163,
164–6
and prostate cancer risk, 165
changes in the hair follicles, 164
consequences of hair loss, 165
grading, 164
incidence, 164–5
link to myocardial infarction, 165
pattern of balding, 164
role of, 164–5
role of androgens, 165–6
role of genes, 165–6
role of the androgen receptor gene,
165
androgenetic alopecia in women, 166
female pattern hair loss (FPHL),
166
grading, 166
incidence, 166
- androgenetic alopecia treatments,
167–8
bimatoprost, 167–8
dutasteride, 168
endocrine-based treatments, 168
finasteride, 168
for eyelashes, 167
latanoprost, 167–8
minoxidil, 167
non-hormonal therapy, 167–8
prostaglandin analogs, 167–8
5 α -reductase inhibitors, 168
surgery, 167
- androgens, 22
effects on SHBG, 62
genomic effects, 24–7
mode of action in the brain,
89–90
non-genomic effects, 27–8
physiological effects, 15
role in spermatogenesis, 130–8
- androkinin (hypothetical male
hormone), 8
- andromedins, 277, 279, 281
- andropause, 336
- androstenedione
intracrine activation, 442
- androst-5-ene-3 β ,7 β ,17 β -triol
(β AET), 440
- androstan-3 α -ol-17-one.
See androsterone
- androsterone
structure, 310–11
- androstane-3 α ,17 β -diol, 16
- 5 α -androstane-3 α ,17 β -diol-
glucuronide (ADG), 24,
340, 440
- 5 α -androstane-3,17-dione, 274
- 5 α -androstane-3,17 β -diol, 275
- 3 α -androstanediol, 24
- androsten-17 α -ol-3-one.
See testosterone
- androsterone-3,17-dione, 17
- androstenedione, 23, 26, 35, 99, 131,
340, 438, 495
administration in clinical studies,
446–7
as a prohormone, 441–2
effects of administration in women,
103
in depressed women, 107
in women, 100, 108
mechanisms of action, 441–2
use as a food supplement, 447
use by athletes, 447
- androstenone (16 ene-5 α -androsten-
3-one), 28
- androsterone, 23
isolation of, 9
- anemia due to bone marrow failure
androgen therapy, 375–6
- anemia of end-stage renal failure
androgen therapy, 378–9
- anemias, 27
- anger
dimensions of, 95
- angina, 214
- angina pectoris, 226
testosterone treatment studies,
217–18
- angioplasty, 214
- angiotensin converting enzyme
inhibitors, 219, 222
- ankle-brachial index, 210
- Annibaldi, Domenico, 4
- anorchia, 39, 292
- anterior hypothalamic/preoptic area,
88
- antiandrogens, 285, 343
effects in women, 101
- anti-arrhythmics, 219
- anticonvulsants, 393
- antiepileptic drugs, 61
- anti-Mullerian hormone (AMH), 35,
39
- anti-thymocyte globulin (ATG), 375
- anxiety, 447
- aortic intima-media thickness, 210
- Aphrodite (Venus)
birth of, 2
- aplastic anemia
androgen therapy, 375–6
- apolipoprotein A1, 348
- apolipoprotein B, 347
- apolipoprotein E, 347
- apoptosis
during brain development, 88
in rat Leydig cells, 21
- AR. *See* androgen receptor
- Arabic medicine, 6
- areal bone density
and testosterone deficiency, 180–1
- Aristotle, 2, 156
- aromatase, 238
action in men, 422
activity in the brain, 89
in adipocytes, 238
- aromatase activity, 23–4
effects of aging, 340
- aromatase cytochrome P450 enzyme,
132
- aromatase deficiency, 423–4, 429, 432,
433
caused by testosterone treatment, 24

- aromatase inhibitors, 238, 350, 432
aromatase knock-out mice, 23, 143, 426
aromatization of testosterone to estradiol, 143–4, 350–1
arousal
 and testosterone level, 94, 96–7
aryl-propionamides, 459, 461
asthma
 androgen therapy, 391
atheroma development
 carotid artery atheroma, 210
 coronary atheroma, 209–10
 peripheral arterial disease, 210–11
atherosclerosis, 224
 age-related effects, 208–9
 and low testosterone, 209–11
 and testosterone levels, 208–9
 effect on testosterone levels, 342
 effects of estrogens, 208
 fatty streak development in animal models, 211–12
 plaque rupture, 215
 role of testosterone in animal models, 211–12
atherosclerosis pathophysiology
 angina pectoris treatment, 217–18
 effects of testosterone on serum cytokine levels, 213
 endothelial adhesion molecule expression, 213–14
 endothelial cell injury, 212
 erythropoiesis, 216
 evidence for effects of low testosterone, 212–17
 fatty streaks, 216
 features of advanced atheroma, 213
 formation of fatty streaks, 212–13
 hemostatic factors, 215–16
 plaque rupture, 213
 role of LDL, 212
 thrombotic process, 215–16
 thrombus formation, 213
 total and LDL cholesterol, 216–17
 treatment studies, 217–18
 vascular reactivity, 214–15
atherosclerotic plaque, 212
athletes
 use of androstenedione, 447
 see also anabolic androgenic steroids.
attention deficit hyperactivity disorder (ADHD)
 and CAG repeat AR polymorphisms, 46
autoimmune disease
 effects of testosterone therapy, 221
azoospermia, 25
 anabolic steroid side-effect, 540
Bartoli, Cecilia, 4
Beck Depression Inventory (BDI), 93, 101, 104
bed nucleus of the stria terminalis (BNST), 88, 89
behavioral effects. *See* activation effects of testosterone
benign prostatic hyperplasia (BPH), 27, 44, 270, 271, 272, 281–2, 285, 343, 416, 431
 and androgen therapy in elderly men, 356–7
 SRD5A inhibitor treatment, 281–2
Berthold, Arnold A., 6, 8
beta-adrenergic receptor blockers, 219, 222
bicalutamide, 199, 285, 459
bicyclic hydantoin, 461
bimatoprost, 167–8
bioassay of testosterone, 78
bioavailable testosterone, 77–8, 210, 211, 224, 226
 effects of aging, 338–9
birth cohort effect, 341
blood–testis barrier, 124
body composition
 effects of DHEA treatment, 448
body mass index (BMI), 240, 341
body weight problems
 androgen therapy, 394–5
bodybuilding
 misuse of anabolic steroids, 520
boldenone, 522
boldenone undecylenate, 520
bone disease
 androgen therapy, 383–4
bone health
 androgen receptor-mediated action on bone cells, 184
 dual actions of testosterone on bone, 183–4
 effects of androgens on bone cells, 184
 osteoblast functions, 184
 osteoclast functions, 184
 role of estrogens, 178
 role of testosterone, 177–8
 testosterone replacement in elderly men, 182
 testosterone replacement in hypogonadal men, 181–2
 see also osteoporosis.
bone homeostasis
 role of estradiol in men, 431
bone marrow cells
 response to androgen therapy, 375
bone marrow failure
 androgen therapy, 375–7
bone mass
 monitoring testosterone therapy, 301
bone maturation
 role of estrogens in men, 430–1
bone metabolism
 in elderly men, 349–51
 influence of estrogens in men, 429–31
bone mineral density (BMD)
 effect of DHEA treatment, 448–9
 effects of testosterone therapy for women, 504
 in elderly men, 350–1
 in hypogonadism, 415–16
 influence of estrogens in men, 431
bone tissue
 effects of CAG repeat AR polymorphisms, 45
bones
 actions of estrogen, 23
 actions of testosterone, 23
 osteoporosis, 23
 risk of fractures in elderly men, 349–51
 side-effects of anabolic steroids, 538–9
boys on hemodialysis
 androgen therapy, 380
 growth of, 380
brain, 24
 action of androgens and estrogens, 89–90
 distribution of androgen receptors, 89–90
brain development
 gender differentiation and testosterone, 88–9
 organizational effects of testosterone, 88–9
 white matter, 89
brain imaging studies, 88
brain natriuretic peptide, 223
breast, 24
breast cancer, 375, 439
 contraindication for testosterone therapy, 303
Brief Index of Sexual Functioning for Women (BISF-W), 106
Brief Psychiatric Rating Scale (BPRS), 95
Brown-Séquard, Charles E., 6–7
buccal administration of testosterone, 314–15
burn injury
 androgen therapy, 385–6
buserelin, 475
Buss and Perry Aggression Questionnaire, 95, 96, 109

Index

- Buss–Durkee Hostility Inventory (BDHI), 95, 96
 Butenandt, Adolf, 8, 9
- C-reactive protein (CRP), 245
 cachectic patients, 216
 cachexia, 222
 effects of testosterone therapy, 221
 CAG repeat polymorphisms.
 See androgen receptor CAG repeat polymorphisms
 CAG repeats (polyglutamine), 25
 calculated free testosterone, 78
 California Verbal Learning Test, 505
 Canadian Physicians' guidelines, 413
 cancers, 193
 cancers in women, 25
 capon comb's test, 8
 cardiac cachexia, 220, 222
 cardiac disease
 and anabolic steroids, 208
 cardiac effects of testosterone treatment, 221
 cardiomyopathy, 223
 cardiovascular disease
 and erectile dysfunction, 245, 252
 epidemiology, 207–8
 see also atherosclerosis; chronic heart failure; coronary artery disease.
 cardiovascular events
 and testosterone levels, 217
 testosterone therapy in older men, 195–6
 cardiovascular events in women
 effects of HRT, 208
 cardiovascular function in women
 effects of testosterone therapy, 504
 cardiovascular mortality
 gender differences, 347
 cardiovascular risk
 and erectile function, 255
 and estrogen, 208
 and metabolic syndrome, 235
 and obesity, 235
 and testosterone levels, 208–9
 and testosterone therapy, 417
 and type 2 diabetes, 235
 androgen deprivation therapy, 209, 238
 CAG repeat androgen receptor polymorphisms, 45–6
 insulin resistance, 235–6
 metabolic syndrome, 236–7
 carotid artery
 intima-media thickness, 210, 211
 carotid artery atheroma
 and low testosterone, 210
 carotid artery atherosclerosis
 effect on testosterone levels, 342
 carotid endarterectomy, 210
 carotid-femoral pulse wave velocity, 211
 Casodex, 285
 castor oil in testosterone preparations, 322–3
 castration, 2–4, 254
 ancient Egypt, 3
 as lawful punishment, 3
 as revenge for seduction and adultery, 4
 as revenge on enemies, 3
 cardiac effects, 221
 castrato singers, 4
 Chinese eunuch system, 2–3
 effects on life expectancy, 4
 Greek mythology, 2
 in the Islamic world, 3
 medieval Scandinavia, 3
 Normans, 3
 of slaves, 2–3
 of Uranos by Chronos, 2
 prepubertal, 4
 range of supposed therapeutic uses, 10
 self-mutilation for religious reasons, 3 *see also* orchidectomy.
 castration before puberty
 effects on hair growth, 161
 castrato singers, 4
 catabolic hormones, 220
 Catharers, 3
 cell membrane
 effects of estradiol, 89
 effects of testosterone, 89
 cellular membrane androgen receptors, 27–8
 cellular therapy, 7
 cetrorelix, 92
 cGMP, 252, 254, 255
 chaperones, 24, 26
 chemiluminescent assay (CLIA), 74
 chemotherapy, 343
 Chinese eunuch system, 2–3
 Chinese medicine, 6
 cholestasis of the liver, 312
 cholesterol, 16, 218
 conversion to pregnenolone in mitochondria, 19
 conversion to testosterone, 16–17
 effect of testosterone therapy, 245
 requirement by Leydig cells, 16
 role in atherogenesis, 216–17
 storage as lipid droplets, 16, 18
 transport to the mitochondria, 18–19 *see also* HDL cholesterol; LDL cholesterol.
 cholesterol ester hydrolase, 18
 chromosome 2, 24
 chromosome 5, 24
 chronic anemia, 216
 chronic heart disease
 anabolic–catabolic imbalance, 220
 cardiac cachexia, 220
 effects of testosterone on physical function, 221
 effects of testosterone on skeletal muscles, 221
 effects on blood pressure, 220
 reduced cardiac output, 220
 vasoconstriction, 220
 chronic heart failure, 216, 218–24, 226
 androgen status, 220
 baroreceptor sensitivity, 224
 brain natriuretic peptide marker, 223
 breathlessness and fatigue, 219, 220, 221
 cachexia, 222
 cardiac cachexia, 222
 cardiac effects of testosterone treatment, 221
 causes, 218
 chronic anemia, 222
 clinical features, 219
 clinical trials of testosterone therapy, 222–4
 drug therapy, 219
 effect of testosterone on exercise capacity, 223–4
 effect of testosterone on hemodynamics, 222
 erythropoietic effects of testosterone, 222
 hematocrit, 222
 hemoglobin concentration, 222
 inflammation, 222
 insulin resistance, 221–2
 metabolic syndrome, 220
 mortality rate of severe heart failure, 220
 non-cardiac effects of testosterone treatment, 221
 pathophysiology, 220
 prevalence, 219
 prognosis, 220
 reduced cardiac output, 222
 systemic vascular resistance, 221, 222
 systolic blood pressure, 224
 theoretical basis for testosterone treatment, 221
 vasoconstriction, 221
 chronic illness
 effects of androgen therapy on physical function, 193–4

- loss of muscle mass and function, 193–4
- chronic obstructive pulmonary disease (COPD), 193, 342, 343
- androgen therapy, 389–90
- effects of androgen therapy on physical function, 194
- chronic renal failure, 343
- chronic respiratory failure, 375
- chronic stable angina, 218
- chronic urticaria
- androgen therapy, 383
- Chronos
- castration of Uranos, 2
- cimetidine, 168
- cingulate cortex, 91
- cingulate gyrus, 91
- circadian variation of serum testosterone, 340
- circannual variations in testosterone levels, 340
- cirrhosis of the liver
- androgen therapy, 374
- claustrum, 91
- clinically available forms of testosterone, 9–10
- clitoris
- fetal development, 36
- clobetasol propionate, 505
- clomifene, 238
- clomipramine, 107
- cluster headaches
- androgen therapy, 392
- coactivator proteins, 34
- cognitive function
- and testosterone levels in women, 500
- effects of androgen therapy, 391–2
- effects of testosterone therapy for women, 504–5
- in elderly men, 351
- Colleoni, Bartolomeo, 4
- common marmoset (*Callithrix jacchus*), 128
- compensated hypogonadism, 344
- competitive androgen receptor antagonists, 285
- complete androgen insensitivity syndrome (CAIS), 10, 24, 27, 33, 35, 36, 38–9, 111
- see also androgen insensitivity syndrome (AIS).
- conduct disorder (CD)
- and CAG repeat AR polymorphisms, 46
- congenital adrenal hyperplasia (CAH), 19, 36
- congenital aromatase deficiency, 423–4
- congestive heart failure, 193, 356
- constitutional delay of puberty
- testosterone therapy, 302
- contraception. *See* male hormonal contraception; oral contraception (women)
- coronary angiography, 210
- coronary artery disease, 212, 213
- and low testosterone, 209
- and sexual dysfunction, 251
- thrombotic process, 215–16
- coronary artery vasodilatation, 218
- coronary atheroma
- and low testosterone, 209–10
- coronary atherosclerosis
- effect on testosterone levels, 342
- coronary disease, 222
- coronary heart disease
- and low testosterone, 208–9
- epidemiology, 207–8
- gender differences in prevalence, 207–9
- coronary thrombosis, 215
- corpus callosum, 88, 91
- cortisol, 62, 438, 442
- in depressed women, 107
- couple relationship
- and testosterone levels, 261
- CREB transcription factor, 136
- critical illness
- androgen therapy, 384–6
- effects on testosterone levels, 342
- Crohn's disease, 446
- cryopreservation of sperm
- Spallanzani, 5
- Cushing syndrome, 62, 166, 343
- Cushing, Harvey W., 7
- cyclic GMP. *See* cGMP
- cyclic quinolinones, 459
- cyclodextrins, 314
- cynomolgus monkeys, 89
- CYP19 aromatase, 461
- CYP19 gene, 340, 350
- cyproterone acetate, 101, 109, 155, 168, 169, 484–5, 537
- cytochrome P450 aromatase, 89
- cytochrome P450 oxido-reductase deficiency (PORD), 432
- cytochrome P450ssc, 19
- cytokine activation, 218
- cytokines, 220, 244–5
- adipocytokines, 238–9
- effects of testosterone, 213
- danazol, 61, 75
- de Graaf, Regnier, 5
- decapeptyl, 475
- deep vein thrombosis (DVT), 393–4
- dehydroepiandrosterone. *See* DHEA
- dehydroepiandrosterone sulfate.
- See* DHEAS
- Deiters, Otto, 1
- delayed puberty in boys, 432
- testosterone therapy, 302
- $\Delta 5$ pathway of steroid synthesis, 16–17
- $\Delta 4$ pathway of steroid synthesis, 16–17
- demasculinization
- in androgen receptor knock-out mice, 36
- in male knock-out mice, 37
- dementia, 439
- denosumab, 183
- depression
- and CAG repeat AR polymorphisms, 46
- and testosterone levels, 46, 96
- androgen therapy, 392–3
- effect of DHEA treatment, 445
- effects of testosterone in men, 93
- effects of testosterone in women, 106–8
- effects of testosterone therapy, 196–7
- in elderly men, 351–2
- Depression Scales, 46
- depressive disorders, 447
- dermal papilla, 161–3
- Derogatis Interview for Sexual Function, 104
- designer steroids, 519, 522–3
- desogestrel, 485–6
- desoxymethyltestosterone (Madol, DMT), 522
- development
- influence of testosterone, 97
- DHEA, 17, 88, 131, 210, 347, 495
- adrenocortical steroid, 437
- and atheroma formation, 211
- and well-being in women, 107
- effects on mood in women, 108
- in women, 98, 100, 108
- mechanisms of action, 439–41
- use as anti-aging drug, 437
- DHEA deficiency
- approach to treatment, 449
- DHEA levels
- age-related decline, 437, 438
- as health status indicator, 439
- epidemiology of effects, 438–9
- gender differences in effects, 438–9
- genetic component, 438
- interindividual variability, 438
- pattern throughout the lifetime, 438
- secretion and age, 438
- DHEA mechanisms
- intracrinology concept, 440
- ligand for a specific DHEA receptor, 440–1

Index

- DHEA mechanisms (*cont.*)
 neurosteroid, 440
 precursor for active sex steroids, 439–40
- DHEA sulfotransferase (SULT2A1), 439
- DHEA therapeutic profile, 447–9
 body composition, 448
 central nervous system effects, 447
 effect on mood, 447
 effect on sexuality, 447
 immune system effects, 449
 metabolic effects, 447–8
 skeletal effects, 448–9
 skin effects, 449
- DHEA treatment
 adrenal insufficiency, 442–4
 Crohn's disease, 446
 diminished ovarian reserve (DOR), 446
 effect on depression, 445
 effect on fatigue, 442–4
 effect on libido, 442–4
 effect on mood, 442–4, 445
 effect on pubic hair growth, 443, 444
 effect on well-being, 442–4, 445
 elderly subjects, 444–5
 future directions, 449–50
 hypopituitarism, 443–4
 immunological disorders, 445–6
 skin effects, 443, 444
 systemic lupus erythematosus (SLE), 445–6
 ulcerative colitis, 446
- DHEAS, 88, 99, 226, 340, 347, 495
 adrenocortical steroid, 437
 and vitality in women, 107
 in women, 98, 100
- DHEAS levels
 age-related decline, 437, 438
 as health status indicator, 439
 epidemiology of effects, 438–9
 gender differences in effects, 438–9
 genetic component, 438
 interindividual variability, 438
 pattern throughout the lifetime, 438
 secretion and age, 438
- DHT, 16, 23, 24, 127, 254
 5 α -reduction of testosterone, 131–2
 binding to AR in the prostate, 277
 cellular effects, 24
 effects of aging on production, 339–40
 formation in the prostate, 273
 glucuronoconjugated, 340
 in depressed women, 107
 measurement of, 78–9
 metabolism in the prostate, 274
 metabolites, 24
 potency compared to testosterone, 23
 production, 23
 production in women, 495
 role in fetal prostate development, 36
 synthesis by 5 α -reductase, 24
 use in doping, 528
- DHT gel
 as osteoporosis therapy, 183
- diabetes mellitus, 24, 42, 46, 218, 222
 and cardiovascular disease, 207
 and sexual dysfunction, 252
- diabetes mellitus type 1, 254
- diabetes mellitus type 2, 24, 226, 254, 347
 and androgen deprivation therapy, 238
 and androgen receptor polymorphism, 240
 and androgen receptor sensitivity, 240
 and cardiovascular disease, 235
 and low testosterone, 235–6
 and metabolic syndrome, 236–7
 and testosterone deficiency, 416
 and testosterone level, 237–8
 clinical implications of low testosterone, 245
 effect of testosterone on body composition, 242
 effect of testosterone on central adiposity, 242
 effect of testosterone on cholesterol and lipoproteins, 245
 effect of testosterone on dyslipidemia, 244
 effect of testosterone on ED, 245
 effect of testosterone on hyperglycemia, 242–4
 effect of testosterone on hypertension, 244
 effect of testosterone on inflammation, 244–5
 effect of testosterone replacement, 242
 effects in elderly men, 342
 effects of testosterone on insulin resistance, 240–1
 insulin resistance, 237, 242
 low testosterone as risk factor, 237
 potential benefits of testosterone replacement, 245
 prevalence of hypogonadism, 235
 systolic blood pressure, 240
- Diana/Artemis Ephesina fertility cult, 2
- diazepam, 103
- dickkopf 1 (DKK1), 164
- dienogest, 485
- diet
 and testosterone levels in elderly men, 342
- diethylstilbestrol (DES), 427–8
- digoxin, 219
- dihydrotestosterone. *See* DHT
- 5 α -dihydrotestosterone. *See* DHT
- dilatative cardiomyopathy (DCM), 538
- diminished ovarian reserve (DOR), 446
- direct free testosterone assays, 76–7
- Djungarian hamster, 139
- DMPA (depot MPA), 101, 476–84
- Doisy, Edmund A., 8
- dominance
 and testosterone level, 93, 94
- doping
 use of anabolic steroids, 9
- doping in sport. *See* anabolic androgenic steroids; SARMs
- doping screens for athletes, 24
- doping tests
 organization of, 523–4
- Doppler ultrasound scanning, 210
- drospirenone, 169
- drostanolone enanthate, 520
- drostanolone propionate, 520
- drug abuse
 and CAG repeat AR polymorphisms, 46
- drug-related hirsutism, 166
- drugs
 effects on testosterone levels, 343
- Duchenne muscular dystrophy
 androgen therapy, 381
- dutasteride, 161, 168, 281–2, 285–6, 311
- dyslipidemia
 effect of testosterone therapy, 244
- echocardiography, 223, 224
- ED. *See* erectile dysfunction
- eflornithine hydrochloride, 168
- embryo
 sexual differentiation, 35–7
- endocrinology
 description of organotherapy, 7
- endocrine function
 and gonadal development, 34–5
 testosterone and the testes, 5–6
- Endocrine Society, 413
- Endocrine Society of Australia, 413
- endocrinology
 history of, 1–2
- endoplasmic reticulum, 16
- endothelial cell adhesion molecule
 expression, 213–14

- endothelial glycocalyx, 21
 endothelial nitric oxide synthase (eNOS), 440–1
 end-stage renal disease, 193, 211
 androgen therapy, 378–9
 effects of androgen therapy on physical function, 194
 energy
 effects of testosterone therapy, 196–7
 ENERKI mice, 143
 enuresis
 androgen therapy, 380
 enzyme-linked immunosorbent assay (EIA/ELISA), 74
 epididymis, 24
 epilepsy, 393
 equilibrium dialysis method, 75–6
 ER. *See* estrogen receptors
 erectile dysfunction (ED)
 and cardiovascular disease, 245, 252
 and hypogonadism, 259–60
 and metabolic disease, 252
 and metabolic syndrome, 237
 and testosterone deficiency, 237
 androgen level and erectile activity, 255–7
 biological dimension, 251
 definition, 251
 effect of testosterone therapy, 245
 effects of sexual activity on testosterone levels, 260–1
 effects of sexual inertia, 261
 effects of treatment on testosterone levels, 260–1
 evaluation of erectile function, 255–7
 impact on quality of life, 251
 intrapsychic dimension, 251
 meta-analyses of testosterone therapy studies, 257
 organic dimension, 251
 PDE5 inhibitor and testosterone combined therapy, 257–9, 261–2
 prevalence, 251–2
 prevalence of testosterone deficiency, 259–60
 relational dimension, 251
 relational domain, 261
 relationship with aging, 251–2
 erectile function
 aging and hypoandrogenism, 346–7
 and cardiovascular risk, 255
 and MACE risk, 255
 and testosterone, 97
 calcium sensitivity of smooth muscle cells, 254
 cavernous peak systolic velocity (PSV), 255
 evaluation of penile blood flow, 255
 influence of sexual interest, 254–5
 nocturnal erections, 255–7
 nocturnal penile tumescence (NPT) test, 257
 penile color Doppler ultrasound (PCDU), 255
 ROC curve analysis, 255
 role of testosterone, 253–5
 sex-related erections, 257
 sleep-related erections (SREs), 255–7
 erectile tissues
 excitatory tone, 91
 inhibitory tone, 91
 erection physiology, 252
 corpora cavernosa, 252
 detumescence, 253
 intracellular calcium, 252
 nitric oxide (NO) formation, 252
 nitric oxide synthase (NOS), 254
 non-adrenergic, non-cholinergic (NANC) nerve endings, 252
 PDE5, 254
 psychogenic erection, 252
 reflexogenic erection, 252
 RhoA/ROCK pathway, 254
 role of cGMP, 252, 254, 255
 role of noradrenaline, 252
 role of phosphodiesterase (PDE5), 252
 role of vasoactive intestinal peptide (VIP), 255
 smooth muscle cells, 252
 venous leak, 254
 erythrocytosis, 355
 risk factor for testosterone therapy, 417
 erythropoiesis
 androgen therapy, 375
 effects of testosterone, 216, 222
 erythropoietin, 222, 375
 esophageal cancer, 25
 estradiol, 16, 24, 26, 87–8
 and aggression in women, 108
 aromatization of testosterone to, 127, 143–4, 350–1
 in men, 422
 production, 23
 production in elderly men, 340
 role in bone homeostasis in men, 431
 SHBG binding, 22
 steroid feedback, 127
 testicular, 132
 estradiol receptors, 89
 estradiol-to-testosterone ratio, 103
 estrogen, 22
 and aggression in women, 109
 and cardiovascular risk, 208
 estrogen in men
 aromatase activity, 427
 estrogen-induced negative feedback, 100
 estrogen receptor knock-out mice, 23
 estrogen receptor α knock-out mice, 143, 426
 estrogen receptor $\alpha\beta$ knock-out mice, 426
 estrogen receptor β knock-out mice, 426
 estrogen receptors (ERs), 25, 275
 estrogen receptor α (ER α), 132
 estrogen receptor β (ER β), 132
 evolution of, 271
 in men, 421–2, 423
 polymorphisms, 45
 estrogen replacement treatment in men, 432, 433
 estrogen resistance, 432, 433
 estrogen response elements (EREs), 132
 estrogen-to-testosterone ratio, 24
 estrogens, 23
 and atherosclerosis, 208
 effects on SHBG, 62
 influence on testosterone effects, 23–4
 mode of action in the brain, 89–90
 estrogens in men
 action on the hypothalamic-pituitary unit, 423–4
 and gender identity, 428–9
 and male infertility treatment, 432
 and sexual behavior, 429
 and sexual orientation, 428–9
 aromatase deficiency, 431, 432, 433
 clinical implications, 432
 congenital aromatase deficiency, 423–4
 congenital estrogen deficiency, 423–4
 effects of aromatase deficiency, 429
 effects of inappropriate exposure, 427–8
 effects of prenatal exposure to diethylstilbestrol, 427–8
 effects on human male reproduction, 427
 effects on male reproduction, 426–8
 estradiol, 422
 estrogen biosynthesis, 422–3
 estrogen deficiency conditions, 432
 estrogen receptors, 421–2, 423
 estrogen replacement treatment, 432, 433
 estrogen resistance, 433
 estrone, 422

Index

- estrogens in men (*cont.*)
 historical development of
 knowledge, 421–3
 influence of circulating estrogens,
 423–4
 influence on bone mineral density,
 431
 influence on glucose metabolism,
 431–2
 influence on lipid metabolism, 432
 influence on male sexuality, 428–9
 knock-out models of estrogen
 deficiency, 426–7
 male rodent reproduction models,
 426–7
 regulation of gonadotropin
 feedback, 423–4
 role in bone maturation, 430–1
 role in bone metabolism, 429–31
 role in boys before puberty, 433
 role in sperm production and
 quality, 427
 role of estradiol in bone
 homeostasis, 431
 testosterone-to-estradiol ratio, 427
 therapeutic implications, 432
 threshold level for estradiol effect,
 431
- estrone, 8, 23
 in men, 422
- ethinyl estradiol, 62, 168
- ethnic differences
 CAG repeat AR polymorphisms,
 43–4
 prostate development and
 malignancy, 43–4
 testosterone levels in elderly men,
 341
- etonogestrel, 485–6
- eunuchoidal body proportions, 299
- eunuchs, 254
- evolution of male accessory glands,
 268–9
- excitatory tone in erectile tissues, 91
- exercise testing in angina studies,
 217–18
- external quality assessment (EQA),
 81–2
- externalizing behaviors
 and CAG repeat AR
 polymorphisms, 46
- extracellular matrix factors, 163
- eyelashes
 treatment for hypotrichosis, 167
- Fallopian tubes
 development of, 35
- falls
 risk in elderly men, 349
- Farinelli, Carlo, 4
- fatal cardiovascular events
 and testosterone levels, 217
- fatigue
 effect of DHEA treatment, 442–4
- fatigue/energy
 effects of testosterone therapy,
 196–7
- fatty acid metabolite receptors, 25
- fatty streak development, 211, 212–13
- female pattern hair loss (FPHL), 166
- female sexual dysfunction (FSD)
 testosterone therapy, 500–4
- fertile-eunuch syndrome, 10
- fertility
 and aging, 336–7
 constant fertility in human males,
 272
- fetal development of the testis, 16
- fetal Leydig cells, 16, 35
- fetus
 development of external genitalia,
 36–7
 development of the genital tubercle,
 36–7
 masculinization, 36–7
 sexual differentiation, 35–7
- fibrinogen, 347, 348
- fibrinolysis, 218
- finasteride, 36, 155, 161, 168, 169, 274,
 281–2, 285–6, 311, 343, 347, 351
- fitness studios
 misuse of anabolic steroids, 520
- flow-mediated brachial artery
 vasodilatation, 215
- flow-mediated brachial reactivity, 211
- fluoroimmunoassay (FIA), 74
- flouxymesterone, 313, 520
- flutamide, 169, 212
- follicle stimulating hormone. *See* FSH
- follicle-stimulating hormone, 127, 199
- forskolin, 26
- fractures
 risk in elderly men, 349–51
- frailty
 androgen therapy, 380
- Free Androgen Index (FAI), 99
- free radicals, 212
- free testosterone, 21, 273
 effects of aging, 338–9
 measurement methods, 75–8
- frontal lobe, 91
- frustration tolerance
 and testosterone level, 93
- FSH (follicle stimulating hormone),
 21, 37–8, 39, 126
 action on Sertoli cells, 127
 and spermatogenesis, 138–40
 feedback regulation, 127
- FSH receptor, 19
- fulvestrant, 212
- functional brain imaging studies, 88
- G-coupled receptor (LGR8), 21
- Galen, 5
- gambling (pathological)
 and CAG repeat AR
 polymorphisms, 46
- gangliosides-associated testosterone
 transport, 23
- gas chromatography–mass
 spectrometry (GC-MS), 63–4
 derivatization, 63
- gender differences
 action of androgens and estrogens
 in the brain, 89–90
 aggression, 94
 and testosterone, 110–12
 AR distribution in the brain, 89–90
 cardiovascular mortality, 347
 differentiation of the brain, 88–9
 effects of DHEA/DHEAS, 438–9
 osteoporosis, 177–8
 prevalence of coronary heart
 disease, 207–9
see also activational effects of
 testosterone.
- gender differences and testosterone
 amount of individual variability,
 110
 by-product hypothesis, 113–14
 desensitization hypothesis, 112–13
 effects of androgen receptor gene
 polymorphisms, 111–12
 explanatory hypotheses, 112–14
 mechanisms of androgen
 production, 111
 relationship between mood and
 sexuality, 110–11
 sensitivity to testosterone, 110
 threshold effect, 111
- gender identity, 428–9
- genetic factors
 testosterone levels in elderly men,
 340–1
- genital skin, 24
- genital tubercle
 development in the fetus, 36–7
- genomic effects of androgens, 24–7
- genomic pathway of androgen
 receptor action, 135–6
- German Democratic Republic
 secret athlete doping program, 518,
 536
- gestagens, 476–86
- gestation
 development of the testis, 16
- GGC repeats (polyglycine), 25

- glucocorticoid receptors, 25, 40, 271
 glucocorticoids, 21, 343, 442
 glucose metabolism
 role of estrogens in men, 431–2
 glucose tolerance
 impaired, 23–4
 glucuronoconjugated DHT, 340
 Glut-4, 241
 glutamine (CAG) repeats, 25
 glycine (GGC) repeats, 25
 glycolysis, 241
 GnRH (gonadotropin-releasing hormone), 27, 37, 126, 127
 secretion in elderly men, 344–5
 GnRH agonists, 192, 193, 474–5
 GnRH analogs, 92, 130, 144, 343, 474–6
 GnRH antagonists, 92, 127, 131, 139, 311, 475–6, 496
 GnRH deficiency, 128
 GnRH immunization, 129, 140
 GnRH receptor, 19
 gonadal development
 and endocrine function, 34–5
 gonadal dysgenesis, 39
 gonadarche, 37
 gonadotropin-releasing hormone.
 See GnRH
 gonadotropins, 16, 126, 127
 levels in elderly men, 343–4
 neuroendocrine control, 344–5
 gonads
 tumor risk in AIS, 39
 Graafian follicles, 5
 Greco-Roman period, 2
 growth factors, 21
 production by dermal papillae, 163
 growth hormone, 62, 345
 excess, 61
 role in testosterone action on muscles, 199
 guidelines for testosterone deficiency
 benign prostatic hyperplasia risk, 416
 bone mineral loss, 415–16
 cardiovascular risk from treatment, 417
 clinical manifestations of hypogonadism, 414–16
 clinically relevant testosterone level, 414
 cognition, 416
 decreased muscle mass and strength, 415
 definition of a guideline, 408
 definition of hypogonadism, 413
 depression, 416
 diabetes mellitus, 416
 diagnosis of hypogonadism, 413
 diagnostic criteria for hypogonadism, 414
 different approaches to guidelines, 413
 erectile dysfunction (ED), 415
 erythrocytosis risk, 417
 evidence-based versus expert opinion criteria, 413
 hormone threshold level, 414
 impaired libido, 414–15
 lower urinary tract obstructive symptoms, 416
 metabolic syndrome, 416
 monitoring patients on testosterone treatment, 417
 mood, 416
 osteoporosis, 415–16
 potential risks from testosterone therapy, 416–17
 principal published guidelines, 408
 prostate cancer contraindication for treatment, 416
 reference to a specific age group, 413
 review committees, 417–18
 screening for androgen deficiency syndrome, 414
 selection of guideline committee members, 413
 specificity of diagnostic tests, 413
 strength of the evidence base, 417–18
 symptoms required for hypogonadism diagnosis, 414
 treatment contraindications, 416–17
 treatment options, 417
 untreated sleep apnea risk factor, 417
 well-being, 416
 gynecomastia, 24, 38, 42, 294, 298–9, 356, 486
 anabolic steroid side-effect, 540
 hair
 functions of hair, 156–7
 male sexual hair pattern, 298
 sexual hair growth in CAIS, 38
 sexual hair growth in PAIS, 38
 social and sexual functions, 154
 structure, 157–8
 hair follicle, 24
 capacity for regeneration, 158–9
 dermal papilla, 157, 158
 epithelial stem cells, 158
 epithelial–mesenchymal interactions, 158
 extracellular matrix components, 163
 hair growth cycle, 158–9
 mechanism of androgen action, 161–4
 melanocyte stem cells, 158
 paracrine factors in mesenchyme–epithelial interactions, 163–4
 structure, 157–8
 hair follicle transplant surgery, 160
 hair growth
 after puberty, 157, 159–60
 axillary hair, 159, 161
 balding inhibitors, 163–4
 balding scalp, 162
 beard, 158, 159, 161, 162, 163
 beard hair color, 163
 beard hair medulla, 163
 before birth, 159
 before puberty, 159–60
 effects of androgens, 159–61
 effects of castration before puberty, 161
 evidence for the role of androgens, 160–1
 eyelashes, 167
 in androgen insensitivity syndrome, 161
 in androgen insufficiency syndrome, 161
 in children, 154
 influence of CAG repeat AR polymorphisms, 47
 intermediate hairs, 159
 lanugo hairs, 159
 male pattern baldness, 161
 mesenchymal–epithelial interactions, 159
 molecular mechanisms, 159
 production of hairs, 157–8
 pubic hair, 159
 regulation by androgens, 154–6
 requirement for DHT in men, 161
 role of androgen receptors, 161
 role of growth hormone, 161
 role of the dermal papilla, 161–3
 seasonal variations, 158–9
 terminal hair, 159, 161
 variations within and between races, 159
 vellus hair, 159
 hair growth cycle, 158–9
 hair growth disorders
 androgen-dependent conditions, 164–7
 androgenetic alopecia, 158, 163–4
 androgenetic alopecia in men, 164–6
 androgenetic alopecia in women, 166
 androgenetic alopecia treatments, 167–8
 balding inhibitors, 163–4

Index

- hair growth disorders (*cont.*)
 hirsutism, 166
 hirsutism treatments, 168–9
 treatment of androgen-dependent conditions, 167
 hair pigmentation, 163
 Hamilton Depression Rating Scale (HDRS), 95
 Hamm, Johan, 5, 155
 Harvey, William, 5
 hCG (human chorionic gonadotropin), 19–20, 144, 343
 in marmosets and humans, 128
 hCG receptors, 20
 hCG therapy
 in hypogonadotropic hypogonadism, 129–30
 HDL cholesterol, 46, 210, 212, 216–17, 237, 240, 244, 347, 348, 432
 headache
 androgen therapy, 392
 heat shock protein 90 (HSP 90), 26
 height
 testosterone therapy to reduce final height, 302–3
 hematocrit
 effects of testosterone, 216
 hematological disorders
 androgen therapy, 375–7
 hemochromatosis, 343
 hemodialysis
 androgen therapy for boys on, 380
 hemoglobin A1c (HbA1c), 242–4
 hemoglobin concentration
 effects of testosterone treatment, 217
 hepatitis
 androgen therapy, 374
 hepatocellular carcinoma, 538, 539
 hepatocytes
 actions of sex steroids, 22
 hepatotoxicity
 androgen-induced, 374
 17 α -methyltestosterone, 312
 hepcidin, 375
 hereditary angioedema
 androgen therapy, 381
 Hershberger assay, 461
 high-altitude residence, 375
 high-density lipoprotein. *See* HDL cholesterol
 high-resolution mass spectrometry (HRMS), 528
 hijras (India), 3
 hip fracture in elderly men, 350
 hippocampus, 89
 hirsutism, 101, 166, 541
 evaluation approach, 166
 hirsutism treatments, 168–9
 efloornithine hydrochloride, 168
 endocrine-based treatments, 168–9
 non-hormonal approaches, 168
 histone acetyltransferase (HAT), 277
 histone demethylases, 25
 histones
 acetylation, 26
 methylation, 26
 phosphorylation, 26
 ubiquitination, 26
 history of testosterone and the testes, 1–11
 anabolic steroids, 9
 ancient Egypt, 2, 3
 androkinin, 8
 Arabic medicine, 6
 capon comb's test, 8
 castration, 2–4, 10
 cellular therapy, 7
 chemical synthesis of testosterone, 8–10
 Chinese eunuch system, 2–3
 Chinese medicine, 6
 clinically available forms of testosterone, 9–10
 early descriptions of hypogonadism syndromes, 10
 first descriptions of sperm, 5
 first descriptions of testicular morphology, 5
 Greco-Roman period, 2
 intramuscular testosterone undecanoate, 10
 Islamic world, 3
 isolation of androsterone, 9
 isolation of testosterone, 9
 Loewe–Voss test, 8
 medieval Scandinavia, 3
 the Netherlands, 5
 Normans, 3
 origins of endocrinology, 1–2
 pharmacokinetic studies, 9
 power through polyorchidism, 4–5
 proof of endocrine function, 5–6
 prostate cancer, 10
 ring structure of steroids, 8
 rise of steroid biochemistry, 8
 Romans, 6
 testicular organotherapy, 6–7
 testis transplantations, 7–8
 testosterone immunoassays, 9
 transdermal testosterone gel, 10
 transdermal testosterone patches, 9
 twentieth century, 8–10
 HIV/AIDS, 193
 androgen therapy for wasting, 386–7
 androgen therapy in patients without wasting, 387–8
 effects of androgen therapy on physical function, 193–4
 effects of testosterone therapy, 221
 purpose of androgen therapy, 222, 386
 HOMA-IR (Homeostatic Model Assessment of Insulin Resistance), 240
 hormone
 origin of the term, 1–2
 hormone replacement therapy (HRT), 45, 216, 496
 and cardiovascular events in women, 208
 effects of testosterone administration, 104–5
 HPG. *See* hypothalamic-pituitary-gonadal axis
 HPT. *See* hypothalamic-pituitary-testicular axis
 Huggins, Charles, 10
 human chorionic gonadotropin. *See* hCG
 Hunter, John, 5–6
 hydantoin derivatives, 461–2
 hydroxyflutamide, 459
 17 α -hydroxylase-17,20-lyase deficiency, 432
 17-hydroxypregnenolone, 17
 17-hydroxyprogesterone, 23
 17 α -hydroxyprogesterone, 17
 17-hydroxyprogesterone capronate, 476
 hydroxysteroid dehydrogenase, 24
 11 β -hydroxysteroid dehydrogenase, 21
 17 β -hydroxysteroid dehydrogenase, 439, 440
 17 β -hydroxysteroid dehydrogenase deficiency, 38
 3 β -hydroxysteroid dehydrogenase, 439, 440
 hypercholesterolemia
 and cardiovascular disease, 207
 hyperglycemia, 237
 effect of testosterone on, 242–4
 hypergonadotropic hypogonadism, 91–2, 181
 hyperlipidemia
 and sexual dysfunction, 252
 hyperprolactinemia, 166, 343, 498
 hypertension, 237, 356
 and cardiovascular disease, 207
 and sexual dysfunction, 251
 effect of testosterone therapy, 244
 hyperthyroidism, 61, 341
 hypertriglyceridemia, 237
 hypoactive sexual desire disorder (DSM-IV), 105
 hypoactive sexual desire disorder (HSDD) in women
 testosterone therapy, 500–4

Index

- hypogonadal (hpg) mice, 128, 132, 137, 143
- hypogonadal men
testosterone replacement, 90–2
- hypogonadal osteoporosis, 180
- Hypogonadal-Obesity-Adipocytokine Hypothesis, 238
- hypogonadism, 2, 6, 27
and erectile dysfunction, 259–60
and estrogen deficiency, 432
and obesity, 236
cardiovascular risk, 255
choice of testosterone therapy, 294–7
classification, 294
effects of testosterone treatment on muscle mass, 192–3
effects on sleep, 96–7
intramuscular testosterone undecanoate, 10
level for initiation of testosterone therapy, 297
non-hormonal anti-osteoporotic drugs, 183
range of applications of testosterone therapy, 292–4
skeletal effects of testosterone replacement, 181–2
symptoms of testosterone deficiency, 294
symptom-specific thresholds for treatment, 297
testosterone treatment for angina, 217–18
transdermal testosterone gel, 10
type 2 diabetes risk factor, 237–8 *see also* guidelines for testosterone deficiency.
- hypogonadism syndromes
early descriptions, 10
- hypogonadism treatment
effects of CAG repeat AR polymorphisms, 47–8
- hypogonadotropic hypogonadism, 91–2, 239, 261
after anabolic steroid abuse, 540
hCG therapy, 129–30
- hypophysectomy, 254
- hypopituitarism, 2, 255, 440, 443–4
in women, 104, 498, 504
- hypospadias, 37
- hypotestosteronemia, 209
- hypothalamic-pituitary-gonadal (HPG) axis, 16, 48, 343
- hypothalamic-pituitary-testicular (HPT) axis, 22, 126–7, 131, 273, 423
interactions with adipose tissue, 238–40
- male imprinting, 272
- hypothalamo-hypophyseal-testicular axis, 126–7
- hypothalamus, 90, 239
- hypothyroidism, 61, 62, 343
- hypoxia, 375
- hysterectomy
effects of, 496
effects on sexuality, 102–3
- hysterectomy and bilateral ovariectomy
effects of testosterone administration, 105–6, 181
- idiopathic male infertility
ineffectiveness of testosterone treatment, 303
- IGF. *See* insulin-like growth factor
- IL. *See* interleukin
- immature Leydig cells, 16
- immune disease
androgen therapy, 386–8
- immune system
effects of DHEA treatment, 449
- immunoglobulin, 220
- immunological disorders
DHEA treatment, 445–6
- importin- α , 26
- importin- β , 26
- impotence. *See* erectile dysfunction (ED)
- impulsivity
and testosterone level, 93
- incremental shuttle walk test, 223
- Indian hedgehog (*Ihh*), 252
- infectious disease susceptibility
effects of testosterone, 28
- inferior frontal gyrus, 91
- infertility (male)
ineffectiveness of testosterone treatment, 303
- inflammation, 218
and obesity, 235
effect of testosterone therapy, 244–5
effects of testosterone, 222
in chronic heart failure, 216, 222
role in prostate carcinogenesis, 282
- inflammatory cytokines, 212
- inhibin B, 39, 127, 336
- inhibitory tone in erectile tissues, 91
- inotropes, 220
- insula, 91
- insulin levels, 341
- insulin receptor substrate 1 (IRS-1), 241
- insulin resistance, 23–4, 209, 218, 222, 235–6, 237
and mitochondrial dysfunction, 241
and obesity, 239
- and ovarian androgen production, 100
- and SHBG, 240–1
- effects in elderly men, 342
- effects of testosterone therapy for women, 504
- in chronic heart failure, 221–2
- mechanisms of testosterone action, 240–1
- insulin sensitivity, 348
effect of testosterone replacement, 241–2
mechanisms of testosterone action, 240–1
- insulin-like growth factor (IGF), 226
- insulin-like growth factor 1 (IGF-1), 163, 164, 168, 281, 341, 345
role in muscle growth and differentiation, 199
- insulin-like factor 3 (INSL3), 21, 35
- interleukin 1 (IL-1), 239
- interleukin 1 β (IL-1 β), 213, 239, 244–5
- interleukin 6 (IL-6), 239, 241, 244–5
- interleukins, 222
- internal quality control
measurement of testosterone, 80
- International Index of Erectile Function (IIEF) questionnaire, 259
- International Index of Erectile Function (IIEF-5), 257
- interstitial nuclei of the anterior hypothalamus (INAH 1–4), 88
- Interviewer Ratings of Sexual Function (IRSF), 101
- intracrine activation of androstenedione, 442
- intracrinology concept, 440
- intrahepatic cholestasis, 538
- intramuscular administration of testosterone, 315–23
- intratesticular leiomyosarcoma, 540
- intratesticular testosterone, 128, 130–2
differences between animals and humans, 130
suppression, 134
- irritability
and aggression, 93
and testosterone level, 93, 96
premenstrual syndrome (PMS), 106
- isolated hypogonadotropic hypogonadism, 292, 294
- isotope ratio mass spectrometry (IRMS), 528–9
- Japanese men
cardiovascular risk, 255
- Kallmann syndrome, 10, 292
- Karolinska Scales of Personality, 46

Index

- Kennedy syndrome (XSBMA), 25, 34, 42–3, 44, 45, 46, 238
- ketoconazole, 285
- 11-ketotestosterone, 28
- kisspeptin, 239–40
- Klinefelter syndrome, 2, 8, 10, 181, 221, 238, 240, 255, 292, 297, 300
- lactation, 98
- sexual interest during, 100
- testosterone level variations, 100
- Laqueur, Ernst, 8, 9
- latanoprost, 167–8
- late-onset hypogonadism, 292, 345, 413
- LDL cholesterol, 16, 218, 244, 245, 347, 432
- role in atherogenesis, 216–17
- role in atherosclerosis
- pathophysiology, 212
- LDL receptor knock-out mice, 211
- Leeuwenhoek, Antoni A., 2, 5
- leptin, 239, 240, 242, 244, 341, 345
- leuporelin, 92, 93, 96, 343
- levonorgestrel, 484
- Leydig cell function
- effects of aging, 337, 343
- effects of drugs, 343
- effects of endocrine diseases, 343
- neuroendocrine control, 344
- Leydig cells, 5, 15, 35, 37, 123, 132, 133, 239, 292
- cholesterol homeostasis, 16
- development from perivascular and peritubular mesenchymal-like cells, 16
- fetal development of the testis, 16
- in the testicular interstitium, 15
- influence of LH, 16
- interactions with Sertoli cells, 21
- ontogeny, 16
- proliferation in the adult testis, 16
- regulation by factors other than LH, 21
- steroidogenesis, 130
- stimulation of androgen secretion, 129–30
- testosterone production, 15–16
- types of, 16
- use of cholesterol, 16
- Leydig, Franz, 5
- LH (luteinizing hormone), 16, 37, 39, 126, 260, 261
- influence on Leydig cell development, 16
- levels in AIS, 39
- regulation of testosterone
- biosynthesis, 19–20
- rise at menopause, 100
- LH receptor, 19–20
- activating mutations, 128
- comparison between human and marmoset, 128
- inactivating mutations, 128
- LH receptor knock-out mice, 19, 128, 131
- LHRH (luteinizing hormone-releasing hormone) super-agonists, 284, 285
- life expectancy
- effects of testosterone, 4
- lifestyle
- effects on testosterone levels, 342
- lipid droplet storage of cholesterol, 16, 18
- lipid metabolism
- role of estrogens in men, 432
- lipoprotein (a), 245
- lipoprotein lipase, 240
- lipoproteins
- effect of testosterone therapy, 245
- liquid chromatography–tandem mass spectrometry (LC-MS/MS), 63, 64–5
- derivatization, 64
- liver, 24
- first-pass metabolism of testosterone, 310, 314
- hepatotoxic effects of 17 α -methyltestosterone, 312
- metabolism of testosterone, 310–11
- liver cirrhosis, 310, 342
- liver disease, 343
- androgen therapy, 374–5
- liver disorders
- androgen induced, 374
- liver function
- during testosterone therapy, 301
- liver tumors, 312
- locus coeruleus, 91
- Loewe, S., 8
- Loewe–Voss test, 8
- loop diuretics, 219
- low-density lipoprotein. *See* LDL cholesterol
- lower urinary tract obstructive symptoms (LUTS), 416
- luteinizing hormone. *See* LH
- Lydston, G. Frank, 7
- lymph circulation, 313
- lymphatic circulation of the testes, 22
- lysine-specific demethylase 1 (LSD1), 26
- MAIS (minimal androgen insensitivity syndrome), 39
- major adverse cardiovascular events (MACE) risk, 255
- major cardiovascular events
- and testosterone levels, 217
- mal descended testes, 292
- male accessory glands, 268–9
- male adulthood
- androgen functions, 37–8
- male climacteric, 10
- male contraception, 27
- condom, 471
- desirable features, 471
- existing methods, 471
- new approaches, 471
- reasons for, 470–1
- vasectomy, 471
- male hormonal contraception, 47, 92, 130, 131, 132, 134, 138, 139, 144, 318
- acceptability, 487
- adverse events, 486
- depression side-effect, 486
- effects on liver function, 486
- efficacy studies, 472–3
- future outlook, 487
- goal of azoospermia, 471–2
- goal of oligozoospermia, 471–2
- gynecomastia side-effect, 486
- MENT (7 α -methyl-19-nortestosterone), 474
- new approaches, 471
- 19-nortestosterone, 474
- 19-nortestosterone plus DMPA, 476–84
- principle, 471–2
- side-effects, 486–7
- testosterone alone, 472–4
- testosterone buciclate, 473
- testosterone enanthate, 472–3
- testosterone pellets, 474
- testosterone plus cyproterone acetate, 484–5
- testosterone plus desogestrel, 485–6
- testosterone plus dienogest, 485
- testosterone plus DMPA, 476–84
- testosterone plus etonogestrel, 485–6
- testosterone plus GnRH agonists, 474–5
- testosterone plus GnRH analogs, 474–6
- testosterone plus GnRH antagonists, 475–6
- testosterone plus levonorgestrel, 484
- testosterone plus 19-norethisterone, 486
- testosterone plus progestins, 476–86
- testosterone undecanoate (castor oil), 473–4
- testosterone undecanoate (oral), 473

- testosterone undecanoate (tea seed oil), 473
- weight gain side-effect, 486
- male imprinting of the HPT axis, 272
- male infertility treatment, 432
- male pattern baldness
- influence of CAG repeat AR polymorphisms, 47
 - see also* androgenetic alopecia.
- male puberty and adulthood
- androgen functions, 37–8
- male sexual development, 34–5
- malignant disease
- androgen therapy, 388–9
- mammalian evolution
- dangers of reproduction, 271–2
 - seasonal breeding, 271–2
 - selection of testosterone as master reproductive regulator, 270–2
- mammary gland development, 38
- mammillary nuclei, 89, 90
- manic behavior
- associated with testosterone level, 96
- MAP-kinase pathway, 27
- Marrian, Guy, 8
- marsupials, 25
- masculinization of the fetus, 36–7
- mass spectrometry
- measurement of testosterone, 63–73
- McCormick, Katherine, 487
- M-CSF (macrophage-colony stimulating factor), 184, 185
- MDV-3100, 285
- measurement of DHT, 78–9
- free and protein-bound forms, 60–2
- measurement of testosterone, 62–78
- assessment of free testosterone, 75–8
 - automatic multianalyzers, 74
 - bioassay, 78
 - bioavailable testosterone, 77–8
 - calculated free testosterone, 78
 - challenges, 60
 - chemiluminescent assay (CLIA), 74
 - choice of kit, 79–80
 - clinical applications, 62
 - comparison of different methods, 65–73
 - direct free testosterone assays, 76–7
 - EIA/ELISA, 74
 - equilibrium dialysis, 75–6
 - external quality assessment (EQA), 81–2
 - fluoroimmunoassay (FIA), 74
 - free and protein-bound forms, 60–2
 - gas chromatography–mass spectrometry (GC-MS), 63–4
 - internal quality control, 80
 - liquid chromatography–tandem mass spectrometry (LC-MS/MS), 63, 64–5
 - mass spectrometry methods, 63–73
 - non-radioactive assays, 74–5
 - quality control, 74–5, 79–82
 - radioimmunoassay, 73–4
 - reference ranges, 62
 - salivary testosterone, 77
 - ultrafiltration, 76
 - validation of methodology, 79–80
 - validation of methods, 74–5
- medial pre-optic area, 89
- medications
- effects on testosterone levels, 343
- Medvei, Victor C., 1
- megalin, 21
- megestrol acetate, 476
- menopause, 98, 100
- effects on mood, 107
 - surgical, 105–6
- menstrual cycle, 98
- influence on mood, 106
 - testosterone level variations, 99
- MENT (7 α -methyl-19-nortestosterone), 91, 474
- MENT implants, 484
- mental retardation, 255
- mesonephric ducts, 35
- mestanolone, 518
- mesterolone, 303, 313, 520
- metabolic clearance rate for testosterone, 337, 339
- metabolic disease
- and erectile dysfunction, 252
- metabolic effects of DHEA treatment, 447–8
- metabolic risk factors in men, 24
- metabolic syndrome, 45, 254, 347
- and androgen deprivation therapy, 238
 - and androgen receptor polymorphism, 240
 - and cardiovascular disease, 235
 - and erectile dysfunction, 237
 - and low testosterone, 235–6
 - and testosterone deficiency, 416
 - cardiovascular risk factors, 236–7
 - clinical implications of low testosterone, 245
 - definitions, 236–7
 - effect of testosterone on body composition, 242
 - effect of testosterone on central adiposity, 242
 - effect of testosterone on cholesterol and lipoproteins, 245
 - effect of testosterone on dyslipidemia, 244
 - effect of testosterone on ED, 245
 - effect of testosterone on hypertension, 244
 - effect of testosterone on inflammation, 244–5
 - effect of testosterone on insulin resistance, 240–1
 - effect of testosterone replacement, 242
 - effects in elderly men, 342
 - insulin resistance, 237, 242
 - low testosterone as risk factor, 237
 - potential benefits of testosterone replacement, 245
 - prevalence of hypogonadism, 235
 - risk of developing diabetes, 236–7
- metandienone, 518, 520, 524
- metenolone acetate, 520
- metenolone enanthate, 520
- metformin, 169
- methandriol dipropionate, 520, 538
- 7 α -methyl-19-nortestosterone.
- See* MENT
- methylation of histones, 26
- methyltestosterone, 96, 105, 520, 538
- 17 α -methyltestosterone, 6, 9, 312, 314
- hepatotoxic side-effects, 312
- micropenis
- testosterone therapy, 303
- microphallus
- testosterone therapy, 303
- mifepristone, 75
- mineralocorticoid receptors, 25, 40, 271
- mineralocorticoids, 442
- minimal androgen insensitivity syndrome. 33 *See* MAIS
- minoxidil, 155, 167
- miRNAs, 136
- mitochondria
- conversion of cholesterol to pregnenolone, 19
 - transport of cholesterol to, 18–19
- mitochondrial dysfunction
- and insulin resistance, 241
- mitogens
- insulin-like growth factor (IGF-1), 163
- Modified Mania Rating Scale (MMRS), 95
- 17 α -mono-oxygenase inhibitors, 285
- monotremes, 25
- mood
- and testosterone level, 95
 - effects of bilateral ovariectomy in women, 107–8
 - effects of DHEA administration in women, 108

Index

- mood (*cont.*)
 effects of DHEA treatment, 442–4
 effects of lowering of testosterone in women, 107
 effects of oral contraceptives in women, 107
 effects of testosterone in men, 93
 effects of testosterone in women, 106–8
 effects of testosterone therapy, 196–7
 effects of testosterone therapy for women, 504
 influence of the menstrual cycle in women, 106
 menopausal symptoms, 107
 premenstrual syndrome (PMS), 106
 relationship to sexuality in women, 107
- mood disorders
 and CAG repeat AR polymorphisms, 46
 effect of DHEA treatment, 445
- Moreschi, Alessandro, 4
- Morris, J.M., 10
- mortality predictive marker
 low testosterone level, 224–6
- mouse model of human AR CAG repeats, 43
- MPA (medroxyprogesterone acetate), 476
- MRI brain scanning, 89
- Mullerian ducts, 35
- Mullerian inhibiting substance (MIS), 35
- Multi-Dimensional Anger Inventory (MAI), 95
- multiple sclerosis, 393
- muscle
 anabolic effects of androgens, 191–2
- muscle function
 in elderly men, 348–9
- muscle mass
 effects of lowering testosterone levels, 192
 in elderly men, 348–9
 influence of CAG repeat AR polymorphisms, 45
 influence of testosterone, 192
- muscle mass and strength
 avoiding negative effects of testosterone, 197–200
 dose-response relationship for testosterone, 193
 effects of androgen therapy in chronic illnesses, 193–4
 effects of testosterone replacement, 192–3
 mechanism of testosterone actions, 197–9
- role of growth hormone, 199
- role of IGF-1, 199
- strategies for selectivity in androgen therapy, 197–200
- testosterone as a function-promoting therapy, 200
- testosterone therapy in healthy older men, 194–6
- testosterone treatment in hypogonadism, 192–3
- muscle performance
 effects of testosterone on reaction time, 197
 influence of testosterone, 192
- muscle wasting
 androgen therapy, 384–5
- muscular disorders
 androgen therapy, 380–1
- muscular dystrophies
 androgen therapy, 380–1
- musculo-skeletal system
 side-effects of anabolic steroids, 538–9
- myeloproliferative disorders
 androgen therapy, 376–7
- myocardial infarction, 213, 215, 217, 238, 245, 355
 and sexual dysfunction, 251
 effects on testosterone levels, 342
 link to androgenetic alopecia in men, 165
- myocyte-specific androgen receptor
 knock-out mice, 199
- myogenic lineage, 254
- myotonic dystrophy
 effects of androgen therapy, 380–1
- nafarelin, 475
- NalGlu (GnRH antagonist), 92
- nandrolone, 351, 461
- nandrolone decanoate, 194, 223
- nasal administration of testosterone, 315
- Nebido®, 10, 218
- negative mood
 and testosterone level, 96
- neocortex, 89
- neonatal androgen secretion, 127–8
- neonatal Leydig cells, 16
- the Netherlands
 early anatomical discoveries, 5
- neuroleptic drugs, 343
- neurological disease
 androgen therapy, 391–3
- neurosteroids, 88
- nexin-1, 163–4
- nifedipine, 218
- nitric oxide synthase (NOS), 252, 254, 346
- nocturnal penile tumescence (NPT), 346
 effects of testosterone, 91
- nocturnal penile tumescence (NPT) test, 257
- non-genomic effects of androgens, 27–8
- non-genomic pathways of androgen receptor action, 136
- non-SHBG-bound testosterone, 77–8
- norboletone, 522
- norethandrolone, 524
- norethindrone, 476
- 19-norethisterone, 476, 486
- norethisterone enanthate, 23
- normal (eugonadal) men
 effects of increasing testosterone, 92–3
 experimental reduction of testosterone, 92–3
- Normans, 3
- Norplant, 101
- nortestosterone, 520, 524
- 19-nortestosterone, 474, 484
- nortestosterone decanoate, 520
- nortestosterone esters, 520
- novelty-seeking behavior
 and CAG repeat AR polymorphisms, 46
- nuclear androgen receptor, 212, 215
- nuclear receptor superfamily
 evolution of, 271
- nuclear receptors, 24–7
- Nussbaum, Moritz, 8
- nutritional supplements
 contamination with prohormones, 523
- obesity, 218
 and cardiovascular disease, 235
 and hypogonadotropic hypogonadism, 342
 and low testosterone, 235–6, 237
 androgen therapy, 394–5
 central obesity and insulin resistance, 240
 effect of testosterone replacement, 242
 effect of weight loss on testosterone levels, 236
 hormones produced by adipose tissue, 238–9
 insulin resistance, 242
 risk factor for metabolic syndrome, 235
 risk factor for type 2 diabetes, 235
- obesity measures
 and testosterone levels, 192
- obstructive sleep apnea
 androgen therapy, 390–1

- Okasa®, 6
- older men
effects of testosterone on sleep, 97
- oligozoospermia, 25
- Olweus Multifaceted Aggression Inventory, 108
- opera
castrato singers, 4
- opiates
effects on testosterone levels, 343
- oppositional defiant disorder (ODD) and CAG repeat AR polymorphisms, 46
- oral administration of testosterone, 310–13
- oral contraceptive use (women), 99, 103, 208, 216, 496
effects on mood, 100–1, 107
effects on sexuality, 100–1
effects on testosterone levels, 100–1
for hirsutism, 168–9
- Oral-Turinabol, 518, 520, 536, 540, 541
- orbitofrontal cortex, 91
- orchidectomy, 240
and prostate cancer, 10
health effects, 209
see also castration.
- orchitis, 292
- organizational effects of hormones
brain development, 88–9
- organotherapy, 6–7
- orphan nuclear receptors, 25
- osteoblasts, 184, 241
- osteocalcin, 182
- osteoclasts, 184
- osteocytes, 184
- osteopenia, 27
diagnosis from bone density, 180–1
- osteoporosis, 23, 27, 294, 301
and testosterone in women, 499–500
functions of osteoblasts and osteoclasts, 184
gender differences, 177–8
in hypogonadism, 415–16
postmenopausal, 183
preclinical rodent models, 183–4
role of testosterone, 177–8
steroid induced, 384
- osteoporosis (men)
and areal bone density, 180–1
and testosterone deficiency, 178–81
diagnosis from bone density, 180–1
hypogonadal osteoporosis, 180
idiopathic male osteoporosis, 179–80
risk factors for senile osteoporosis, 178–9
- secondary osteoporosis, 180
- osteoporosis (women)
postmenopausal, 179
- osteoporosis therapy
anastrozole, 183
aromatase inhibitor, 183
DHT gel, 183
non-aromatizable androgen, 183
non-hormonal drugs for
hypogonadal men, 183
raloxifene, 182
SARMs, 182
SERMs, 182
testosterone replacement in elderly men, 182
testosterone replacement in hypogonadal men, 181–2
- osteoprotegerin (OPG), 184
- ovarian androgens, 100
- ovariectomy (bilateral)
effects of hormone replacement, 102–3
effects of testosterone administration, 105–6
effects on mood, 107–8
effects on sexuality, 102–3
effects on well-being, 102–3
- ovary, 24
function of the interstitial cells, 100
- oxandrolone, 461, 520, 538
- oxymetholone, 520
- P450 aromatase, 439, 440
- P450c17 enzyme, 439
- paramesonephric ducts, 35
- parathyroid hormone (PTH), 183
- paraventricular nuclei, 90
- Parkinson's disease, 393
- Parsifal*, 3
- partial androgen insensitivity syndrome (PAIS), 10, 24, 33, 38–9
see also androgen insensitivity syndrome (AIS).
- Partner Aggression Questionnaire (AQ-P), 96
- peliosis hepatis, 312, 374, 538
- penile color Doppler ultrasound (PCDU), 255
- penile growth and development
role of testosterone, 252–3
- penis
fetal development, 36
testosterone therapy for micropenis, 303
- pentoxifylline, 220
- peripheral arterial disease
and low testosterone, 210–11
- peripheral vascular disease
and sexual dysfunction, 252
peripheral vascular venous disease, 393–4
- peritubular cells, 21, 23, 126
- peritubular myoid cells, 35, 123, 124, 132, 133, 135
- personality traits
influence of CAG repeat length, 46
- Pézard, A., 8
- PGE1, 255
- pharmacogenetics
CAG repeat AR polymorphisms, 47–8
- pharmacokinetic studies of testosterone preparations, 9
- pharmacokinetics of testosterone esters, 315–16
- Philipp Magnanimous, Count of Hesse, 5
- phorbol esters, 26
- phosphodiesterase inhibitors, 6
- phosphodiesterase type 5 (PDE5), 254
- phosphodiesterase type 5 inhibitor (PDE5i), 346, 415
and testosterone combined therapy, 257–9
- phosphorylation
androgen receptors, 26
histones, 26
- physical function
androgen therapy for chronically ill patients, 193–4
effects of testosterone therapy in older men, 194–6
in older men, 192
influence of testosterone, 192
potential use of testosterone therapy, 200
- pineal-hypophysis-pituitary system, 158
- pioglitazone, 169
- pituitary, 123, 126
expression of hGC in marmosets, 128
gonadotropin inhibition, 144
hypothalamo-hypophyseal-testicular axis, 126–7
- pituitary insufficiency, 292, 343
- pituitary tumors, 343
- pituitary-gonadal function, 341
- placenta, 24
- plaque rupture, 213
- plasminogen activator inhibitor 1 (PAI-1), 215, 239
- plasminogen activator type 1, 347
- Point Subtraction Aggression Paradigm (PSAP), 95
- polycystic ovary syndrome (PCOS), 166, 169, 541

Index

- polycythemia, 300, 355
 androgen induced, 375
 polyglutamine polymorphisms, 25
 polyorchidism
 power associated with, 4–5
 polyproline (TGG repeats), 25
 positive mood
 and testosterone level, 96
 prairie dog (*Cynomys ludovicianus*), 139
 prefrontal cortex, 90
 pregnancy, 61, 62
 pregnandiol, 8
 pregnane, 16
 pregnenolone, 16, 23
 conversion of cholesterol to, 19
 Premarin, 105
 premenstrual syndrome (PMS), 106
 prepubertal castration, 4
 primary spermatocytes, 124
 primates
 SHBG, 61
 testis development, 16
 Profile of Female Sexual Function (PFSF), 99
 Profile of Mood States (POMS), 96
 progenitor Leydig cells, 16
 progestagen receptors, 271
 progesterone, 17, 23, 26, 89
 progesterone receptors, 23, 25, 28, 40
 progestins, 28, 168, 476–86
 progestogens, 92
 programmed cell death
 during brain development, 88
 prohormones
 androstenedione, 441–2
 contamination in nutritional supplements, 523
 of anabolic androgens, 521–2
 of dihydrotestosterone, 521
 of nortestosterone, 521
 of testosterone, 521
 testosterone as, 277
 testosterone for estrogen, 421
 use in doping in sports, 519
 prolactin, 97
 prolactinoma, 2, 343
 proline (TGG) repeats, 25
 prostaglandin D synthase, 35
 prostate, 23, 24, 271
 age-related effects, 286–7
 AR integration of androgen signaling, 275–7
 autoregulation of androgen metabolism, 277
 development of the urogenital sinus, 277–8
 DHT binding to AR, 277
 dual agonist/antagonist effects of androgen, 273
 evolution of male accessory glands, 268–9
 gene transcription and growth, 24
 interactive stem cell units, 277–9
 intermediate cells, 279
 maintenance of steady-state size, 279
 mechanism of androgen action, 277–9
 mesenchymal stem cells, 281
 monitoring testosterone therapy effects, 301
 neuroendocrine cells, 279
 organization of epithelial and stromal cell units, 279–81
 regenerative capacity, 279
 role of testosterone in development and growth, 272–3
 role of testosterone in maintenance, 273
 secretory products in humans, 270
 secretory-luminal cells, 279–81
 self-renewal of stem cells, 279
 side-effects of testosterone therapy, 286–7
 steady-state self-renewing tissue in adults, 273
 stromal–epithelial cell interactions, 277–9
 testosterone as a prohormone, 277
 testosterone binding to AR, 277
 testosterone metabolism in, 273–5
 transit-amplifying (TA) cells, 279
 transition zone, 281
 variations between animal species, 269–70 *see also* benign prostatic hyperplasia (BPH).
 prostate cancer, 25, 43, 165, 269, 270, 271, 272
 and androgen therapy in elderly men, 356–7
 and orchidectomy, 10
 and testosterone treatment, 10
 androgen ablation therapy for metastatic cancer, 284–5
 androgen deprivation therapy, 209, 236, 238, 240
 AR conversion to oncogene, 284
 autonomous autocrine AR signaling pathway, 283–4
 bipolar androgen therapy, 286
 cardiovascular risk from treatment, 209
 castration-resistant prostate cancer, 284–5, 286
 cell of origin, 282–4
 contraindication for testosterone therapy, 303, 416
 effects of hormonal treatment, 343
 ethnic differences, 43–4
 high-grade prostatic intraepithelial neoplasia (HGPIN), 282–4
 intratumoral steroid synthesis, 285
 preventative role for SRD5A inhibitors, 285–6
 proliferative inflammatory atrophy, 283
 role of androgens in carcinogenesis, 282–4
 role of chronic and acute inflammation, 282
 treatment side-effects in aging men, 286–7
 use of supraphysiological levels of testosterone, 286
 prostate cancer cells, 28
 prostate cancer risk, 165
 and androgenetic alopecia in men, 165
 and CAG repeat AR polymorphisms, 43–4
 prostate development
 and CAG repeat AR polymorphisms, 43–4
 role of androgens in the fetus, 35–6
 prostate ontogeny, 277–8
 paracrine interactions, 277–8
 prostate-specific antigen (PSA), 26, 27, 270
 proteohormone, 21
 Provera, 105
 psychological effects
 CAG repeat AR polymorphisms, 46–7
 psychosexual function
 and testosterone level, 95
 PTM-ARKO mice, 135
 puberty, 21
 androgen functions, 37–8
 effects of androgen receptor defects, 27
 hair growth after, 159–60
 hair growth before, 159–60
 testosterone therapy for delayed puberty, 302
 timing of, 88–9
 pubic hair growth
 effect of DHEA treatment, 443, 444
 pulsatile testosterone production, 20
 quality control
 immunoassay methods, 74–5
 measurement of testosterone, 79–82
 quality of life
 effects of testosterone therapy, 196–7
 quinolinones, 461

- radioimmunoassay for plasma testosterone, 73–4
- raloxifene, 182
- RANKL (receptor activator of nuclear factor- κ B ligand), 184, 185
- rat Leydig cells
- apoptosis, 21
- Rathus Assertiveness Schedule, 96
- reaction time
- effects of testosterone, 197
- reactive oxygen species (ROS), 185
- rectal administration of testosterone, 315
- 5 α -reductase, 440, 461
- expression in the skin, 62
 - synthesis of DHT, 24
 - 274 *see also* SRD5A isoenzymes
- 5 α -reductase activity
- effects of aging, 340
 - in the brain, 89
- 5 α -reductase deficiency, 38
- 5 α -reductase genes, 165
- 5 α -reductase inhibitors, 168, 311, 343, 347, 351
- 5 α -reductase isoenzymes, 131
- 5 α -reductase type 1, 24
- 5 α -reductase type 2, 24, 36, 340
- 5 α -reductase type 2 deficiency, 36, 161
- 5 α -reductase type 2 inhibitors, 168
- rehabilitation after surgery
- androgen therapy, 384–6
- Reifenstein, E.C., 10
- relaxin, 21
- religious reasons for castration, 3
- REM sleep
- nocturnal erections, 255–7
- renal disease
- androgen therapy, 377–80
- renal failure, 343
- renal function
- effects of androgen therapy, 378
- renal insufficiency, 356
- renal transplantation, 377
- renin-angiotensin-aldosterone axis, 220
- reproductive function
- effects of CAG repeat androgen receptor polymorphisms, 44–5
- respiratory disease
- androgen therapy, 389–91
- retinal atherosclerosis, 210
- retinol receptors, 25
- Reynaud's phenomenon
- androgen therapy, 260, 383
- rhesus monkeys, 89
- rheumatic diseases, 343
- rheumatoid arthritis, 439
- androgen therapy, 381–2
- rheumatological disorders
- androgen therapy, 381–3
- RhoA/ROCK pathway, 254
- risedronate, 183
- RNA synthesis, 25
- rodents
- testis development, 16
- RoDH, 24
- rosiglitazone, 169
- Ryneerson, E.H., 7
- Sabbatsberg Sexual Self-Rating Scale, 104
- salivary testosterone measurement, 77
- Sanger, Margaret, 487
- SARMs (selective androgen receptor modulators), 27, 177, 182, 373
- characteristics, 459
 - conformational hypothesis of action, 463–5
 - discovery programs, 459–60
 - early phase I and II trials, 466
 - history of development, 459–60
 - impetus for development, 459
 - mechanisms of tissue-selective actions, 463–5
 - misuse in sports, 529
 - non-steroidal SARMs, 460, 461–3
 - potential therapeutic use, 459
 - preclinical studies with first-generation non-steroidal SARMs, 465–6
 - prohibition in sports, 529
 - regulatory challenges to development, 466
 - role of co-regulator proteins, 463–5
 - sports drug testing, 529–30
 - steroidal SARMs, 460–1
 - structural classes, 460
- schizophrenia, 393, 445, 447
- Scoptic sect, 3
- scrotal testosterone patches, 9, 296
- scrotum
- fetal development, 36
- seasonal breeding in mammals, 271–2
- selective androgen receptor modifiers (SARMs), 287
- self-emulsifying drug delivery system (SEDDS)
- for testosterone undecanoate, 314
- semen
- Artistotle's theory of, 2
- seminal emission
- effects of testosterone withdrawal, 91
- seminal vesicle, 24
- seminiferous tubules, 124, 126
- senescence. *See* aging
- sensitive window
- for masculinization of the fetus, 36–7
- septic shock, 440
- SERMs (selective estrogen receptor modulators), 182
- Sertoli cell AR knock-out (SCARKO) mice, 133, 134, 136
- Sertoli-cell-only syndrome, 10, 292
- Sertoli cells, 5, 16, 21, 35, 127
- action of testosterone on, 126
 - effects of aging, 336–7
 - interactions with Leydig cells, 21
 - role in spermatogenesis, 124, 126, 132–5
 - role in testis development, 35
 - stimulation by FSH, 44
 - tight junctions, 135
- Sertoli, Enrico, 5
- serum amyloid A, 239
- sex hormone-binding globulin. *See* SHBG
- sex hormones
- complexity of functions, 87–8
- sexual activity
- effect on testosterone level, 259–60
- sexual arousal
- and testosterone, 97
 - and testosterone level, 94, 96
- sexual desire and response (men)
- and testosterone level, 90
 - components of sexual arousal, 90
 - effects of testosterone, 90–3
 - experimental reduction of testosterone, 92–3
 - increasing testosterone in eugonadal men, 92–3
 - testosterone replacement in hypogonadism, 90–2
 - testosterone threshold theory, 90
 - visual erotic stimuli, 91
- sexual desire and response (women)
- activational effects of testosterone, 98–106
 - central arousal, 98
 - during lactation, 100
 - effects of antiandrogens, 101
 - effects of bilateral ovariectomy, 102–3
 - effects of hysterectomy, 102–3
 - effects of oral contraceptive use, 100–1
 - genital response, 98
 - incentive motivation, 98
 - influence of the menstrual cycle, 99
 - masturbation, 99
 - oral contraceptive use, 99
 - orgasm, 98
 - ovarian androgens, 100
 - patterns of sexuality in women, 106

Index

- sexual desire and response (women) (*cont.*)
 problems of low sexual desire, 99
 role of estradiol, 98–106
 role of testosterone, 98–106
 sexuality of older women, 100
 testosterone deficiency in women, 98
 vaginal pulse amplitude (VPA), 98
 sexual differentiation of embryo and fetus, 35–7
 Sexual Experience Scale, 92
 sexual interest
 influence on erectile function, 254–5
 sexual offenders
 contraindication for testosterone therapy, 303
 sexual orientation, 428–9
 sexuality
 influence of estrogens in men, 428–9
 monitoring testosterone therapy, 298
 sexuality in women
 relationship to mood, 107
 sexually dimorphic development, 35–7
 SHBG (sex hormone-binding globulin), 15, 21, 24, 130, 423
 and bone loss in men, 178
 and insulin resistance, 240–1
 binding properties, 60
 effects of aging, 338–9, 345
 effects of HRT in women, 104
 in women, 100
 levels in blood, 60–2
 levels in elderly men, 341–2
 levels in women, 495–6
 SHBG test, 40
 short tandem repeats (STRs), 25
 Silber, Sherman J., 7
 sildenafil, 257, 258–9
 Sjögren's syndrome
 androgen therapy, 383
 skin
 genital, 24
 non-genital, 24
 skin healing
 androgen therapy, 385–6
 slaves
 castration, 2–3
 sleep
 effects of testosterone in men, 96–7
 sleep apnea, 300–1, 342, 356, 375
 and testosterone level, 96
 androgen therapy, 390–1
 contraindication for testosterone therapy, 417
 sleep-related erections (SREs), 255–7
 small intestine muscle
 effects of androgens, 28
 smoking
 and cardiovascular disease, 207
 and testosterone levels in elderly men, 342
 somatic mosaicism
 androgen receptor gene mutations, 41
 somatotrophic axis, 345
 sonic hedgehog (Shh), 37, 252
 Sox9 expression, 34–5
 Spallanzani, Lazzaro, 2, 5
 specificity-affecting androgen receptor knock-in mice, 135
 sperm
 first descriptions of, 5
 sperm concentrations
 influence of CAG repeat AR polymorphisms, 45
 normal range, 45
 sperm cryopreservation
 Spallanzani, Lazzaro, 5
 sperm maturation, 21
 spermatid vein, 23
 spermatids, 124
 development, 134
 release from Sertoli cells, 134
 spermatogenesis, 123–4
 adult spermatogenesis, 129–30
 and FSH, 138–40
 and testosterone, 127–30
 and testosterone levels, 28
 aromatization of testosterone to estradiol, 143–4
 basic and common features, 124–6
 cooperative effects of androgen and FSH, 140–3
 effects of aging, 336–7
 effects of progestogens, 92
 effects of testicular androgen concentration, 137–8
 evaluation of the process, 126
 genomic pathway of androgen receptor action, 135–6
 germ cell development, 124–5
 hypothalamo-hypophyseal-testicular axis, 126–7
 in primates, 126
 in rodents, 126
 influence of CAG repeat AR polymorphisms, 44–5
 intratesticular testosterone, 128, 130–2
 mechanisms of androgen action in the testis, 135–6
 meiotic arrest, 137
 meiotic divisions, 124
 mitotic divisions, 124
 neonatal androgen secretion, 127–8
 non-genomic pathways of androgen receptor action, 136
 primary spermatocytes, 124
 pubertal initiation in rodents, 131
 role of androgens, 130–8
 role of androgens in initiation, 128
 role of androgens in maintenance, 128
 role of the Sertoli cells, 124, 126, 132–5
 sites of androgen action, 132–5
 species-specific features, 126
 spermatid development, 134
 spermatids, 124, 134
 spermatogonia, 124, 140
 spermatogonial development, 134–5
 spermiation, 124
 spermiation failure, 134, 138
 spermiogenesis, 124, 137–8
 suppression by anabolic steroids, 540
 suppression by testosterone therapy, 304
 testicular androgen production and metabolism, 130–2
 testicular androgen receptor, 132–5
 treatment implications for male hormonal contraception, 144
 treatment of secondary hypogonadism, 144
 spermatogonia, 124, 140
 spermatozoa
 progesterone receptors, 23
 spermiation, 124
 spermiation failure, 138
 spermiogenesis, 124, 137–8
 spinobulbar muscular atrophy (XSBMA). *See* Kennedy syndrome
 spironolactone, 168, 169, 343, 537
 sports doping. *See* anabolic androgenic steroids; SARMs
 SRD5A inhibitors, 281–2
 role in prostate cancer prevention, 285–6
 SRD5A isoenzymes, 273–4
see also 5 α -reductase.
 SRD5A1 gene, 165
 SRD5A2 gene, 165
 SRY (sex-determining region of the Y chromosome), 34
 Stanley, Leo, 7
 stanozolol, 40, 518, 520, 524, 538
 StAR expression, 21
 StAR gene, 19
 State Self-Esteem Scale, 96
 statin drugs, 216
 statin therapy, 241
 Steinach, Eugen, 7, 8

Cambridge University Press

978-1-107-01290-5 - Testosterone: Action, Deficiency, Substitution: Fourth Edition

Edited by Eberhard Nieschlag and Hermann M. Behre

Index

[More information](#)

Index

- stem cell factor (SCF), 163, 164
- stem cells, 254
 - properties of, 279
- stem Leydig cells, 16
- stereology, 126
- steroid biochemistry, 8
- steroid-induced osteoporosis, 384
- steroid receptors
 - evolution of, 271
- steroid sulfatase (STS), 439, 440
- steroidogenesis, 15
 - adrenal glands, 16
 - Leydig cells, 15–16
- steroidogenic acute regulatory (StAR) protein, 18–19
- steroids
 - androgens, 15
 - discovery of ring structure, 8
- stroke, 217, 342
- structural brain imaging studies, 88
- stump-tailed macaque
 - androgenetic alopecia, 163, 164
- subdermal testosterone pellet
 - implants, 323–4
- sublingual administration of
 - testosterone, 314–15
- sudden cardiac death
 - and anabolic steroids, 208
- sudden death caused by thrombosis, 213
- supraoptic nuclei, 90
- surgery rehabilitation
 - androgen therapy, 384–6
- surgical trauma
 - effects on testosterone levels, 342
- Sustanon, 97
- Sveinsson, Jonas, 7
- Swammerdam, Jan, 5
- Swedish guidelines on testosterone deficiency, 413
- Symptom Checklist-90-R, 95
- synthetic androgens, 310
- systemic lupus erythematosus (SLE), 439, 445–6
 - androgen therapy, 382–3
- systemic sclerosis
 - androgen therapy, 383
- tadalafil, 257, 259
- T-cells
 - effects of testosterone, 28
- tea seed oil in testosterone
 - preparations, 321–2
- temporal cortex, 89, 90
- testicular androgen production and metabolism, 130–2
- testicular androgen receptor, 132–5
- testicular estradiol, 132
- testicular feminization, 10, 27
- testicular feminized mice, 212, 215, 217, 240
- testicular interstitium
 - Leydig cells, 15
- testicular lymphatic circulation, 22
- testicular morphology
 - first descriptions of, 5
- testicular organotherapy, 6–7
- Testifortan®, 6
- testis, 24
- testis cords, 35
- testis development, 34–5
- testis sicca*, 6
- testis transplantation, 7–8
- testosterone
 - 5 α -reduction, 23, 24
 - aromatization to estradiol, 350–1
 - chemical synthesis in the twentieth century, 8–10
 - clinically available forms, 9–10
 - evolution of reproductive regulatory role, 270–2
 - first-pass metabolism in the liver, 310, 314
 - isolation of, 9
 - levels in depressed women, 107
 - normal range in men, 90
- testosterone and gender differences, 110–12
- testosterone binding protein (TeBG), 273
- testosterone biosynthesis, 16–19
 - conversion of cholesterol, 16–17
 - $\Delta 5$ pathway, 16–17
 - $\Delta 4$ pathway, 16–17
 - regulation by factors other than LH, 21
 - regulation by LH, 19–20
- testosterone buciclate, 320–1, 473
- testosterone cream, 303
- testosterone cyclohexanecarboxylate, 318–19
- testosterone cypionate, 11, 95, 217, 295, 303, 318–19
- testosterone decanoate, 319, 323
- testosterone deficiency symptoms, 294
- testosterone enanthate, 9, 92, 94, 96, 193, 211, 295, 303, 317–18, 319–20, 472–3
- testosterone esters, 295
 - forms misused in sports, 520
 - pharmacokinetics, 315–16
- testosterone gel, 10, 46, 62, 195, 295, 297, 325–8
 - advantages over patches, 327
 - risk of interpersonal transfer, 327, 328
 - scrotal application, 329
- testosterone immunoassays, 9
- testosterone in the blood
 - free and protein-bound forms, 60–2
- testosterone isocaproate, 319
- testosterone levels
 - and cardiovascular risk, 208–9
 - predictive marker for mortality, 224–6
- testosterone microcapsules, 323
- testosterone patches, 9, 62, 324–6
 - non-scrotal, 296, 325
 - scrotal, 296, 324–5
- testosterone pellet implants, 296, 323–4
- testosterone pellets, 474
- testosterone phenylpropionate, 319
- testosterone preparations
 - buccal administration, 314–15
 - derived from androstane, 310–11
 - fluoxymesterone, 313
 - goal of testosterone therapy, 309–10
 - hepatotoxic side-effects, 312
 - history of clinical use, 309–12
 - in castor oil, 322–3
 - in tea seed oil, 321–2
 - intramuscular administration, 315–23
 - mesterolone, 313
 - 17 α -methyltestosterone, 312, 314
 - nasal administration, 315
 - oral administration, 310–13
 - pharmacokinetic studies, 9
 - pharmacokinetics of testosterone esters, 315–16
 - range of approaches, 310
 - rectal administration, 315
 - subdermal testosterone pellet implants, 323–4
 - sublingual administration, 314–15
 - synthetic androgens, 310
 - testosterone buciclate, 320–1
 - testosterone
 - cyclohexanecarboxylate, 318–19
 - testosterone cypionate, 318–19
 - testosterone decanoate, 323
 - testosterone enanthate, 317–18
 - testosterone ester combinations, 319–20
 - testosterone esters, 315
 - testosterone gel, 325–8
 - testosterone microcapsules, 323
 - testosterone patches, 324–6
 - testosterone propionate, 316–17, 319–20
 - testosterone topical solution, 330
 - testosterone undecanoate, 313–14, 321–3
 - transdermal administration, 324–30
 - unmodified testosterone, 310–12

Index

- testosterone propionate, 9, 303, 315, 316–17, 319–20
- testosterone rebound therapy, 303
- testosterone replacement
- effects of testosterone withdrawal, 90–2
 - effects on muscle mass, 192–3
 - hypogonadal men, 90–2
 - timing of effects, 98
- testosterone therapy
- adverse events in older men, 195–6
 - age-related differences in response, 193
 - and prostate cancer, 10
 - aromatase deficiency, 24
 - cardiac effects, 221
 - choice of preparation, 294–7
 - delayed puberty in boys, 302
 - effects in healthy older men, 194–6
 - effects on chronically ill patients, 193–4
 - effects on depression, 196–7
 - effects on fatigue/energy, 196–7
 - effects on mood, 196–7
 - effects on quality of life, 196–7
 - effects on well-being, 196–7
 - for micropenis, 303
 - for microphallus, 303
 - goal of, 309–10
 - guidelines for monitoring patients, 417
 - guidelines on potential risks, 416–17
 - HIV patients, 193–4
 - ineffective applications, 303
 - influence of CAG repeat AR polymorphisms, 47–8
 - level for initiation of therapy, 297
 - long-term effects, 348
 - mechanisms of effects on muscle, 197–9
 - overall effect, 304
 - potential benefits for hypogonadal men, 304
 - potential use to improve physical function, 200
 - range of potential benefits, 292–4
 - role of growth hormone, 199
 - role of IGF-1, 199
 - routes of administration, 295–7
 - side effects, 24
 - strategies for selective action, 197–200
 - strategies to avoid adverse effects, 197–200
 - suppression of spermatogenesis, 304
 - symptoms of testosterone deficiency, 294
 - symptom-specific thresholds for treatment, 297
 - to reduce final height, 302–3
 - transdermal route, 62
 - use in types of hypogonadism, 292–4 *see also* androgen therapy.
- testosterone therapy
- contraindications, 303–4
 - breast cancer, 303
 - patients who wish to father children, 304
 - prostate carcinoma, 303
 - reduced spermatogenic function, 304
 - sexual offenders, 303
- testosterone therapy for women, 500–5
- adverse androgenic effects, 505
 - amenorrheic women, 104
 - assessing women with low sexual desire, 508–9
 - breast cancer risk, 505–6
 - effects on bone mineral density, 504
 - effects on cardiovascular function, 504
 - effects on cardiovascular risk, 504
 - effects on cognition, 504–5
 - effects on insulin resistance, 504
 - effects on lean mass, 504
 - effects on mood, 504
 - effects on well-being, 504
 - endometrial cancer risk, 506–7
 - female sexual dysfunction (FSD), 500–4
 - following bilateral ovariectomy, 105–6
 - healthy pre-menopausal women, 103
 - hypoactive sexual desire disorder (HSDD), 500–4
 - issues related to, 494–5
 - naturally postmenopausal women, 104–5
 - need for an approved formulation for women, 509
 - premenopausal women with endocrine abnormalities, 104
 - premenopausal women with sexual problems, 103–4
 - safety concerns, 505–7
 - surgical menopause, 105–6
 - transdermal testosterone, 503
 - treatment options, 509
 - vulval lichen sclerosis treatment, 505
 - women likely to benefit, 507–8
 - women using HRT, 104–5
- testosterone therapy surveillance, 297–302
- behavior, 297–302
- blood pressure, 299
- bone mass, 301
- cardiac function, 299
- erythropoiesis, 300–1
- gonadotropins, 300
- gynecomastia, 298–9
- lean body mass, 298
- lipid metabolism, 301
- liver function, 301
- male sexual hair pattern, 298
- monitoring for prostate carcinoma, 301
- mood, 297–302
- penis growth, 299
- phenotype, 298–9
- prostate-specific antigen (PSA), 301
- prostate volume, 301
- sebum production, 298
- serum DHT, 300
- serum estradiol, 300
- serum testosterone, 299–300
- sexuality, 298
- sleep apnea, 300–1
- voice mutation, 299
- testosterone-to-epitestosterone ratio, 528–9
- drug testing in sport, 519
- testosterone-to-estradiol ratio, 427
- testosterone topical solution, 330
- application site erythema, 330
 - risk of interpersonal transfer, 330
- testosterone transport, 21–3
- entry into target cells, 22
 - free testosterone in serum, 21
- testosterone undecanoate, 9, 91, 96, 104, 218, 242, 244, 295, 296, 303, 313–14, 315, 321–3
- in castor oil, 473–4
 - in tea seed oil, 473
 - intramuscular form, 10
 - oral, 473
 - self-emulsifying drug delivery system (SEDDS), 314
- Testoviron® Depot, 319, 320
- tetrahydrogestrinone (THG), 522
- tetrahydroquinoline analogs, 461
- tetrahydroquinoline derivatives, 462
- TGF- β (transforming growth factor beta), 164
- TGG repeats (polyproline), 25
- threshold level of testosterone, 98
- thrombocytopenia
- androgen therapy, 377
- thrombosis formation, 215–16
- thrombotic occlusion of arteries, 217
- thrombus formation, 213
- thyroid hormones, 21, 341
- effects in elderly men, 342

Cambridge University Press

978-1-107-01290-5 - Testosterone: Action, Deficiency, Substitution: Fourth Edition

Edited by Eberhard Nieschlag and Hermann M. Behre

Index

[More information](#)

Index

- thyroid hormone receptors, 22, 25, 62
- thyroid-stimulating hormone, 341
- thyrotoxicosis, 62
- tibolone, 541
- tight junctions
between Sertoli cells, 135
- tissue plasminogen activator (tPA), 215
- TNF- α (tumor necrosis factor alpha), 213, 239, 241, 244–5
- transactivation function
and short tandem repeats, 25
- transcriptional coactivator or co-repressor proteins, 275
- transdermal testosterone
administration in women, 104
- transdermal testosterone gel.
See testosterone gel
- transdermal testosterone patches, 9, 223, 295
- transdermal testosterone preparations, 296–7, 324–30
- transgender identity, 88
- transgendered individuals
effects on mood and aggression, 109
- transplantation
testicular, 7–8
- transsexuals, 88
- trauma
androgen therapy, 384–6
- trenbolone, 521
- trenbolone acetate, 521
- triglycerides, 244, 347
role in atherogenesis, 217
- tuberculosis, 193
- tumors of gonads
in AIS, 39
- Turner syndrome, 504
- ubiquitination of histones, 26
- ulcerative colitis, 446
- ultradian pattern of episodic
testosterone secretion, 340
- ultrafiltration method, 76
- unilateral anorchia, 2
- unmodified testosterone, 310–12
- urogenital epithelium, 36
- urogenital sinus, 35–6, 272, 277–8
- uterus, 24
development of, 35
- vagina
development of, 35
- varденаfil, 257
- varicocele, 292
- Vasari, Giorgio, 2
- vascular disease
androgen therapy, 393–4
- vascular endothelial growth factor (VEGF), 281
- vascular reactivity
and low testosterone, 211
influence of testosterone, 214–15
- vascular tone, 214
- vasoactive intestinal peptide (VIP), 255
- Vatican
castrato singers, 4
- venous thromboembolism risk, 215–16
- ventromedial hypothalamic nuclei, 89
- vertebral fractures in elderly men, 350
- veterans
cardiovascular risk, 255
- violence in women, 108–9
- voice mutation, 299
- Voronoff, Serge, 7
- Voss, H.E., 8
- vulval lichen sclerosis
testosterone therapy, 505
- Wagner, Rudolph, 6
- wasting
androgen therapy, 394
- weight loss
effects of testosterone therapy, 221
- well-being
effect of DHEA treatment, 442–4
effects of testosterone therapy, 196–7
effects of testosterone therapy for women, 504
- William the Conqueror, 3
- Wolffian ducts, 35
- women
cardiovascular disease and testosterone, 499
- causes of low testosterone, 496–8
- cognitive function and testosterone, 500
- effects of adrenalectomy, 496
- effects of oophorectomy replacement therapy (HRT), 496
- effects of hyperprolactinemia, 498
- effects of hypopituitarism, 498
- effects of hypothalamic amenorrhea, 498
- effects of hysterectomy, 496
- effects of oophorectomy, 496
- effects of oral contraceptives, 496
- effects of premature ovarian failure, 498
- endogenous testosterone and health, 498–500
- osteoporosis and testosterone, 499–500
- postmenopausal ovarian testosterone, 496
- sexual function and testosterone, 498
- SHBG levels, 495–6
- testosterone physiology in reproductive years, 495–6
- testosterone therapy issues, 494–5
- well-being and testosterone, 499
see also testosterone therapy for women.
- World Anti-Doping Agency (WADA), 519, 520, 523–4
- X chromosome
androgen receptor gene, 25
- XSBMA. *See* Kennedy syndrome
- Y chromosome
SRY (sex-determining region of the Y chromosome), 34
- yohimbine, 6, 261
- Young Mania Rating Scale (YMRS), 95
- zoledronic acid, 183
- zona reticularis, 438