Index

A

Abdominal acupuncture, 232

Acupuncture

autonomic activity, 231–232
daily abdominal acupuncture, 232
DHT-induced PCOS rat model, 234
hypothetical mechanism, 228
in infertility and subfertility cofactors, 236–239
and insulin resistance, 237–238
intramuscular needle insertion and stimulation, 229
low-frequency electroacupuncture, 230, 231, 233
and mental health, 238–239
modulation, 231–232
molecular mechanism, 233
and obesity, 236–237
in ovarian dysfunction, 232–234
during pregnancy, 234–236
protocols, 229
randomized controlled trials, 227
stimulation and physiological responses, 229–230
Western medical perspective, 228–232

Androgen excess (AE)-PCOS Society criteria, 13, 16

Aneuploidy, 33, 34, 37, 281, 313

Anovulation, 8, 24–25

Anti-estrogens. See Selective estrogen receptor modulators (SERMs)

Anti-Müllerian hormone (AMH)

assay, 6
foetal life, 26
follicle excess
clinical application, 95
immuno-analysers, 96
inter-laboratory variability, 96
molecular heterogeneity, 95–96
serum concentration, 94–95
and FSH concentrations, 27
functions, 26, 27
levels, 15
and LH concentrations, 28
male sexual differentiation, 94
mechanisms, 27
ovarian reserve, indirect reflection, 94
in ovary, 94, 95
role, PCOS anovulation, 26, 27
transforming growth factor-beta family, 26

Antral follicular count (AFC), 5

Aromatase inhibitors (AI)
aminogluthethimide, 120
anastrozole, 120
breast cancer and fertility preservation, 128
CC resistance, 124–125
clinical studies, 123–125
exemestane, 120
foetal safety and teratogenic effects, 126–127
formestane, 120
half-life, 121
history, 120
hormonal balance and interactions, 123
letrozole, 119
LOD, 125
mechanism of action, 122–123
oestrogen biosynthesis, 119
OHSS prevention, 129
Aromatase inhibitors (AI) (cont.)
pharmacodynamics, 121–122
pharmacokinetics, 121–122
protocols and doses, 125
side effects, 126
unexplained infertility, 127
Assisted reproductive technologies (ARTs), 3, 7–8, 43, 122, 126, 221, 267
biological manipulations, 311
elective single embryo transfer, 314
and lifestyle interventions, 173, 174, 176–178
luteal phase support, 267
male/tubal cofactors, infertility, 328
maturational and developmental
competence, 298
medical treatments, 311
vitamin D supplementation, 173

Chinese herbal medicine (CHM)
Berberine, 187
Cinnamon, 187
formula, 186–187
glucose metabolism, 188, 189
limitations, 187–189
mechanisms of action, 187, 188
physiological mechanisms, 185–186
plantain, 189
side effects, 187, 188
Tanshinones, 187
TCM, 184–185
therapeutic strategies, 186

Chronic stress exposure adaptation, 171
Classic PCOS (phenotypes A and B), 83–84
Clomiphene citrate (CC)
adjuvant infertility therapies, 113–114
adverse events, 111–112
anovulatory infertility treatment, 110
CC-resistant patients, metformin
co-treatment, 144–145
gonadotrophins, 145–147
pretreatment, 145
treatment, 143–144
chemical structure, 110
genital birth defects, 112
efficacy, 110–111
estrogenic effect, 110
hormone-dependent breast cancer, 109
induced withdrawal bleed, 113
mechanism of action, 110, 115
predictive factors, 110, 111
protocols, 112–113
uncertainty, 114
Combined oral contraceptive (COC) pretreatment, 35, 264, 266, 267, 274
Controlled ovarian hyperstimulation (COH), 259
after first IVF
dual-suppression protocol, 266
GnRH-agonist suppressive protocol, 265
low-dose FSH stimulation protocol, 266
low-dose gonadotrophin stimulation, 264–265
modified ultra-long GnRH-agonist protocol, 266–267
first IVF cycle
COC pretreatment, 264
GnRH antagonist co-treatment, 262–264
GnRH vs. multiple-dose GnRH antagonist protocol, 261–262
luteal phase defect, 267
metformin, 260–261
ovarian morphology, 260
strategies, 260
Cord blood androgen studies, 25
Couples with mild male subfertility, 255
Couples with unexplained subfertility, 255–256

D
Daily abdominal acupuncture, 232
Defective deep placentation
classification, 42
vs. normal placental bed, 43
Diagnostic criteria
AE-PCOS Society, 16
AMH assay, 19
ESHRE/ASRM, 14–16
follicle distribution, 18, 19
limitations, 16, 17
NIH, 12–14
patient characterisation, 17
Dietary supplements, 171–173
beneficial effects, 181
cinnamon extract, 183
green and spearmint tea, 182–183
micronutrients, 184
polyunsaturated fatty acids, 183–184
vitamin B12 and folate, 182
vitamin D deficiency, 182
ω-3 fatty acids, 183–184

E
Embryo culture, 272, 275, 278
Embryo transfer (ET), 57, 128, 206, 259, 264, 266, 279
Endometrial abnormalities, 4
Endometrial receptivity
  abnormal endometrial competence, 51–53
cell adhesion molecules, 48
clinical protocol, 57
decidualization and placentation, 53–55
differential gene regulation, 47
embryo implantation, 56
endometrial apolipoprotein A1 expression, 47
ER expression, 48
folliculogenesis, 46
and functions, 44–48
and glucose metabolism, 55
glucose transporter 4, 48
HOXA10 expression, 46
impairment, subfertile women, 44
implantation, 44
micronized progesterone, 47
molecular analysis, 56
ontogenetic progesterone resistance, 44
progesterone, role, 46
sequential gene expression, 44
subfertility pathogenesis, 45
treatment, 55
Endometrial scratching, 56
Endometrium competence, 8
Epidemiological findings, fertility, 6
Epigenetics, 49, 281, 313
ESHRE/ASRM criteria, 13–16

F
Ferriman-Gallwey scoring system, 12, 13
Fertility
  enhancement, PCOS
    bariatric surgery, 292–293
    behaviour modification, 292
dietary interventions, 291
exercise, 292
insulin resistance, 289
intra-and extra-ovarian factors, 290, 291
IVF cycles management, 300
IVM, 298–300
lifestyle algorithm management, 293, 294
lifestyle therapy, 291
mono-follicular ovulation, 291
ovulation induction methods, 294–298
weight loss, 291
evaluation
  BBT measurements, 71
  laboratory test, 71–72
medical and reproductive history, 70–71
physical examination, 71
semen analysis, 72–73
transvaginal ultrasound, 72
tubal patency, 72

Follicle excess
  AMH regulation, 90, 91, 94–96
  clinical role
    diagnostic performance, 96, 97
    infertility treatment, 98–99
  PCOS phenotypes, 97–98
  elevated serum anti-Müllerian hormone level, 90
  intraovarian hyperandrogenism, 91
  ovarian reserve, 89
  pathophysiology, 89–91
  Rotterdam classification, 91, 93, 99
ultrasound
  B-mode ultrasonography, 92–93
  magnetic resonance imaging, 94
  ovarian polycystic aspect, 91, 92
  three-dimensional ultrasonography, 93

Follicular apoptosis defect, 90
Folliculogenesis, 35

G
Gene expression, 41
Genetic approach, oocyte quality, 33–34
Genome-wide association studies (GWAS), 85
Gonadotrophins
  administration, 3–4, 124
  CC-resistant patients, 145–147
  COH after first IVF, 264–265
  in human ovarian physiology, 154–156
  infertility treatment, 153
  metformin, 145–146
  mono-ovulation induction, 153
  in mono-ovulatory induction, 146–147, 160–161
  in multiple ovulatory cycles, IVF procedures, 147
  oocyte retrieval, 128
  ovarian response, predictive markers, 161–162
  release abnormalities, 25
  single ovulation, 153
  step-down protocol, 159, 160
  step-up protocol, 158–160
  treatment, women, 156–157
  types, 157–158
  in unexplained infertility, 127
H

Health-related quality of life (HRQoL), 170–171
Healthy diet, 171–173
Hirsutism, 24, 171, 183, 186
AE-PCOS, 16
chronic treatments, 109
Ferriman-Gallwey score, 12, 13, 71
NIH/NICHD criteria, 14
2003 Rotterdam criteria, 15
signs, 11
Homeostatic model assessment (HOMA) index, 218
Hormonal priming, 271–273
Human ovarian physiology, 154–156
Hyperandrogenemia, 3
Hyperandrogenism, 3, 12, 14, 17, 25–26, 44, 47, 66, 81–85, 94, 97, 98
anovulation and infertility, 65
biochemical, 7, 83, 203, 227, 291, 308–309
central obesity, 66
definition, 12
evaluation, 65
and insulin resistance, 67–68, 200, 213
metformin, 138
occurrence, 65
ovarian environment, 65
PCOS-related factors, 65
reproductive abnormalities, 111
tanshinone, 187
Hyperinsulinaemic insulin resistance, 43, 213, 214, 217, 221, 312

I

Immature oocyte collection, 273–274
Infertility

AMH assay, 326
definition, 63
diagnostic criteria, 326–327
endometrial receptivity, 68–69
endometriosis, 64
evaluation, 63, 64
fertility evaluation, 70–73
hyperandrogenism, 64
integrated strategy of treatment, 328, 329
irregular menses, 64
management, 327–328
oligo-anovulation, 64, 325
oocytes and embryo quality, 69
ovulatory disorder, 64
PCOS-related factors
anovulation, 325
characteristics, 64
hyperandrogenism, 65
insulin resistance, 67–68
obesity, 66–67
phenotypes, 85
pelvic inflammatory disease, 64
treatment, follicle excess
clofemphine citrate, 98
LOD, 99
in vitro stimulation, 98–99
vitamin D/calcitriol, 69–70

Inositisls
abnormal epimerase activity, 216–217
data efficacy, 222
effects, women with PCOS
D-chiro-inositol administration, 218–219
myo-inositol administration, 219–220
myo-inositol and D-chiro-inositol monotherapies, 220–221
as fertility drug, 221–222
insulin-sensitising effects, 214
mechanisms of action, 214–216
post-treatment fertility, 222
structure, 214, 215
Insulin-sensitising drugs. See Metformin
Intrauterine insemination (IUI), 8
countraindications, 250
data efficacy, 252–253
density gradient centrifugation, 251
indications, 250
mild male subfertility couples, 255
swim-up technique, 251
vs. timed intercourse, 254, 255
unexplained subfertility couples, 255–256
in women, PCOS, 250–252

In vitro fertilisation (IVF) cycles, 8, 259
after first IVF
dual-suppression protocol, 266
GnRH-agonist suppressive protocol, 265
low-dose FSH stimulation protocol, 266
low-dose gonadotrophin stimulation, 264–265
modified ultra-long GnRH-agonist protocol, 266–267
fertility enhancement, 300
first IVF cycle
COC pretreatment, 264
GnRH antagonist co-treatment, 262–264
luteal phase defect, 267

In vitro oocyte maturation (IVM)
anueplody, 281
birth outcomes, 279–281
embryo culture, 278
epigenetic variation, 281
fertilisation, 278
fertility enhancement, 298, 300
hormonal priming, 272–273
immature oocyte collection, 273–274
multi-follicular growth, 271
oocyte maturation and culture, 274–278
reproductive outcomes, 279
stimulated IVF treatment, 271
transfer/cryopreservation, 279
treatment method, PCOM/PCOS, 272

L
Laparoscopic ovarian drilling (LOD)
AMH assay, 99
in clomiphene citrate resistant patients, 125, 145, 311
efficacy, 196
evidence-based data, 201
fixed vs. dose-adjusted energy, 197–198
indications and data efficacy
in CC-resistant PCOS, 199, 200
OHSS, 200, 201
theoretical advantages, 200
mechanism of action, 196–198
metformin, 144, 145
vs. oral ovulation induction treatments, 196
oral ovulatory drugs, 207
ovarian adhesions, 125
ovulation induction, 99, 125
ovulation/pregnancy predictors, 201–203
PCOS-related anovulation, 195
reproductive outcomes, 203
safety concerns
IVF outcomes, 206
ovarian reserve, 204–206
periadnexal adhesions, 204
surgical technique, 196–198
surgical treatment, infertility, 195
unilateral vs. bilateral, 197
Lifestyle interventions
bariatric surgery, 176
clinical effectiveness, 174–175
definition, 174
methodological aspects, 177
and natural and assisted reproduction (see Assisted reproductive technologies (ARTs))

O
Obesity, 3–4
adiponectin, 67
characteristics, 66
leptin, 66–67
SHBG, 66
Oligo-anovulation, 3
OMICS technologies, oocyte quality, 34–35
Ontogenetic progesterone resistance, 52
Oocyte/embryo
cryopreservation, 128, 206, 267, 279
maturation and culture
coronal cells, 275–278
culture media additives, 274
culture timing, 275–278
hormonal additives, 274
serum/follicular fluid, 274–275
therapeutic procedure, 176
weight loss, 174
Luteal phase defect, 50, 51, 84, 113, 219, 262, 267
Luteinising hormone/follicle-stimulating hormone (LH/FSH) ratio, 12

M
Metformin
cotreatment, 144–145
data efficacy
in anovulatory infertility, 141–143
in CC-resistant patients, 143–147
infertility diagnosis prevention, 141
drug safety profile, 139–140
gonadotrophins
for mono-ovulatory cycles, 146–147
in multiple ovulatory cycles, IVF procedures, 147
ovarian gluconeogenesis, 138
patients selection, 140
pharmacology, 136–138
pretreatment, 145
therapeutic regimens, 138–139
treatment, 143–144
Morphological approach, oocyte quality, 32–33

N
National Institutes of Health (NIH) criteria, 12–14
Neonatal morbidity, 7
Normoandrogenic PCOS (phenotype D), 84
Oocyte/embryo (cont.)
quality, 8
body mass index, 36
embryonic development, 32
fertilization, 32
fertilization, 32
genetic approach, 33–34
implantation, 32
meiotic maturation, 32
meiotic/mitotic cell cycle pathway, 37
molecular specificities, 36
morphological approach, 32–33
nuclear maturation status, 32
OMICS technologies, 34–35
pregnancy, 32
pregnancy rates, 32
Ovarian hyperstimulation syndrome (OHSS),
264, 266, 267, 327
complications rates, 114
drainage and hospitalisation, 262
follicle excess, 98
gonadotrophin protocols, 146, 158
IVM, 298, 300
LOD, 195, 200
occurrence, 262
ovarian hyperstimulation, 271
ovulation induction, 260
predictive markers, 99
prevention, 129, 250, 262
Ovulation induction methods
with antiestrogens (see Selective estrogen
receptor modulators (SERMs))
clomiphene citrate, 294–295
gonadotrophin therapy, 296–297
letrozole, 295–296
management, 298, 299
metformin, 295
ovarian drilling, 297–298
Ovulatory PCOS (phenotype C), 84

P
PCOS phenotypes
classic (A and B), 83–84
and infertility, 85
normoandrogenic (D), 84
ovulatory (C), 84
pathogenesis, 84–85
prevalence, 82–83
Rotterdam criteria, 82
PCOS-related ovulatory dysfunction, 8
Pharmacology, metformin
pharmacodynamics, 136–138
pharmacokinetics pathway, 136
Phytotherapy, 181, 185, 328
Pipelle for Pregnancy (PIP), 56
Placenta function, 7
Polycystic ovarian morphology (PCOM), 3
Pregnancy
acupuncture
depression, 236
labor induction, 236
low-frequency electrical stimulation,
234–235
for pelvic girdle pain, 235
pregnatal androgenized rat PCOS model,
235
complications
abnormal inflammatory and metabolic
pattern, 313
acetylsalicylic acid, 315–316
causes, 308, 309
clinical data, 306–308
foetal and perinatal outcomes, 307
gestational diabetes mellitus, 306
hormone-independent alterations, 312
hyperandrogenic states, 309
iatrogenic multiple pregnancies, 308
incidence, 308
large for gestational age, 308
lipid abnormalities, 312
low-frequency electroacupuncture, 316
low molecular weight heparin, 315–316
management, 313–316
metformin administration, 315, 316
miscarriage, 306
non-pharmacological intervention, 310
oligo-amenorrhea, 310
pathophysiology, 308–313
pharmacological measures, 315
pregnancy-induced hypertension, 307
prevention, 313–316
sleep-disordered breathing, 311–312
small for gestational age, 308
Pregnancy in Polycystic Ovary Syndrome I
and II (PPCOS-I and PPCOS-II)
trials, 5
Preterm delivery (PTD), 7, 52, 307, 308,
310–312, 314, 315
Progesterone resistance, 48–50
abnormal endometrial competence,
51–53
decidualization and placentation, 53–54
embryonic implantation, 51
late-onset preeclampsia, 52
luteal dysfunction, 50
ovulation/corpus luteum formation, 52
ovulatory cycles, 53
subnuclear vacuolization, 52
Psychological disorders, 170–171
R
Raloxifene, 109, 114
Reproductive medicine, 6, 305, 328
Rotterdam or Androgen Excess-PCOS Society criteria, 3, 15

S
Selective estrogen receptor modulators (SERMs)
clinical role, 109
clophene citrate, 109–114
raloxifene, 109, 114, 115
tamoxifen, 109, 110, 114, 115

T
Tamoxifen, 109, 110, 114, 115, 120, 124, 128
Traditional Chinese Medicine (TCM), 184–185
Transvaginal ultrasound (TVS), 12, 72
Tubal disease, 72
Two cell-two gonadotrophin theory, 155