

INDEX

Page numbers in *italics* indicate figures or tables.

- f-actin 38
activin receptor-like kinase 54
adenosine diphosphate *see* ADP
adenosine triphosphate *see* ATP
adenylation control element 70
adnexal torsion 213
ADP 16
adult respiratory distress syndrome 215, 223
aging oocytes 115
A-kinase-anchoring-proteins 86
albumin 299
 intravenous 210–11
alpha-keto acids 19
androgen excess 165
androgens 158
 free androgens index 165
Angelman syndrome 103, 117
angiotensin converting enzyme inhibitors 189,
 206
antihistamines 215
anti-Müllerian hormone 52, 131–2, 138, 158
antiphospholipid antibodies 337
antral follicles 124
antrum 1
APGAR score 316
apoptosis 150, 151, 363
ascites 216–17
aspirin, low dose 337
ATP 16
atresia 150
aurora A kinase 88, 92

Balbiani body 18
basic fibroblast growth factor 53, 130
Beckwith-Weidemann syndrome 103
birthweight 315–16
blastocyst transfer 307, 307, 328

bone morphogenetic protein 7, 8, 52, 53, 129
8-bromo guanosine 3'5'-cyclic
 monophosphate 131

cAMP 3, 43, 86–7, 87, 131
cancer treatment 132, 137
catalase 19
cdc25 phosphatase 89
cell cycle control 64–8, 65
cell interactions
 folliculogenesis 41–3, 41
 oocyte maturation 43–4
 oogenesis 40–1
cellular metabolism 16–17, 16, 17
 folliculogenesis 19–23, 20, 21
 mitochondria 17–19
 in oogenesis 23–8, 25
 in vitro vs. ex vivo 30
cesarian section rates 315, 315
chromatin condensation 89–91, 90
chromatin structure 56–9
c-kit proto-oncogene 42
clast-4 56
cleft palate 314
clomiphene citrate 322
coasting 210, 217
condensin 89
conflict hypothesis 104
congenital abnormalities 313–14, 314
congenital adrenal hyperplasia, late onset
 164
connective tissue growth factor 158
connexins 9, 38, 149
 see also Cx
connexon 38
cord pH 316
corpus luteum 152–3

- CPEB *see* cytoplasmic polyadenylation element
binding protein
- cryopreservation
conventional 365
embryos 210, 363–4, 365–6
oocytes 363–4
immature 364–5
mature 365
ovarian tissue 363
- culture systems 126–7, 126, 127
embryo culture 295–7, 296
problems of 298–9, 299
supplements and concentrations 140, 299–300
- cumulus granulosa cells 37, 39, 41
cumulus-oocyte complex 15, 20, 27, 38, 149, 149, 233, 248
- Cx37 39
Cx43 39
- cycle cancellation 323–5
high miscarriage rate 325
low implantation rate 325
poor embryo quality 323, 325
- cyclic AMP *see* cAMP
- cytokinesis 94–5
- cytoplasmic maturation 84–5
- cytoplasmic polyadenylating elements 50
- cytoplasmic polyadenylation element binding protein 50, 61
- cytostatic factor 66
- danazol 215
- deadenylation 61, 63
- dehydroepiandrosterone 156
- diet 321–2
- diuretics 216
- DNA methylation 57, 104, 107
- DNA methyltransferase 110–15, 111
DNMT1 110–13
DNMT3a/b 113–14
DNMT3L 114–15
Dnmt1p 112
Dnmt3a 115
Dnmt3b 114
Dnmt3L 114–15
DNMT *see* DNA methyltransferase
- dominant follicle growth 152
- dopamine 216
- Early Ectoderm Development 59
- early mitotic inhibitor 57
- early oogenesis 128–32, 129
- early unilateral ovarian follicular aspiration 209
- Edwards, Robert 232
- eggs *see* oocytes
- embryo cryopreservation 210, 363–4, 365–6
- embryo culture 286, 295–312, 295
culture system 295–7, 296
day 3 to blastocyst 303–4
day of embryo transfer 307, 307
embryo grading 304–5
gas phase, pH and incubation chamber 300–1
incubation volume and number of embryos per drop 301–2
media 297–8
oil 302
problems of 298–9, 299
pronucleate to day 3 303
protocol 302–4
quality control 302
sequential scoring techniques 305–7, 306
supplements 299–300
- embryo grading 304–5
blastocyst 305
cleavage stage embryos 304–5
pronucleate embryos 304
- embryo-maintenance medium 280
preparation of 285–6
- embryonal poly(A) binding protein 68
- embryo transfer 225, 286–8, 287
blastocyst transfer 307, 307
embryo developing stage 286–7
embryo loading and transfer 286–7, 286
endometrial thickness 287
frozen-thawed 264–5
IVF/IVM 356
over-responders 347
scoring 287
- Emi1 66
Emi2 66–7
- endometrial preparation 226, 263–72
drugs used in 265
gonadotropin priming 266
IVF/IVM 356
optimal thickness 265–6, 266
over-responders 347

- receptive endometrium 263–4
- stimulated cycles for IVF 264
- endometrial thickness 287
- epidermal growth factor 44, 55, 156
- epigenetic dysregulation 117–18
- epigenetics 103–22
 - in assisted reproduction 115–18
 - dynamics and timing 104–11, 106–8
- estradiol 159
 - concentration in poor responders 334
- estradiol priming 326–7, 327
- estrogens 158
- ethylenediaminetetraacetic acid (EDTA) 300
- exercise 321–2
- FAD 17
- F-box genes 57
- fertile age span, extension of 362
- fertility preservation 361–7
 - avoidance of hormone stimulation 364
 - cryopreservation 364–6
 - experience of 366
 - indications for 361–2
 - options for 362–4
 - timing of oocyte retrieval 364
- fertilization, identification of 286
- fetal follicles 133
- fetal oocytes 125, 125
- FIG- 52, 59
- flavin adenine dinucleotide *see* FAD
- flushing medium 280–1, 281
- follicles
 - antral 124
 - fetal 133
 - growth 21–3, 21
 - nutrition 28–30, 29
 - ovulatory 23
 - in PCOS 178–9, 179
 - primary 123, 148
 - primordial *see* primordial follicles
 - secondary 123
- follicle development 138–9
 - cyclic recruitment 150–5, 151, 152, 154
 - initial recruitment 149–50, 150, 151
 - intraovarian modulators 156–9, 157
- follicle number in poor responders 334
- follicle stimulating hormone *see* FSH
- follicular aspiration 209–10
- follicular size 275–6
- folliculogenesis 19–23, 20, 21, 40
 - cell interactions 41–3, 41
 - early 128–32, 129
 - gene expression 51–9
 - growing follicle 21–3, 21
 - in-vivo 123–36
 - ovulatory follicle 23
 - primordial follicle 19–21, 20
- free androgens index 165
- FRGY2 69
- frozen-thawed embryo transfer 264–5
- FSH 42, 117
 - administration 198
 - basal level in poor responders 334
 - cyclic follicular recruitment 153–5, 154
 - dose 198
 - injection technique 199
 - IVM 224–5, 277–9
 - and oocyte development 7–9, 9
 - ovarian stimulation 198–9, 198
 - preparation 198
 - primordial follicles 130
 - storage 198
 - window/threshold concept 152
- FSH priming 224–5, 237–41, 244–5, 326
 - clinical variables and outcome 247
 - combined hCG/FSH priming 246–8
 - immature oocytes
 - from normal women 238–9
 - from PCOS patients 237–8
- gap junctions 5, 9–10, 37–40, 38, 149
- gene expression 49–82, 105
 - differential 59–70, 60, 62
 - follicle and oocyte growth 51–9
 - genomic integrity 50–1
 - oocyte growth and chromatin structure 56–9
- genetic abnormalities 362
- genomic imprinting 104
- genomic integrity 50–1
- germinal vesicle 2, 49, 83
 - breakdown 2, 3, 53, 83, 84, 85–9, 86, 232, 233, 243
- gestational age
 - at delivery 316
 - weight for 316
- gestational trophoblastic disease 109
- gestational diabetes 316, 316
- Gleevec 54

- glomerular nephropathy 189
glucocorticoids 211
glucose-6-phosphate dehydrogenase 26
glucose 17, 21, 22, 29
glutamine 29
glutathione 39, 84
glutathione peroxidase 19
glycogen synthase kinase *see* GSK
glycolysis 16, 17
GnRH agonists 208, 211, 327–8
 downregulation with 336
 ovarian protection 363
GnRH antagonists 336–7
GnRH pumps 327–8
gonadotoxic treatments 361–2
gonadotropin-releasing hormone *see* GnRH
gonadotropins 115–16, 322
 high dose in poor responders 336
 IVM supplementation 277–9
Gpr3 protein 3
Graafian follicle 149
granulosa cells 123, 148
Grb7 116
growth/differentiation factor-9 6–7, 7, 42, 54,
 129, 157
growth factors 53–5, 128–30, 129, 140
 IVM supplementation 279–80
growth hormone 337
GSK-3 92, 93, 95
Gs protein 3

H19 106, 116
hCG 117, 153, 326
 coasting 210, 217
 IVM 224–5
 and OHSS 209
 ovarian stimulation 199
hCG priming 238, 244–6, 245–6
 combined hCG/FSH priming 246–8
 IVF/IVM 354
 prior to oocyte retrieval 338, 339
heteroplasmy 18
histamine 188
histone-H1 kinase 91
histone mRNAs 56
hormone supplementation 265–9, 266–8
hormone synthesis 155–6, 156
human chorionic gonadotrophin *see* hCG
hydatidiform mole 109

hydrogen peroxide 17
hyper-androgenic insulin resistant acanthosis
 nigricans syndrome 166
hyperinsulinemia 166
hypoxanthine phosphoribosyltransferase 59

Igf2r 109
Igf2 116
imaging
 IVM 224
 oocyte retrieval 255
 polycystic ovary syndrome 166–7
 see also ultrasound
immature oocytes
 collection 231, 253–61, 280–2, 281, 282
 cryopreservation 364–5
 identification of 281–2, 281, 282
 IVF/IVM 355
 IVM 274–80, 282–5, 283–5
 retrieval 346
immunodeficiency, centromeric instability and
 facial anomalies 114
implantation rate 319–31
incubation chambers 300–1
infertility, and aging oocytes 115
inhibins 156, 158, 334
inhibitory factors 131–2
insulin 128–9, 139
insulin-like growth factor 128–9, 139
insulin-like 3 protein 64
insulin resistance 166
insulin-sensitizing agents 168–70, 168, 169
interleukin-6 130
intracisternal A particle 105
intracytoplasmic sperm injection 103, 286, 286
intraovarian modulators 156–9, 157
Inverdale fecundity gene (*FecX*) 7
in-vitro fertilization 137
 holistic analysis 296
 live birth rates 295
 natural cycle, with IVM 269, 353–60
 oocyte retrieval 254–6, 256
 outcome 313–18
 over-responders 347
 in PCOS 223, 322
 risks of 223
in-vitro growth 15
in-vitro maturation 15, 83, 123–36
 advantages of 224, 322–3

- clinical importance of 124–5
 cycle cancellation 323–5, 324
 development of 256–7
 embryo transfer 225
 endometrial preparation 226, 263–72
 fertility preservation 361–7
 fertilization 225
 fetal oogonia/oocytes 125, 125
 FSH priming 224–5, 237–41, 326
 hCG priming 224–5, 326
 history 231–6, 244
 hormone supplementation 265–9, 266–8
 immature oocytes 274–80, 282–5,
 283–5
 laboratory aspects 273–93
 luteal support 226
 media 276–7, 280
 in OHSS 211
 oocyte donation 226–7
 oocyte retrieval 257–9, 258, 259
 outcome 226
 over-responders 345–52
 patient selection 326
 and PGD 227
 polycystic ovary syndrome 221–30
 in poor responders 333–44
 pregnancy outcome 354
 prevention of OHSS 349–50
 primordial follicles 125–8, 126–8
 problems 323, 324
 retrieval of immature oocytes 225
 stimulated cycles 248–9
 supplements 277–80
 treatment cycle 224–6
 ultrasound 224
see also IVF/IVM
 in-vivo maturation 221–2
 3-isobutyl-1-methylxanthine 43
 IVF *see* in-vitro fertilization
 IVF/IVM 269, 353–60
 embryo quality 358–9
 endometrial preparation and embryo
 transfer 356
 immature oocytes 355
 oocyte retrieval 355, 355
 outcome 356–7, 356–8
 patient selection 354
 potential problems 357–8
 IVM *see* in-vitro maturation
 keratinocyte growth factor 53, 54
 Kit ligand 5–6, 42, 53
 KL *see* Kit ligand
 Krebs cycle 17

 labour and delivery 315, 315
 lactate 21, 29
 leptin 189
 letrozole 167
 leukemia inhibiting factor 130, 149
 Leventhal, Michael 163
 LH
 cyclic follicular recruitment 153–5, 154
 inappropriate secretion 165
 IVM supplementation 277–9
 and OHSS 208
 lifestyle modification 321–2, 321
 limited ovarian stimulation 350
 liver dysfunction 212
 long interspersed nuclear element 1 105
 low implantation rate 325
 luteal support 226
 luteinizing hormone *see* LH

 MAP kinase 92
 meiotic re-arrest 96
 polar body extrusion 95
 Maskin 61, 70
 MATER 58
 maternal imprinting 105–10, 106–8
 maturation promoting factor 49, 50, 64, 87–8,
 88, 93–4, 94
 chromatin condensation 90–1
 meiotic re-arrest 96
 segregation of homologs 93–4, 94
 maturation, regulation of 64–8, 65
 mature oocytes
 identification of 285
 insemination of 285–6, 286
 media
 embryo culture 297–8
 in-vitro maturation 276–7, 280
 meiotic arrest 2–4, 3
 meiotic division 123
 meiotic re-arrest 95–6
 meiotic resumption 85–9, 86
 meiotic spindle apparatus formation 91–2, 91
 menstrual cycle 152
 messenger RNA *see* mRNA

- metabolic profiling 28
 metabolic shift 23
 metformin 167, 211–12, 322, 327
 Minimum Essential Medium 28
 miscarriage 320–1
 high rate of 325
 MISS protein 67
 mitochondria 17–19
 mitogen activated protein kinase 43
 Mn-superoxide dismutase 59
 Mos kinase 66
 MPF *see* maturation promoting factor
 mRNA 60
 polyadenylated 68–9
 post-translational mechanisms 69–71
 translational inactivation 63–4
 Müllerian inhibiting substance 54
 multicystic ovaries 179–80
 multiple growth factors 131
 multiple pregnancy 314–15, 314
- NAD 16
 NADH 16
 natural cycle IVF with IVM *see* IVF/IVM
Ndn 109
 neurotrophins 129, 130
 nicotinamide adenine dinucleotide *see* NAD
 Nobox 55
 non-surrounded nucleolus 58
 nuclear lamins 85
 nuclear maturation 83–4, 84
 nuclear transfer 108, 109
 nucleolar precursor bodies 304
 nucleotide derivatives 131
 nutrition of follicle/oocyte 28–30, 29
- obesity 165–6, 321–2
 ocadaic acid 88
 Oct-4 56
 OHSS *see* ovarian hyperstimulation syndrome
 oil overlay 302
 oligo-amenorrhea 320
 omphalocele 314
 oncostatin M 130
 oocytes
 aging 115
 cryopreservation 363–4
 immature *see* immature oocytes
 in-vitro maturation *see* in-vitro maturation
 in-vivo maturation 221–2
 mature *see* mature oocytes
 nutrition 28–30, 29
 preovulatory 26–8
 oocyte capacitation 2
 oocyte collection 199–201
 anesthesia/analgesia 199–200
 bleeding 200
 bruising/discomfort 200
 infection 201
 organ damage 200–1
 ovarian torsion 201
 surgical trauma 200
 oocyte donation 124, 226–7, 264–5
 oocyte-granulosa complexes 4, 8, 9
 see also gap junctions
 oocyte maturation 83–101, 243–4
 cell interactions 43–4
 cytoplasmic maturation 84–5
 nuclear maturation 83–4, 84
 regulation of 85–96
 see also in-vitro maturation
 oocyte-maturation medium 280
 preparation of 282–3, 282–4
 oocyte redox state 19
 oocyte retrieval 253–4, 253, 254, 346
 anesthesia/analgesia 254–5, 257
 aspiration pressure 258
 aspiration technique 255–6, 256, 258–9, 258,
 259
 cleaning and antisepsis 255, 257–8
 fertility preservation 364
 IVF 254–6, 256
 IVF/IVM 355, 355
 IVM 256–8, 257, 258
 laparoscopic 253
 materials 255
 needles 255, 258
 risks 256
 timing of 364
 transabdominal ultrasound-guided 254
 tubes and blocks 258
 ultrasound technique 255
 oocyte stripping 285, 285
 oocyte-washing medium 280
 preparation of 282
 oogenesis-1 56
 oogenesis 1–2, 2
 cell interactions 40–1

- early 128–32, 129
 FSH in 7–9, 9
 gene expression 51–9, 56–9
 growing oocyte 24–6, 25
 in-vitro models 4
 in-vivo 123–36
 metabolism during 23–8, 25
 paracrine control 4–7, 5, 7
 preovulatory oocyte 26–8
 primordial germ cell 23–4
 primordial oocyte 24
 oral contraceptive pill 337
 ovarian anatomy 147–9, 148, 149
 ovarian cryopreservation 124, 137–8
 ovarian drilling 322
 ovarian hyperstimulation syndrome 170–1,
 187–96, 203–20, 313, 322–3
 abandoning treatment 210
 aspiration of ascitic fluid 216–17
 classification 204–5, 205
 clinical presentation 205
 complications 212–13
 criteria for hospitalization 188
 management 213–15, 214
 mild 213–14
 moderate 214
 pathophysiology 187–9, 188, 205–6
 pleural effusion 216–17
 prediction 209–10
 prevalence 203–4
 prevention/reduction 189–91, 190, 209–12
 through IVM 349–50
 risk factors 190, 207–8, 207
 severe 214–15
 surgical treatment 216
 treatment 191–2
 ovarian prorenin-renin-angiotensin system 206
 ovarian protection 363
 ovarian steroid and protein synthesis 155–6,
 156
 ovarian stimulation 197–202, 346
 choice of FSH dose 197–9, 198
 hCG 199
 limited 350
 luteal support 199
 monitoring 199
 oocyte collection 199–201
 ovarian tissue
 autotransplantation 138
 collection 139
 cryopreservation 363
 culture 139–41, 140, 141
 ovarian transposition 363
 over-responders 345–52
 embryo transfer and endometrial
 preparation 347
 identification of 346
 IVF and IVM 347
 oocyte retrieval 346
 pregnancy outcome 347–9, 348, 349
 ovulation induction 115–16, 167–8
 ovulatory follicle 23

 paracentesis 171, 192, 216–17
 PARD6A 67
 parthenogenesis 106, 107, 109
 paternal imprinting 106, 107
 patient selection for IVM 326
 PCO *see* polycystic ovaries
 PCOS *see* polycystic ovary syndrome
Peg1 116
Peg3 109
 pentose phosphate pathway 23
 PGD *see* preimplantation genetic diagnosis
 pH buffering systems 300–1
 phosphodiesterase 4
 phosphodiesterase inhibitors 4, 43
 phospho-ribosyl-pyrophosphate 27
 Pincus, Gregory 231
 pleural effusion 216–17
 polar body extrusion 94–5
 polo-like kinase-1 92
 polyadenylated mRNA 68–9
 polyadenylation 59–62, 60, 62
 poly(A) polymerases 61
 Polycomb gene products 59
 polycystic ovaries 207, 222–3, 223
 risks of IVF 223
 polycystic ovary syndrome 7, 222, 222, 313,
 319–21
 androgen excess 165
 assisted reproductive technology
 strategy 321–3, 322
 blood flow 181
 clinical aspects 163–74
 definition 182, 320
 diagnosis 164
 histologic appearance 164

- polycystic ovary syndrome – *continued*
 history 163–4
 imaging 166–7
 inappropriate LH secretion 165
 insulin resistance 166
 insulin-sensitizing agents 168–70, 169
 in-vitro maturation 221–30, 322–3
 obesity 165–6, 321–2
 reproductive abnormalities 320–1
 risks of IVF 223
 size/no. of follicles 178–9, 179
 stromal area/volume 180–1
 stromal echogenicity 180
 surface area and volume of ovary 177–8
 treatment 167–8
 ultrasound diagnosis 175–85
 uterine size 178
 workup 164–5
 polymerase chain reaction 104
 poor embryo quality 323, 325
 poor responders 333–44
 definition of 334
 etiology 335–6
 IVM for 337–9, 338, 339
 management 336–7
 prediction of 334–5
 PP1 89–90, 90, 93
 PP2A 91–2
 pregnancy 313–18
 complications 316–17, 316
 multiple 314–15, 314
 pregnancy outcome
 IVF/IVM 354, 356–7, 356–8
 over-responders 347–9, 348, 349
 preimplantation embryos 116
 preimplantation genetic diagnosis, and
 IVM 227
 premature menopause 141
 preovulatory oocytes 26–8
 see also cumulus-oocyte complex
 primary follicles 123, 148
 primordial follicles 19–21, 20, 123
 culture systems 126–7, 126, 127
 development in culture 132
 follicle stimulating hormone 130
 gene expression 51–9
 inhibitory factors 131–2
 in-vitro maturation 124–5, 125–8, 126–8
 maturation 137–45
 nucleotide derivatives 131
 primordial germ cells 23–4, 123
 primordial oocyte 24, 25
 progesterone 199
 synthesis 156
 prolactin 188
 proliferating cell nuclear antigen 125
 prostaglandin synthetase inhibitors 215
 protein kinase A 86–7, 87
 protein kinase C 87
 protein phosphatase-1 88–9, 88
 protein synthesis 155–6, 156
 pyruvate 17, 19, 25, 26, 29

 quality assurance 297
 quality control 297, 302

 radiotherapy 137
 reactive oxygen species 17, 19, 30
 renal complications of OHSS 213
 renin-angiotensin system 206
 respiratory complications of OHSS 213
 restriction fragment length polymorphism 106
 Rfpl4 66
 RNA polymerase 54

 Saunders, Barbara 231
 scoring techniques 305–7, 306
 secondary follicles 123
 serotonin 188
 Sertoli cells 40
 serum supplementation 277
 sex hormone binding globulin 156
 signaling pathways 53–5
 single nucleotide polymorphisms 106
Snrpn 105, 109, 110, 115
 Sonic hedgehog 55
 Southern blotting 104
 sperm preparation 283, 285
 spindle attachment checkpoint 66
 Stein, Irving 163
 Stein-Leventhal syndrome 163
 stem cell factor 42, 130
 stem-loop binding protein 56
 steroids, IVM supplementation 279
 steroid synthesis 155–6, 156
 stromal area/volume 180–1
 stromal echogenicity 180
 SU5416 207

- superoxide anion 17
- superoxide dismutase 19
- supplements
 - embryo culture 299–300
 - ovarian tissue culture 140
- survival factors 53–5
- synaptonemal complex protein 1 51

- theca-interstitial cells 148
- three-dimensional ultrasound 177
- thromboembolism 212
- Tissue Culture Medium-199 28
- transabdominal ultrasound 175–7
- transcription factors 55–6
- transcription silencing 2
- transforming growth factor- 129
- transforming growth factor- 55
- translation 68–9
- transvaginal ultrasound 177
- transzonal processes 9–10
- Trichostatin A 58
- Trounson, Alan 233
- Turner's syndrome 124, 137, 141
- two-cell, two-gonadotropin concept 154

- ultrasound
 - IVF/IVM 354
 - ovarian stimulation 199
 - PCOS 175–85, 176
 - prior to IVM 224
 - three-dimensional 177
 - transabdominal 175–7
 - transvaginal 177

- vascular endothelial growth factor 188, 206–7
- Veeck, Lucinda 232
- ventriculo-septal defect 314
- vitrification 365

- Wood, Carl 233

- Zeste 59
- Znf127* 109
- zona pellucida 1, 41, 124, 148
 - formation 157
- zona proteins 59

