

## Index

Note: Page numbers followed by *f* indicate a figure on the corresponding page. Page numbers followed by *t* indicate a table on the corresponding page.

- Active Lives Survey, 30  
acute lymphoblastic leukemia (ALL), 99, 146  
advanced maternal age (AMA)  
  aneuploidy and, 61  
  antenatal care, 134–135, 136*f*  
  Caesarean delivery, 134  
  cardiac complications, 133  
  care in labour, 135  
  chromosomal abnormalities, 131, 132*t*, 135  
  congenital malformations, 131  
  defined, 131  
  fertility declines, 59  
  gestational diabetes, 27, 31, 61, 132–133  
  hypertensive disorders, 132  
  introduction to, 131  
  malpresentation, 134  
  maternal death, 134  
  medical and psychosocial risks, 174  
  medical ethics and, 176  
  placental disorders, 133  
  postnatal care, 135  
  postpartum hemorrhage, 134  
  practical management of, 134–135  
  preterm delivery, 133  
  small for gestational age, 133  
  stillbirth, 133–134  
  summary, 135  
  Venous Thrombo-Embolism, 120, 121*f*, 133  
age-related fertility decline  
  as barrier to reproduction, 12–13  
  biological basis for, 19–20  
  knowledge of, 59–60  
  male fertility and, 99  
  ovarian aging and, 81, 82*f*  
  rates of, 12, 58, 59  
age related subfertility, 20*f*  
agonist control, 89  
alcohol impact on fecundity, 30, 33  
algorithms in diagnostic testing, 48–51, 49*t*  
altered blood flow, 19, 22  
American College of Obstetricians and Gynecologists (ACOG), 31, 52, 174  
American Society for Reproductive Medicine (ASRM), 30, 56, 76, 81, 106, 149, 153, 156, 174, 176  
amniocentesis in multiple pregnancies, 123–124  
amyloid-like substance infiltration, 19, 22  
androgen receptor (AR), 85, 86  
androgens pre-treatment, 85–86  
aneuploidy  
  advance maternal age and, 61  
  correction through gene editing, 166, 167*f*, 168*f*, 169*f*  
  preimplantation genetic testing for aneuploidy, 75, 157  
  premature separation of chromatids, 99  
  in reproductive aging, 19  
  screening for, 122–123  
antagonist control, 89  
antenatal care, 134–135, 136*f*  
anti-müllerian hormone (AMH)  
  age-specific values, 71–72  
  cumulative live birth rate and, 45*t*  
  diagnostic testing of reproductive aging, 43–46, 45*t*, 47, 48*t*, 51–52  
  evaluating levels, 101  
  follicle development and, 83  
  normal population values, 65*f*  
  ovarian aging and, 64, 65*f*, 82  
  ovarian reserve and, 40, 47, 48*t*, 51–52, 71–73, 72*f*  
  overview of, 43–46, 101  
Antiphospholipid syndrome  
  testing, 125  
antral follicle count (AFC), 40, 42–43, 63, 71–73, 72*f*, 100–101  
antral follicle pool, 74  
APGAR score, 142, 143  
Apple, 60  
aromatase inhibition, 90–91  
artificial ovaries, 168, 170*f*  
Asherman's Syndrome, 23  
aspirin therapy to prevent pre-eclampsia, 119–120, 132  
ASRM Committee Opinion, 155  
Assisted Reproductive Technology (ART) over age forty. *See also* in-vitro fertilisation  
  age related subfertility and, 20*f*  
  child development concerns, 141, 143–145, 144*t*  
  ectopic pregnancy and, 126  
  ethical principles of, 177–179  
  guidelines for, 173–174  
  how often and how many attempts, 77*f*, 77–78  
  how to use, 73–77  
  introduction to, 1, 71  
  medical ethics in, 174–176  
  ovarian reserve testing, 39–40, 71–73, 72*f*  
  overestimating effectiveness, 57  
  parental death concerns, 176–177  
  preconception consultation, 73  
  prevalence of, 173  
  psychosocial ethics, 176–177  
  social egg freezing and, 56  
  success rates, 1  
  uterine aging and, 22–23  
  when to stop, 78  
Attention Deficit/Hyperactivity Disorder (ADHD), 148  
Autism Spectrum disorder (ASD), 73, 99, 147–148  
autologous eggs, 93, 173, 175  
autologous germline mitochondrial energy transfer (AUGMENT), 164  
autonomy concerns, 177–178  
behavior issues in children conceived by mothers over forty, 147  
beneficence concerns in ART over age forty, 178  
birth defects, 73  
body mass index (BMI), 27–28, 33, 41, 50, 102  
BRCA gene, 98, 102  
British Infertility Counseling Guidelines (BICA), 109, 110*t*

## Index

- C-reactive protein (CRP), 31  
 Caesarean delivery, 134, 135  
 caffeine impact on fecundity, 30, 33  
 caloric restriction, 19, 22  
 cancer history and limited reproduction, 102  
 cancers in childhood, 146–147  
 cardiac complications, 133  
 cardiomyopathy risks, 73  
 cardiovascular disease risk, 63, 73, 133  
 care in labour, 135  
 cell free fetal DNA (cffDNA), 122–123  
 cellular fragmentation, 19  
 Center for Disease Control (CDC), 48, 73, 145  
 Center for Human Reproduction in NYC (CHR), 81  
 chiasmata formation, 19, 20–21  
 child development with mothers over forty  
   Attention Deficit/Hyperactivity Disorder, 148  
   Autism Spectrum disorder, 147–148  
   behavior and cognition issues, 147  
   cancers in childhood, 146–147  
   childhood outcomes, 146  
   community support, 150–151  
   infant parenting strategies, 149–150  
   introduction to, 141  
   morbidity and hospitalizations, 147  
   neurodevelopment diseases, 147–148  
   over 18 parenting strategies, 150  
   parenting strategies in, 148–151  
   perinatal and neonatal outcomes, 141–146  
   school-aged parenting strategies, 150  
   teen and tween parenting strategies, 150  
   toddler parenting strategies, 150  
   using donor eggs/oocytes, 145–146, 149  
   using donor sperm, 149  
   using their own oocytes, 143–145, 144*t*  
 childlessness, 3, 7–10, 12–13  
 chorionicity in multiple pregnancies, 123–124  
 chromosomal abnormalities, 99, 131, 132*t*, 135, 175. *See also* aneuploidy  
 circadian rhythm, 31  
 clinic support structures, 108–109  
 clinical pregnancy rate (CPR), 42  
 clock gene expression, 31  
 clomiphene citrate (CC), 73, 89–90, 91*f*  
 clomiphene citrate challenge test (CCCT), 40, 101  
 Cochrane Database, 75  
 Cochrane Meta-analysis, 132  
 Coenzyme Q-10 (CoQ10), 29, 76, 88  
 cognition issues in children  
   conceived by mothers over forty, 147  
 cohesin defects, 19, 21  
 congenital malformations, 131  
 corporate subsidizing of social egg freezing, 60  
 cost effectiveness of social egg freezing, 58  
 COVID pandemic, 13, 106, 107*t*  
 CRISPR-Cas9 gene editing, 166, 168*f*, 169*f*  
 crown rump length (CRL), 122, 124  
 cryopreserved eggs, 10, 12, 13, 51, 52, 153. *See also* social egg freezing  
 cumulative LBR (CLBR), 56, 57  
 cumulus-oocyte complex (COC), 84  
 cytogenetic testing, 125–126  
 Danish Cancer registry, 146  
 decision-tree model, 58  
 dehydroepiandrosterone acetate (DHEA), 30, 63, 75, 85–86  
 dehydroepiandrosterone (DHT), 75  
 diagnostic testing of reproductive aging  
   algorithms in, 48–51, 49*t*  
   anti-müllerian hormone and, 43–46, 45*t*, 47, 48*t*, 51–52  
   antral follicle count and, 40, 42–43  
   chronological age and, 41  
   deciding on, 46, 47*t*  
   discordant tests, 47, 48*t*  
   follicle stimulating hormone and, 40, 41–42, 47, 48*t*  
   future needs, 52–53  
   historical and limited value tests, 40  
   ideal ovarian reserve test, 40–41  
   introduction to, 39  
   oocyte declines and, 39, 45  
   ovarian reserve, 39–40, 71–73, 72*f*  
   patient choices and, 51–52  
 diet and natural conception over age of forty, 28, 33  
 digitization of patient support for fertility care, 114–115  
 diminished ovarian reserve (DOR), 40, 52  
 discordant tests results, 47, 48*t*  
 distributive justice in ART over age forty, 178  
 donor eggs/oocytes  
   child development with mothers using, 145–146, 149  
   epigenetic changes, 157  
   fresh vs. frozen, 153–155  
   IVF with, 10  
   legal considerations, 156–157  
   medical and obstetric events with, 159  
   medical ethics of, 175  
   menopause and, 99, 145, 156, 173  
   postmenopausal recipients, 156  
   pregnancy risks with, 153  
   preimplantation genetic testing for aneuploidy, 157  
   preparing recipient endometrium, 155  
   progesterone needs in older women, 23  
   programmed vs. natural endometrium preparation, 155–156, 158, 159*f*  
   protocols for, 158, 159*f*  
   recurrent implantation failure, 157–158  
   screening of, 156  
   source of, 153  
   success rates using, 153, 154*f*  
   uterine aging and, 22  
 donor sperm, 61, 62*f*, 149  
 dormant follicle activation, 164  
 dyskeratosis congenital, 21  
 early ovarian aging (EOA)  
   background on, 62–63  
   fertility counseling/screening, 63, 65*f*  
   in-vitro fertilisation with, 63  
   management of fertility, 63  
   overview of, 62–65  
   social egg freezing with, 62–65  
 early pregnancy unit (EPU), 119  
 East Asian marriage expectations, 5  
 eating disorders, 28  
 ectopic pregnancy  
   defined, 126  
   expectant management of, 127  
   heterotopic pregnancy, 127, 128  
   management of, 126–128  
   medical management of, 127  
   surgical management of, 127–128  
 Ectopic Pregnancy Trust, 129  
 education  
   fertility and, 9–10, 10*t*  
   highly-educated women, 3  
   late reproduction and childbearing trends, 5–6, 6*f*, 12, 15*f*, 51  
   link to first births, 4  
   lower educated women, 3  
   tertiary education, 4  
 Egg Freezing Counseling Tool, 50

- egg-freezing technology. *See* cryopreserved eggs; social egg freezing
- egg vitrification, 153
- eggs. *See* donor eggs/oocytes; oocyte decline; oocytes; social egg freezing
- embryonic stem cells (ESC), 164
- Endometrial Function Test (EFT), 157
- Endometrial Receptivity Assay (ERA), 157
- endometrial telomerase, 23
- endometrium preparation for donor eggs/oocytes, 155–156, 158, 159f
- epigenetic changes, 73, 157, 175
- ESHRE guideline on patient support, 109–110
- estradiol levels, 40, 100
- estradiol priming, 87, 158
- estrogen supplementation, 91–93
- ethics of ART over age forty
- autonomy concerns, 177–178
  - beneficence concerns, 178
  - justice concerns, 178–179
  - medical ethics in, 174–176
  - nonmaleficence concerns, 178
  - overview of principles, 177–179
  - prevalence of ART over age forty, 173
  - psychosocial ethics, 176–177
- ethinyl estradiol (EE), 92
- euploid embryos, 76
- European Society of Human Reproduction and Embryology (ESHRE), 56, 125
- European trends in late reproduction
- age-related infertility, 12–13
  - fertility intentions vs. actual fertility, 7f, 8f, 9f, 9t, 10t, 10, 15f
  - fertility rates, 14f
  - introduction to, 3–4
- expectant management, 63, 125, 127
- Facebook, 60
- fertility
- actual fertility vs., 7f, 8f, 9f, 9t, 10t, 10
  - childlessness and, 7–10
  - education and, 9–10, 10t
  - late fertility, 3, 12–13
  - live-birth declines after IVF, 10–12
  - male fertility and aging, 99, 175
  - management with early ovarian aging, 63
  - paternal age and, 99, 175
  - screenings, 63, 65f
- Fertility Assessment and Counselling Clinic (FAC), 64
- fertility counseling
- after failed cycle, 94
  - early ovarian aging and, 63, 65f
  - evaluation, 99–101
  - general considerations, 101–102
  - introduction to, 98
  - needs and wants of women in, 63, 65f
  - special considerations, 102–103
- fertility evaluation beyond age forty
- anti-müllerian hormone levels, 101
  - antral follicle count, 100–101
  - clomiphene citrate challenge test levels, 101
  - estradiol levels, 40, 100
  - follicle stimulating hormone levels, 100
  - follicular pool depletion and, 98–99
  - overview, 99–101
- fertility-limiting behaviours, 4
- Fetal Anomaly Screening Programme (FASP), 122
- Finnish Birth Registry, 142
- FMR-1 gene, 98, 102
- folic acid, 28, 30, 33, 119
- follicle atresia, 84
- follicle development, 83f, 84
- follicle stimulating hormone (FSH)
- diagnostic testing and, 40, 41–42, 47, 48t
  - evaluating levels, 100
  - human menopausal gonadotropins and, 92
  - impact of sleep on, 31
  - IVF over forty and, 75
  - with or without LH activity, 92
  - ovarian reserve assessment, 71–73, 72f, 82
  - screening tests for, 64
- follicular activation technology, 164
- follicular microenvironment, 19
- follicular pool depletion, 98–99
- freeze-all approach, 76
- functional ovarian reserve (FOR), 82. *See also* ovarian reserve
- futility of treatment, 81
- gender revolution, 4, 13
- gene editing, 166, 167f, 168f, 169f
- Generation Z, 13
- germinal vesicle transfer (GVT), 164
- germline stem cells (GSCs), 89, 164
- gestational diabetes, 27, 31, 61, 132–133
- gestational trophoblastic disease, 125
- global financial crisis (2008–2012), 4
- globalisation, 4
- Glucose Tolerance testing (GTT), 132–133
- gonadotoxic treatments, 56
- gonadotropin (GnRH) stimulation cycles, 40, 73, 74–75
- Google, 60
- Graafian follicle, 83–84
- granulosa cells. *See also* anti-müllerian hormone
- androgen receptor and, 86
  - Coenzyme Q-10 and, 29
  - follicle-stimulating hormone and, 75
  - IGF-1 receptors on, 88
  - importance to developmental competence, 19
  - loss of, 100
  - in oocyte development, 84
  - premature luteinization of follicles, 93
  - primordial follicles and, 83–84
  - vitamin D and, 29
- growth factors, 75, 83–84, 87, 88–89, 164, 166
- growth hormone (GH) production, 75, 87–88
- health advice in first trimester, 119
- heterotopic pregnancy, 127, 128
- high-risk combined screening, 122
- highly-educated women, 3
- Highly Individualized Egg Retrieval (HIER), 93, 94f
- hormonal contraceptives, 43, 64, 87
- hormonal pre-treatment
- androgens, 85–86
  - estradiol priming, 87
  - estrogen supplementation, 91–93
  - Human Growth Hormone, 87–88
  - to improve ovarian reserve, 85–88
  - luteal oral contraceptives, 87
  - progesterin supplementation, 87
- hospitalizations of children conceived by mothers over forty, 147
- human chorionic gonadotropin,  $\beta$  subunit ( $\beta$ hCG), 122, 127, 128–129
- human embryonic stem cells (hES), 166
- Human Fertilisation and Embryology Authority (HFEA), 10, 76, 108–109, 110–111
- Human Fertilisation and Embryology (HFE) Acts, 166
- Human Growth Hormone (HGH), 87–88
- human menopausal gonadotropins (HMG), 92
- hypertensive disorders, 27, 132

## Index

- hypothalamic-pituitary-adrenal (HPA) axis, 31
- hypothalamic pituitary ovarian (HPO) axis, 40, 41–42, 46
- hysterectomy risks, 23, 73
- immunity compromises, 31
- in-vitro fertilisation (IVF)
- age factors, 41
  - autologous eggs and, 93, 173, 175
  - coordination issues in patient support, 113
  - with early ovarian aging, 63
  - exercise following, 31
  - follicle stimulating hormone and, 75
  - live birth rates and, 74
  - ovarian response in, 42
  - reproduction plans and, 12–13
  - stimulation tests and, 40
  - study of granulosa cells, 93
- in-vitro fertilisation (IVF) with ovarian aging
- age-related fertility decline, 81, 82*f*
  - back-to-back cycles of, 93
  - counseling after failed cycle, 94
  - cycle control, 89, 90*f*
  - embryos and, 93–94
  - estrogen supplementation, 91–93
  - Highly Individualized Egg Retrieval, 93, 94*f*
  - hormonal pre-treatment, 85–88
  - introduction to, 81
  - mini IVF, 92–93
  - pre-treatment to improve ovarian reserve, 85–89
  - stimulation protocols, 89–93
  - summary of, 103
  - treatment expectations, 81
- in-vitro gametogenesis (IVG), 164–166, 167*f*
- in vivo study of granulosa cells, 93
- induced pluripotent stem cells (iPSCs), 166, 168
- infant parenting strategies, 149–150
- inherited thrombophilia testing, 125
- inherited thrombophilias testing, 125
- inositols, 86–87
- insulin like growth factor (IGF-1), 75, 87
- interactive communication in fertility care, 114*f*, 114
- International Society for Stem Cell Research (ISSCR), 166
- intrauterine adhesions, 125
- intrauterine death, 27
- justice concerns in ART over age forty, 178–179
- lambda sign, 123
- late mother, defined, 12
- late reproduction and childbearing
- education and global trends, 5–6, 6*f*
  - fertility intentions vs. actual fertility, 7*f*, 8*f*, 9*f*, 9*t*, 10*t*, 10
  - importance of late fertility to reproductive plans, 12–13
  - introduction to, 1, 3–4
  - social and economic trends in, 4–5
- letrozole (LTZ), 73, 89–91
- leuprolide administration, 158
- levothyroxine use in euthyroid women, 126
- life expectancy, 1, 177
- lifestyle advice in first trimester, 119
- live birth rate (LBR)
- anti-müllerian hormone and, 45*t*
  - declines after IVF, 10–12
  - DHEA and, 75
  - diagnostic testing and, 40, 44, 50, 51
  - futility of treatment and, 81
  - in-vitro fertilisation and, 74
  - IVCF treatment delays and, 106
  - maternal death risks, 73
  - rates with IVF, 74
  - social egg freezing and, 56
  - testosterone supplementation and, 63
- long agonist cycles, 89
- low functional ovarian reserve (LFOR), 82, 86
- lower educated women, 3
- luteal inhibition of advanced follicular recruitment, 84, 85*f*
- luteal oral contraceptives, 87
- luteinizing hormone (LH), 31, 90
- macrosomia, 27, 77
- male fertility and aging, 99, 175
- malpresentation, 134
- maternal death, 73, 134, 176–177
- maternal mortality ratio (MMR), 134
- maternal spindle transfer (MST), 164, 165*f*
- mean gestational sac diameter (MSD), 124
- MedCalc, 50
- medical ethics in ART over age forty, 174–176
- medical management, 125, 127
- medically assisted reproduction (MAR), 4, 5, 10–12, 13, 109
- Mediterranean diet, 33
- menopause
- age-related onset, 12, 19, 163
  - age-specific androgen levels, 86
  - anti-müllerian hormone and, 46
- antral follicle count and, 42, 43, 101
- delay/reversal of, 163
- donor eggs and, 99, 145, 156, 173
- early ovarian aging and, 62–63
- fecundability prior to, 39
- fertility counseling and, 101–102
- follicle stimulating hormone levels and, 41
- follicular pool depletion and, 98–99
- functional menopause, 82
- germ cells and, 24
- iatrogenic menopause, 89, 102
- oocyte numbers at, 39
- ovarian reserve testing and, 39
- ovarian volume and, 42
- ovulation frequency before, 98
- pregnancy and, 173
- smoking and, 30
- symptoms of, 63
- uterine age and, 22–23
- vitamin D and, 29
- menstrual cycle
- age-related changes in, 100
  - anti-müllerian hormone and, 46, 64, 101
  - antral follicle count and, 42
  - clomiphene citrate administration, 90
  - embryo transfers and, 158
  - follicle development, 83*f*, 84
  - hypothalamic-pituitary-adrenal axis and, 31
  - hypothalamic-pituitary-ovarian axis and, 41
  - irregularity of, 63, 98, 102, 124
  - luteal inhibition of advanced follicular recruitment, 84, 85*f*
  - monthly fecundity and, 39
  - normal functioning of, 83–84
  - ovarian pool and, 43
  - in over forty women, 84, 85*f*
  - sleep impact on, 31
  - telomerase and, 23
- methotrexate in ectopic pregnancy, 127
- microdose agonist protocol, 89
- Millennial generation, 13
- mini in-vitro fertilisation (IVF), 92–93
- miscarriage
- age-related, 3, 12, 19, 23, 98, 107
  - aneuploidy rate and, 39
  - anti-müllerian hormone and, 45–46
  - antral follicle count and, 42, 63
  - BMI and, 27
  - chromosomal abnormality and, 99
  - diagnosis of, 124
  - donor eggs and, 153, 154*f*



- family history of, 102  
 in first trimester, 124–126  
 first trimester management, 119  
 late reproduction and, 13  
 management of, 124–125  
 oocyte quality and, 24  
 PGT-A and, 75  
 rates of, 42, 45, 98  
 recurrence of, 119, 125–126  
 risks of, 27, 45, 124*t*, 129  
 smoking and, 102
- Miscarriage Association, 129  
 misoprostol use in miscarriage, 125  
 mitochondrial DNA (mtDNA), 19, 21, 82, 88, 99  
 mitochondrial replacement therapy (MRT), 163–164, 165*f*
- Model Act Governing Assisted Reproductive Technology, 157  
 mono-follicular development, 74  
 monozygotic twins. *See* multiple pregnancies  
 morbidity in children conceived by mothers over forty, 147  
 multidisciplinary team (MDT)  
 approach to infertility care, 113  
 multiple partnerships, 5  
 multiple pregnancies  
 determining chorionicity and amnionicity, 123–124  
 first trimester management, 123–124  
 general advice, 123  
 reduction of, 124  
 screening in, 122  
 myoinositol, 87
- National Institute for Health and Care Excellence (NICE), 108, 119, 132–133
- The National Organ Transplant Act, 156
- natural conception over age forty  
 alcohol impact on, 30, 33  
 body mass index and, 27–28, 33  
 caffeine impact on, 30, 33  
 diet and, 28, 33  
 introduction to, 27  
 miscarriage rates, 98  
 physical activity and, 30–31  
 sleep and, 31–32, 33  
 smoking impact on, 30, 33  
 stress reduction and, 32–33  
 vitamin supplementation, 28–30
- NEETs (not in employment, education, or training), 4  
 negative lifestyle variables, 27  
 neonatal outcomes. *See* perinatal and neonatal outcomes  
 neurodevelopment diseases in children conceived by mothers over forty, 147–148
- Non-Invasive Prenatal Testing (NIPT), 122–123  
 nonmaleficence concerns in ART over age forty, 178  
 nuchal translucency (NT) measurements, 122  
 nuclear DNA, 82  
 nuclear transfer (NT) technology, 163–164  
 nulliparous women, 41, 142
- obstetric and gynecologic histories, 102  
 obstetric management in first trimester  
 aspirin therapy to prevent pre-eclampsia, 119–120, 132  
 co-morbidity assessment, 120  
 early pregnancy unit role, 119  
 ectopic pregnancy, 126–128  
 general points, 119–120  
 health and lifestyle advice, 119  
 introduction to, 119  
 miscarriage during, 124–126  
 multiple pregnancies, 123–124  
 pregnancy of unknown location, 128–129  
 psychological impact of, 129  
 Recurrent Implantation Failure, 126  
 screening during, 122–123  
 Venous Thrombo-Embolic risk, 120, 121*f*
- obstetric screening  
 in first trimester, 122–123  
 high-risk combined screening, 122  
 multiple pregnancies and, 122  
 Non-Invasive Prenatal Testing, 122–123
- obstetrics and gynecology (OB/GYN) physicians, 51  
 Office for National Statistics (UK), 56  
 omega-3 supplementation, 29  
 oocyte quantity/quality decline. *See also* in-vitro fertilisation (IVF) with ovarian aging; ovarian aging  
 age-related, 19–21  
 amyloid-like substance infiltration, 19, 22  
 chiasmata formation, 19, 20–21  
 cohesin defects, 19, 21  
 diagnostic testing of reproductive aging and, 39, 45  
 introduction to, 19–20  
 mitochondrial DNA (mtDNA), 19, 21  
 omega-3 supplementation against, 29  
 oxidative stress and, 29
- Production Line and, 19, 21–22  
 reactive oxygen species, 19, 21  
 sirtuins and caloric restriction, 19, 22  
 summary of, 23–24  
 telomere attrition, 19, 21
- oocytes. *See also* donor eggs/ oocytes; social egg freezing  
 autologous eggs, 93, 173, 175  
 child development with mothers using their own, 143–145, 144*t*  
 cryopreserved eggs, 10, 12, 13, 51, 52, 153  
 efficiency of, 56  
 granulosa cells and, 84  
 improving quality of, 163  
 miscarriage and, 24  
 numbers at menopause, 39  
 quality decreases, 99  
 retrieval before follicles fail, 93  
 social egg freezing, 58–59  
 unused oocytes, 61  
 vitrification techniques, 56
- oral contraceptives, 42, 44, 87, 92, 101, 102  
 osteoporosis risk, 63  
 other surgical subspecialist (OSS), 51  
 ovarian age algorithm (OvAge), 50  
 ovarian aging. *See also* early ovarian aging; in-vitro fertilisation (IVF) with ovarian aging; oocyte declines  
 altered blood flow, 19, 22  
 amyloid-like substance infiltration, 19, 22  
 chiasmata formation, 19, 20–21  
 cohesin defects, 19, 21  
 introduction to, 19–20  
 mitochondrial DNA (mtDNA), 19, 21  
 mitochondrial dysfunction in, 88  
 physiology of, 83–84  
 Production Line and, 19, 21–22  
 reactive oxygen species, 19, 21  
 resveratrol and, 19, 22  
 sirtuins and caloric restriction, 19, 22  
 summary of, 23–24  
 telomere attrition, 19, 21  
 theories of, 20
- ovarian assessment report (OAR), 50  
 ovarian cortex cryopreservation and transplantation (OCT), 65–66  
 ovarian hyperstimulation syndrome (OHSS), 39, 41, 42, 46, 61  
 ovarian reserve (OR)  
 anti-müllerian hormone, 40, 47, 48*t*, 51–52, 71–73, 72*f*

## Index

- ovarian reserve (OR) (cont.)  
 antral follicle count and, 71–73, 72f  
 ART testing, 39–40, 71–73, 72f  
 assessment of, 71–73, 72f  
 diminished ovarian reserve, 40, 52  
 diminished without genetic risk factors, 98  
 follicle stimulating hormone and, 71–73, 72f  
 functional ovarian reserve, 82  
 gonadotropin dose and, 92  
 hormonal pre-treatment to improve, 85–88  
 low functional ovarian reserve, 82, 86  
 menopause and, 39  
 pre-treatment to improve, 85–89  
 ovarian stem cells (OSC), 89  
 ovarian stimulation  
 in aging women, 57, 73–74, 163  
 anti-müllerian hormone and, 44, 71, 101  
 GnRH antagonist protocol, 74  
 in Highly Individualized Egg Retrieval, 93  
 Human Growth Hormone (HGH) supplementation, 88  
 IVF and, 102  
 ovarian cortex cryopreservation and transplantation, 65  
 risks with, 61, 63  
 stromal blood flow and, 22  
 testosterone supplementation and, 63  
 ovulation frequency before menopause, 98  
 own eggs and donor sperm (OEDS), 61, 62f  
 oxidative stress, 29  
 panic partnering, 59, 60  
 parental death concerns, 176–177  
 parental health concerns, 177  
 parenting strategies for children of mothers over forty, 148–151  
 passive coping mechanisms, 110  
 paternal age and fertility, 99, 175  
 patient support for fertility care  
 business growth and, 113  
 clinic support structures, 108–109  
 complaint management, 112–113  
 COVID pandemic and, 106, 107t  
 digitization framework, 114–115  
 ESHRE guideline on, 109–110  
 formal counseling, 109, 110t  
 HFEA guidelines on, 108–109, 110–111  
 infertility management and, 108, 109t  
 interactive communication, 114f, 114  
 introduction to, 106  
 IVF coordination issues, 113  
 multidisciplinary team (MDT) approach, 113  
 personalized care and, 113  
 practical elements of, 111  
 reorganization of outpatient clinics, 111, 112t  
 summary of, 115  
 support for staff, 111–112  
 treatment packages, 113  
 wider concept of, 107–108  
 pelvic inflammatory disease (PID), 126  
 perinatal and neonatal outcomes, 141–146  
 placental disorders, 133  
 platelet-rich plasma (PRP), 88–89, 164  
 polar body transfer (PBT), 164  
 polycystic ovary syndrome (PCOS), 32, 87  
 postnatal care, 135  
 postpartum hemorrhage, 73, 134  
 pre-eclampsia, 61, 73, 76, 119–120, 120t, 132  
 preconception counseling, 27, 73  
 pregnancy of unknown location (PUL)  
 defined, 128  
 management in first trimester, 128–129  
 progesterone levels, 128–129  
 $\beta$ hCG levels, 128  
 preimplantation genetic testing for aneuploidy (PGT-A), 75, 157  
 preimplantation genetic testing (PGT), 102  
 premature ovarian failure (POF), 164  
 premature ovarian insufficiency (POI), 62–63, 64  
 preterm birth risks, 123  
 preterm delivery, 133  
 primordial follicles, 81  
 primordial germ cells (PGCs), 164–166  
 PRISM trial, 126  
 Production Line Hypothesis, 19, 21–22  
 progesterone, 23, 31, 126, 128–129  
 progesterone intrauterine devices, 44  
 progesterone only oral contraceptives, 44  
 progestin supplementation, 87  
 pronuclear transfer (PNT), 164  
 psychological impact of pathology in over forty women, 129  
 psychological support for patients, 107  
 psychosocial ethics of ART, 176–177  
 pulmonary embolism risks, 61  
 reactive oxygen species (ROS), 19, 21, 76  
 ReceptivaDx test, 158  
 reciprocal nuclear transfer, 19  
 Recurrent Implantation Failure (RIF), 126, 157–158  
 recurrent miscarriage, 125–126  
 reduction of multiple pregnancies, 124  
 reorganization of outpatient clinics, 111, 112t  
 reproductive aging delays/reversals  
 aneuploidy correction through gene editing, 166, 167f, 168f, 169f  
 artificial ovaries, 168, 170f  
 dormant follicle activation, 164  
 follicular pool depletion, 98–99  
 improving quality of oocytes, 163  
 in-vitro gametogenesis, 164–166, 167f  
 introduction to, 163  
 mitochondrial replacement therapy, 163–164, 165f  
 platelet-rich plasma and, 164  
 reproductive plans, 12–13  
 reproductive specialists (REI), 178  
 resveratrol, 19, 22  
 RhD negative women, 122  
 Royal College of Obstetricians and Gynaecologists (RCOG), 56, 125  
 salpingostomy for ectopic pregnancy, 127–128  
 SART-CORS database, 146  
 schizophrenia, 73, 99  
 school-aged parenting strategies, 150  
 second demographic transition, 5  
 selective estrogen receptor modulator (SERM), 90  
 selenium supplementation, 30  
 senescence-accelerated mice (SAM), 21  
 sex-hormone-binding globulin (SHBG), 85, 86  
 sirtuins and caloric restriction, 19, 22  
 skill-biased technological change, 4  
 sleep and natural conception over age of forty, 31–32, 33  
 small for gestational age (SGA), 133  
 smoking impact on fecundity, 30, 33, 102  
 social egg freezing (SEF)

- background on, 56  
 corporate subsidizing of, 60  
 cost effectiveness, 58  
 debate surrounding, 60–61  
 donor sperm use, 61, 62*f*  
 early ovarian aging and, 62–65  
 general public attitude toward, 59–60  
 knowledge of age-related fertility decline, 59–60  
 motivations toward, 59  
 optimal age for freezing eggs, 56–57  
 optimal number of eggs for freezing, 57  
 ovarian cortex cryopreservation and transplantation *vs.*, 65–66  
 social egg freezer attitudes toward, 60  
 summary of, 66  
 using stored oocytes, 58–59  
 societal injustice of career *vs.* motherhood choice, 61  
 Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), 44–45  
 Society for Assisted Reproductive Technology (SART), 50  
 stem cells  
   embryonic stem cells, 164  
   germline stem cells, 89, 164  
   human embryonic stem cells, 166  
   induced pluripotent stem cells, 166, 168  
   ovarian stem cells, 89  
 stillbirth, 133–134  
   age-related, 23, 73  
   multiple pregnancy and, 123  
 stress reduction and natural conception over age of forty, 32–33  
 subsidizing social egg freezing, 60  
 surgical management of ectopic pregnancy, 127–128  
 Swedish Medical Birth Register, 141*f*  
 teen parenting strategies, 150  
 telomerase expression by endometrium, 23  
 telomere attrition, 19, 21  
 tertiary education, 4  
 testosterone (T), 75  
 thrombosis risks, 73  
 thrombotic disease, 27  
 thyroid function testing, 125  
 toddler parenting strategies, 150  
 transvaginal egg collection risks, 61  
 Trisomy 16, 124  
 Trisomy 22, 124  
 Trisomy 21 (Down's Syndrome), 122, 124  
 Trisomy 18 (Edward's Syndrome), 122  
 Trisomy 13 (Patau's Syndrome), 122  
 tumour necrosis factor (TNF), 31  
 tween parenting strategies, 150  
 two-child family model, 3, 9  
 ultrasound scan  
   antral follicle count and, 42, 100  
   estimating ovarian reserve, 46–47  
   for fetal complications, 27–28  
   fetal reduction with, 124  
   in miscarriage, 124, 125  
   for multiple pregnancies, 123  
   for pregnancy of unknown location, 128  
   response to estradiol, 158  
   transvaginal ultrasound, 100, 119, 128  
 uniform parentage act (UPA), 156  
 Univfy, 50  
 unused oocytes, 61  
 U.S. Food and Drug Administration, 75, 156  
 uterine aging, 22–23, 99  
 utility of treatment, 81  
 vascular endothelial growth factor (VEGF), 164  
 Venous Thrombo-Embolicism (VTE), 120, 121*f*, 133  
 virtual clinics, 115  
 vitamin C supplementation, 29  
 vitamin D insufficiency, 29, 33  
 vitamin D supplementation, 119  
 vitamin E supplementation, 29  
 zinc supplementation, 30