

Index

ACC. <i>See</i> adrenocortical carcinoma	AI. <i>See</i> adrenal insufficiency	autoimmune thyroid disease
acromegaly, 87–89	aldosterone, 69, 167	chronic autoimmune thyroiditis,
ACT. <i>See</i> antenatal corticosteroid	excess of, 173, 175–176	144–147
therapy	in PE, 156–157	euthyroid, 147–148
ACTH. <i>See</i> adrenocorticotrophic	allopregnanolone, 8–9, 45	AVP. <i>See</i> arginine vasopressin
hormone	alpha-adrenergic receptor blockers,	
activin, 35	for pheochromocytoma or	bacterial vaginosis (BV), 123, 131
ADH. <i>See</i> antidiuretic hormone	paraganglioma, 177	bariatric surgery
adipokines, 93	amiloride, 175–176	for maternal obesity, 112
adiponectin, 93	analgesia, OT administration for, 29	offspring outcomes after, 113
adipose tissue, estrogen synthesis in,	androgens	pregnancy and prenatal outcomes
42	CAH excess of, 170–173	after, 112–113
adrenal disease, 158	fetal production of, 168	barusiban, 27–29
ACC, 177–179	normal pregnancy changes in,	birth trauma, GDM association
CAH, 170–173	166–167	with, 97–98
Cushing’s syndrome, 164–173	in PTB, 126–128	birth weight
PA, 175–176	androstenedione, 152–153, 166–167	adult plasma volume and, 61–62
pheochromocytoma or	anemia, physiological, 61–62	chronic disease risk in later life
paraganglioma, 176–178	angiogenesis, estrogen role in, 44–45	and, 189–190
primary and secondary AI, 168–170	angiotensin, 69, 156–157, 167	GDM association with increased,
adrenal gland. <i>See also</i>	ANP. <i>See</i> atrial natriuretic peptide	97–98
hypothalamus–pituitary–	antenatal corticosteroid therapy	maternal bariatric surgery effects
adrenal axis	(ACT), 132–133, 192	on, 112–113
anatomy and histology of, 164	antibiotics, PTB management with,	maternal BMI role in, 108–109
fetal, 168	130–133	placental role in, 190–191
normal pregnancy function of,	antidiuretic hormone (ADH),	reproductive function in later life
164–165	61–62	and, 193–194
androgens, 166–167	antihypertensive therapy, for PA,	blastocyst implantation. <i>See</i>
catecholamines, 167–168	175–176	implantation
glucocorticoids, 165–167	antithyroid drugs (ATDs), 143–144	blood flow, uterine, 45
mineralocorticoids, 167	apoplexy, pituitary, 79–80	blood pressure. <i>See also</i>
adrenal insufficiency (AI), 170	arginine vasopressin (AVP),	hypertension
chronic corticosteroid	157–158, 165–167	birth weight relationship to,
replacement for, 164–169	aromatase deficiency, 45–46, 153	189–190
diagnosis of, 168–169	ART. <i>See</i> assisted reproductive	maternal, 62
etiology of, 169	technology	BMI. <i>See</i> body mass index
monitoring of, 169	ASD. <i>See</i> autism spectrum disorder	BNP. <i>See</i> brain natriuretic peptide
stress dosing of corticosteroid	assisted reproductive technology	body mass index (BMI). <i>See also</i>
replacement for, 169–170	(ART)	obesity
adrenalectomy, 175–177	OT receptor antagonist use in, 27	birth weight association with,
adrenaline, 167–168	thyroid autoimmunity in	108–109
adrenocortical carcinoma (ACC),	outcomes of, 147–148	neonatal and early infancy, 190
177–179	ATD. <i>See</i> antithyroid drugs	PTB association with, 122
adrenocorticotrophic hormone	atosiban, 27–28	bonding, mother–infant, 6, 24–25
(ACTH), 1–5, 14–16	PTL prevention with, 27–29	brain. <i>See</i> fetal brain; maternal
chronic disease risk in later life	spontaneous abortion prevention	brain
and, 191–193	with, 27	brain natriuretic peptide (BNP), 157
normal pregnancy changes in,	atrial natriuretic peptide (ANP),	breast, placental signals to, 18
165–167	157	breast-feeding
pituitary tumors secreting,	autism spectrum disorder (ASD),	maternal obesity challenges in, 115
164–174	26–27	OT administration for, 25–26

Index

- breast-feeding (cont.)
 OT role in, 24
 PRL role in, 73–74
 prolactinoma management after, 82–83
 prolactinoma management during, 80–82
 somatostatin analogs during, 89
broad spectrum chemokine inhibitors (BSCIs), 135–136
bromocriptine, 67–68
 before pregnancy, 76–77
 during pregnancy, 77–79
 safety of, 80
BSCIs. *See* broad spectrum chemokine inhibitors
BV. *See* bacterial vaginosis
cabergoline
 for acromegaly, 88–89
 for Cushing’s syndrome, 164–174
 for hyperprolactinemia, 73–83
 before pregnancy, 76–77
 during pregnancy, 77–79
 safety of, 80–81
CAH. *See* congenital adrenal hyperplasia
calcineurin, 62–63
caloric intake
 for GDM management, 101–102
 for maternal obesity, 112
CAPs. *See* contraction-associated proteins
carbimazole, 143–144
carbohydrate metabolism, 91–92
cardiac adaptations, maternal, 62–63
cardiac output (CO), 62
cardiovascular disease (CVD)
 developmental programming theory of, 189–190
 GDM association with risk for maternal, 100–101
 in GDM offspring, 100–101
cardiovascular system. *See* maternal cardiovascular system
catecholamines, 167–168
catecholestrogens, 43
catechol-O-methyltransferase (COMT), 45–46
CCK. *See* cholecystokinin
cerebral palsy (CP), 133
cervical cerclage, 132
cervical length (CL), 130
cervical pessary, 132
cervical surgery, PTB association with previous, 123
Cesarean section
 GDM association with, 98
 PTB association with previous, 122–123
chemokine inhibitors, 135–136
cholecystokinin (CCK), 29
cholesterol
 maternal levels of, 17–18
 oxytocin receptor membrane localisation and, 21
 progesterone synthesis from, 14–16
chorionic disease, 38
chorionic gonadotropin. *See* human chorionic gonadotropin
chronic autoimmune thyroiditis, 144–147
chronic disease. *See* non-communicable disease
chronic ectopic pregnancy, 38
CL. *See* cervical length; corpus luteum
CO. *See* cardiac output
COMT. *See* catechol-O-methyltransferase
conception, OT role in, 22
congenital adrenal hyperplasia (CAH), 170–171
 diagnosis of, 170
 fertility effects of, 170–172
 management of, 172–173
 rare types of, 173
contraction-associated proteins (CAPs), 54–55
copeptin, 157–158
corin, 157
corpus luteum (CL)
 estrogen synthesis in, 42
 hCG maintenance of, 35
 historical studies of, 52–53
 in PE, 155
 progesterone production by, 51, 54
corticosteroids
 for AI, 164–170
 for CAH, 172–173
 chronic disease risk in later life and, 189–193
 deficiencies in synthesis of, 170–173
 fetal production of, 168
 normal pregnancy changes in, 165–167
 placental response to, 190–191
 for PTB, 132–133, 192
corticosterone, 1–2, 189–190
corticotropin-releasing hormone (CRH), 14–16
 anti-insulin effects of, 17–18
 estrogen ratios and, 16
 in labor onset, 1–4, 16–17, 128–129
 maternal, fetal, and placental, 1–4
 in multiple pregnancies, 184
 normal pregnancy changes in, 165–167
 in PE, 154–155
placental maturational trajectory effects on, 13
POMC stimulation by, 8, 15
in PTB, 128–129
regulation of placental production of, 16
cortisol, 1–4, 14–16
 for AI, 164–170
 anti-insulin effects of, 17–18
 chronic disease risk in later life and, 189–193
 deficiencies in synthesis of, 170–173
 excess of, 164–173, 177–179
 fetal production of, 168
 insulin resistance role of, 93
 normal pregnancy changes in, 165–167
 in PE, 154
 placental metabolism of, 13
COVID-19 pandemic, 192–194
CP. *See* cerebral palsy
CRH. *See* corticotropin-releasing hormone
CRH binding protein (CRH-BP), 3–4
CRHR1 and CRHR2, 3–4
CT. *See* cytotrophoblast
Cushing’s syndrome
 diagnosis of, 173–174
 etiology of, 174
 management of, 164–174
CVD. *See* cardiovascular disease
cytotrophoblast (CT), 14, 42–44
DA. *See* dopamine agonists
decidua, 54
decidualization, 17, 54
dehydroepiandrosteredione (DHEA)
 estrogen ratios and, 16
 estrogen synthesis from, 14–16, 42–43
 normal pregnancy changes in, 166–167
delivery. *See* labor
deoxycorticosterone (DOC), 167
depression
 OT administration for, 26–27
 postpartum, 8–9, 26–27
Developmental Origins of Health and Disease (DOHaD, developmental programming), 189, 194
early background of, 189–190
human studies of, 190
maternal microbiome role in, 194
placenta role in, 189–191
reproductive health effects, 193–194
stress and glucocorticoid role in, 191–193

- dexamethasone
for AI, 164–169
for CAH, 172–173
maternal
chronic disease risk in later life
and, 189–193
placental response to, 190–191
dexamethasone suppression test,
173–174
DHEA. *See* dehydroepiandrosterone
diabetes mellitus. *See also*
gestational diabetes
acromegaly with, 89
developmental programming
theory of, 189–190
GDM association with risk for
maternal, 99–100
in GDM offspring, 100–101
prevalence of, 107–108
diet. *See also* malnutrition
for GDM, 101–103
for maternal obesity, 112, 115–117
DNA methylation, in zygote, 14
DOC. *See* deoxycorticosterone
DOHaD. *See* Developmental Origins
of Health and Disease
dopamine, 6–7, 73–74, 167–168
dopamine agonists (DA)
for acromegaly, 88–89
for Cushing’s syndrome, 164–174
for hyperprolactinemia, 73–83
before pregnancy, 76–77
during pregnancy, 77–79
safety of, 80–81
doxazosin, 177
dynorphin (DYN), 8

E1. *See* estrone
E2. *See* estradiol
E3. *See* estriol
E4. *See* estetrol
ectopic pregnancy, 37–39
ejaculation, 22
embryo implantation. *See*
implantation
embryogenesis, OT role in early, 22
END. *See* endorphin
endometriosis, 193–194
endometrium
estrogen effects on, 42–44
placental signals to, 17
progesterone effects on, 42–44, 54
endorphin (END), 8
enkephalin (ENK), 8
environment
chronic disease risk in later life
and, 189–193
gene interactions with, 189, 194
placental response to, 190–191
reproductive function in later life
and, 193–194

epigenetic programming
chronic disease risk in later life
and, 189–190, 192–193
of fetal metabolism, 100–101
in zygote, 14
epinephrine, 167–168
eplerenone, 175–176
ER. *See* estrogen receptors
estetrol (E4)
in PTB, 126–127
synthesis of, 14–16
estradiol (E2), 42
in angiogenesis, 44–45
in brain adaptation and
development, 45
changes in ratio of, 16, 47
maternal cardiovascular system
effects of, 64–65
in multiple pregnancies, 183–184
in myometrial invasion, 42–44
in PE, 45–46, 152–153
in placenta development, 42–45
in PTB, 126–127
synthesis of, 14–16, 42–43
in uterine artery remodeling,
42–44
in uterine blood flow and
systemic vasodilation, 45
estriol (E3)
changes in ratio of, 16, 47
maternal cardiovascular system
effects of, 64–65
in multiple pregnancies, 183–184
in PE, 152–153
in PTB, 126–127
synthesis of, 14–16
in uterine blood flow and
systemic vasodilation, 45
estrogen receptors (ER), 16, 65,
126–127
estrogens, 42–47
changes in ratios of, 16, 47
CRH regulation of, 3
maternal cardiovascular system
effects of, 64–66
in multiple pregnancies, 183–184
in PE, 45–46, 152–153
placental maturational trajectory
effects on, 13
PRL regulation by, 73–74
in PTB, 126–127
reproductive physiology roles of
angiogenesis, 44–45
myometrial invasion, 42–44
neuroestrogens, 45
parturition, 46–47, 126–127
placenta development, 42–45
uterine artery remodeling,
42–44
uterine blood flow and systemic
vasodilation, 45
synthesis of, 14–16, 42–43

estrone (E1)
maternal cardiovascular system
effects of, 64–65
in PE, 152–153
in PTB, 126–127
synthesis of, 14–16, 42–43
ethnicity, PTB association with, 122

family history, PTB association with,
122
Ferguson reflex, 23
fertility
CAH effects on, 170–172
Cushing’s syndrome effects on,
173–174
developmental programming
theory of, 193–194
GH role in, 87
hyperprolactinemia effects on,
74–76
OT role in, 22, 29
fertilized ovum, placental signaling
of presence of, 13–14
fetal adrenal gland, 168
fetal brain
estrogen effects on, 45
neurosteroid impacts on, 8–9
thyroid hormone role in
development of, 36–37
fetal death
of GDM offspring, 98
maternal obesity association with,
113–115
fetal fibronectin (fFN), 130–131
fetal growth restriction (FGR)
chronic disease risk in later life
and, 189–190
CRH expression in, 4
hPL levels in, 7
maternal obesity association with,
113–115
maternal plasma volume and,
61–62
placental role in, 190–191
Ucn expression in, 5
fetal liver function, 42–43
fetal lungs, maturation of, 3–4,
132–133, 192
fetal metabolism
GDM effects on, 100–101
glucose utilization, 91–92
fetal neuroendocrine system, 1–2, 9
HPA axis, 1–5
hypothalamus–growth hormone
axis, 5
hypothalamus–pituitary–gonadal
axis, 5
hypothalamus–pituitary–thyroid
axis, 5–6
neurosteroids, 8–9
NPY, 7
opioids, 8

Index

- fetal neuroendocrine system (cont.)
OT, 6
PRL and hPL, 6–7
PTHrP, 8
relaxin, 7–8
fetal testis, hCG stimulation of, 35–36
fFN. *See* fetal fibronectin
FGR. *See* fetal growth restriction
fludrocortisone, 164–169, 172–173
follicle-stimulating hormone (FSH), 5, 33
follistatin-like-3, 92–93
food intake. *See also* diet
OT administration for regulation of, 29
FSH. *See* follicle-stimulating hormone
fuel mediated teratogenesis, 97–98

GA. *See* gestational age
Gaq pathway, 62–63
GDM. *See* gestational diabetes
genes, environment interactions with, 189, 194
gestational age (GA), 120–121
gestational diabetes (GDM), 91, 103
acromegaly and, 89
CRH levels in, 15
diagnostic thresholds for, 95–96
fetal complications of
long term, 100–101
short term, 96–98
management of, 101
insulin therapy, 102
lifestyle intervention and self blood glucose monitoring, 101–102
metformin, 102–103
maternal complications of
cardiovascular disease, 100–101
short term, 98–99
type 2 diabetes, 99–100
maternal metabolism during pregnancy and, 91
carbohydrate metabolism, 91–92
inflammation molecules and adipokines in, 93
insulin resistance, 91–93
lipid metabolism, 92
maternal hormones in, 93
placental hormones in, 92–93
pathophysiology of, 93–94
prevention of, 103
risk factors for, 94–95
universal or selective screening for, 96
gestational hypertension, 173
gestational transient thyrotoxicosis (GTT), 36, 140–143
gestational trophoblastic disease, 38

GH. *See* growth hormone
GHD. *See* growth hormone deficiency
GH-releasing hormone (GHRH), 5
ghrelin, 110–111
GHRH. *See* GH-releasing hormone
glucocorticoids, 1–4
for AI, 164–170
for CAH, 172–173
chronic disease risk in later life and, 189–193
fetal production of, 168
normal pregnancy changes in, 165–167
placental response to, 190–191
glucose utilization, maternal and fetal, 91–92
glycemic control, 101
insulin therapy, 102
lifestyle intervention and self blood glucose monitoring, 101–102
metformin, 102–103
GnRH. *See* gonadotropin-releasing hormone
gonadotropic axis. *See* hypothalamus–pituitary–gonadal axis
gonadotropin-releasing hormone (GnRH), 5, 35
gonadotropins, 5, 33. *See also* human chorionic gonadotropin
GPR30 receptor, 16
Graves’ disease, 140–144, 148–149
growth hormone (GH), 87. *See also* placental growth hormone
anti-insulin effects of, 17–18
excess of, 87–89
fertility and, 87
maternal, fetal, and placental, 5
maternal cardiovascular system effects of, 67
placental maturational trajectory effects on, 13
regulation of placental production of, 16
growth hormone deficiency (GHD), 87–88
GTT. *See* gestational transient thyrotoxicosis

hCG. *See* human chorionic gonadotropin
heart rate (HR), maternal, 62
hemodynamics, maternal, 62, 64
hemorrhage, postpartum, 23–24, 26
home pregnancy tests, 37–38
HPA axis. *See* hypothalamus–pituitary–adrenal axis
17HPC. *See* 17 α -hydroxyprogesterone
hPL. *See* human placental lactogen

HR. *See* heart rate
11 β -HSD 2. *See* 11- β hydroxysteroid dehydrogenase 2
human chorionic gonadotropin (hCG), 33
biological functions of, 35
corpus luteum maintenance, 35
decidualization promotion, 17
dNK cell expansion regulation, 37
fetal testicular stimulation, 35–36
lymphocyte suppression, 37
maternal thyroid stimulation, 5–6, 36–37
myometrial relaxation promotion, 17
pregnancy presence signaling, 13–14
relaxin secretion promotion, 37
clinical applications of, 38
chorionic disease detection, 38
ectopic pregnancy detection, 37–39
pregnancy tests, 37–38
gonadotropin family of, 33
multimodality diagnosis with β -hCG, 38
levels above discriminatory thresholds, 38–39
levels below discriminatory thresholds, 38–39
in multiple pregnancies, 38–39, 183
in PE, 154–155
placental maturational trajectory effects on, 13
production of, 16, 33
regulation of, 16, 35
serum and urine concentrations of, 34–35
abnormal levels of, 38–39
measurement of, 37
synthesis of, 33–34
thyroid stimulation by, 5–6, 36–37, 140–141
human placental lactogen (hPL), 6–7
anti-insulin effects of, 17–18
insulin resistance role of, 92–93
maternal cardiovascular system effects of, 67
in multiple pregnancies, 184
hydatidiform mole, 38
hydrocortisone, 164–170, 172–173
21-hydroxylase deficiency. *See* congenital adrenal hyperplasia
17 α -hydroxyprogesterone (17HPC), 50, 52, 56–57
11- β hydroxysteroid dehydrogenase 2 (11 β -HSD 2), 154, 167, 190–192

- hyperemesis gravidarum, 36, 141
- hyperglycemia, 91, 97–98. *See also* gestational diabetes
- hyperprolactinemia, 73–83
 - gonadotropic axis and fertility effects of
 - in men, 76
 - in women, 74–75
 - management of
 - during breast-feeding, 80–82
 - before pregnancy, 76–77
 - during pregnancy, 77–80
 - after pregnancy and breast-feeding, 82–83
 - safety of DA treatment for, 80–81
- hypertension
 - acromegaly with, 89
 - clinical features of endocrine causes of, 173
 - in Cushing’s syndrome, 173–174
 - developmental programming theory of, 189–190
 - GDM association with, 98–99
 - in PA, 173, 175–176
 - phaeochromocytoma or paraganglioma with, 176–178
- hypertensive disorders of pregnancy, 151. *See also* pre-eclampsia; pregnancy-induced hypertension
- discriminatory clinical features of, 173
- maternal plasma volume and, 61–62
- metabolic and cardiovascular adaptations of pregnancy compared with, 152, 158–159
- hyperthyroidism, 140
 - clinical features and diagnosis of, 141–142
 - definition, epidemiology and etiology of, 140–141
 - fetal and neonatal, 142–143
 - hCG role in, 36, 140–141
 - maternal-fetal consequences of, 142–143
 - pre-pregnancy counseling for women with, 144
 - treatment of, 143–144
 - universal screening for, 147
- hypertrophy, cardiac, pregnancy-induced, 62–63
- hypoglycemia, 5
- hypogonadism, male, 76
- hypothalamus–growth hormone axis. *See also* growth hormone
 - GHRH, 5
 - maternal, fetal, and placental, 5
 - SST, 5
- hypothalamus–pituitary–adrenal (HPA) axis. *See also* corticotropin-releasing hormone
 - chronic disease risk in later life and, 189–193
 - maternal, fetal, and placental, 1–5
 - normal pregnancy changes in, 165–167
 - Ucn, 3–5
- hypothalamus–pituitary–gonadal axis
 - hyperprolactinemia effects on
 - in men, 76
 - in women, 74–75
 - maternal, fetal, and placental, 5
- hypothalamus–pituitary–thyroid axis
 - maternal, fetal, and placental, 5–6
 - normal pregnancy physiology of, 140
- hypothyroidism, 140
 - clinical features and diagnosis of, 145
 - definition, epidemiology and etiology of, 141, 144–145
 - maternal-fetal consequences of, 142, 145–146
 - PPT, 148–149
 - treatment of, 146–147
 - universal screening for, 147
- hypothyroxinemia, 145–147
- hypoxia, placental, 45–46, 151–152
- ICP. *See* intrahepatic cholestasis of pregnancy
- IGF-1. *See* insulin-like growth factor 1
- immune response, maternal
 - progesterone effects on, 54
 - syncytin suppression of, 14
- implantation
 - estrogen role in, 42–44
 - placental signals promoting, 17
- in vitro fertilization and embryo transfer (IVF-ET)
 - GH therapy role in, 87
 - OT receptor antagonist use in, 27
- induction of labor, 25–26
- infant care, OT role in, 6, 24–25
- infection, PTB association with, 123, 129–135
- inflammation
 - in cardiovascular disease, 100
 - in insulin resistance, 93
 - in labor onset, 129, 135–136
 - parturition as state of, 54–57
 - in PE, 151–152
- inhibin, 35
- insulin
 - for GDM management, 102
 - maternal levels of, 17–18
 - insulin resistance (IR), 91–92
 - in GDM pathophysiology, 93–94
 - inflammation molecules and adipokines in, 93
 - maternal hormones in, 93
 - placental hormones in, 92–93
 - pre-eclampsia association with, 98–99
- insulin-like growth factor 1 (IGF-1), 5, 17–18, 87
- intrahepatic cholestasis of pregnancy (ICP), 183
- intrauterine environment
 - chronic disease risk in later life and, 189–193
 - placental response to, 190–191
 - reproductive function in later life and, 193–194
- intrauterine infection, 123, 129–135
- intrauterine pregnancy (IUP),
 - diagnosis of, 38–39
- iodine intake, 144–145
- IR. *See* insulin resistance
- iron deficiency, 144–145
- IUP. *See* intrauterine pregnancy
- IVF-ET. *See* in vitro fertilization and embryo transfer
- kappa (κ) receptors, placental, 8
- ketoconazole, 164–174
- labor
 - AI management during, 169–170
 - androgen role in, 126–128
 - CRH role in, 1–4, 16–17, 128–129
 - definition of preterm, 121
 - END levels in, 8
 - estrogen role in, 46–47, 126–127
 - induction of, 25–26
 - inflammation role in, 129, 135–136
 - OT receptor antagonist administration to prevent, 27–29
 - OT role in, 6, 23–24
 - phaeochromocytoma or paraganglioma management during, 177–178
 - progesterone role in, 46–47, 55–57, 125–126
 - progestin therapy to prevent, 56–57
 - prostaglandins role in, 17, 23
 - PTHrP role in, 8
 - thyroid hormones in, 128
- lactation. *See* breast-feeding
- lactotrophs, estrogen effects on, 73–74
- lanreotide, 88–89
- large for gestational age (LGA),
 - GDM association with, 97–98

Index

- leptin, 93, 110–111
- levothyroxine (LT4) therapy, 144–149
- LGA. *See* large for gestational age
- LH. *See* luteinizing hormone
- LH–hCG receptor, 33–36
- life expectancy, placental
maturation trajectory and, 13–14
- lifestyle interventions
for GDM, 101–103
for maternal obesity, 112, 115–117
- linea nigra, 15
- lipid metabolism, 92
- liver, fetal, 42–43
- low birth weight
chronic disease risk in later life and, 189–190
reproductive function in later life and, 193–194
- LT4 therapy. *See* levothyroxine therapy
- lungs, maturation of fetal, 3–4, 132–133, 192
- luteinizing hormone (LH), 5, 33
- luteo-placental shift, 53
- lymphocytes, hCG suppression of, 37
- macrosomia
in GDM offspring, 97–98
maternal obesity association with, 113–115
- magnesium sulphate, for PTB, 133
- male fetus, PTB association with, 124
- male infertility, 29
- male sexual differentiation, 35–36
- malnutrition
chronic disease risk in later life and, 189–190
placental response to, 190–191
reproductive function in later life and, 193–194
stress and glucocorticoid response to, 191–193
- mastitis, 25–26
- maternal age, PTB association with, 121
- maternal behavior
OT role in, 6, 24–25
placental hormone effects on, 18
- maternal brain
estrogen effects on, 45
neurosteroid impacts on, 8–9
placental signals to, 18
- maternal cardiovascular system, 61
pregnancy adaptations of, 61, 64, 152, 158–159
cardiac changes, 62–63
estrogen role in, 64–66
hemodynamic changes, 62, 64
plasma volume, 61–62
pre-eclampsia and, 63–64
progesterone role in, 65–67
prolactin role in, 67–68
RAAS role in, 69
relaxin role in, 68–69
- maternal metabolism. *See also* gestational diabetes
cardiac, 62–63
placental signals to, 17–18, 92–93
pregnancy changes to, 91, 152, 158–159
carbohydrate metabolism, 91–92
inflammation molecules and adipokines in, 93
insulin resistance, 91–93
lipid metabolism, 92
maternal hormones in, 93
placental hormones in, 92–93
- maternal microbiome, 194
- maternal mortality, PTB impact on, 124–125
- maternal neuroendocrine system, 1–2, 9
HPA axis, 1–5
hypothalamus–growth hormone axis, 5
hypothalamus–pituitary–gonadal axis, 5
hypothalamus–pituitary–thyroid axis, 5–6
neurosteroids, 8–9
NPY, 7
opioids, 8
OT, 6
PRL and hPL, 6–7
PTHrP, 8
relaxin, 7–8
- maternal nutrition
chronic disease risk in later life and, 189–190
placental response to, 190–191
reproductive function in later life and, 193–194
stress and glucocorticoid response to, 191–193
- maternal obesity, 107
adverse pregnancy outcomes associated with, 110
bariatric surgery and, 112–113
GDM risk with, 94–95
global chronic disease epidemic and, 107
insulin resistance in pregnancy and, 93
lactation issues associated with, 115
management of pregnancies complicated by, 115–117
microbiome effects of, 194
- neonatal issues associated with, 113–115
- offspring obesity association with, 108–109, 113–115
- phenotypes of, 109–110
- physiology and pathophysiology leading to, 110–112
- pregnancy complication risk and, 109–110
- prevalence of, 107–108
- PTB association with, 122
- reproductive function of offspring and, 193–194
- weight management approaches to, 112
- maternal stress
chronic disease risk in later life and, 189–193
placental response to, 190–191
- maternal thyroid
fetal brain development and, 36–37
hCG stimulation of, 5–6, 36–37
- maternity blues
allopregnanolone levels in, 8–9
OT administration for, 26–27
- maturation, placental, 13–14
- mental disorders, OT
administration for, 26–27
- metabolic syndrome
GDM risk with, 94–95
maternal obesity association with, 113–115
- metabolism. *See* maternal metabolism
- metformin
for CAH, 172
for GDM, 102–103
- methimazole, 143–144
- methoxyestrogens, 43
- metyrapone, for Cushing’s syndrome, 164–174
- microbiome, maternal, 194
- milk-ejection reflex, OT role in, 24
- mineralocorticoid antagonists, for PA, 175–176
- mineralocorticoids
for AI, 164–169
for CAH, 172–173
normal pregnancy changes in, 167
- miscarriage
CRH expression in, 4
OT receptor antagonist
administration to prevent, 27
relaxin levels in, 7–8
thyroid autoimmunity association with, 147–148
- mitotane, 179
- mood, OT administration for, 26–27
- motherhood. *See* maternal behavior
- multiple pregnancy, 183–187
hormone levels in, 183
CRH, 184
estrogens, 183–184

- hCG, 38–39, 183
- hPL, 184
- progesterone, 183–184
- testosterone, 184
- twin pregnancy effects of, 185
- PTB association with, 123
- PTB in
 - epidemiology and pathophysiology of, 185–186
 - hormonal profiles and, 186
- myoinositol, 103
- myometrial contractility
 - CRH regulation of, 3–4, 17
 - estrogen role in, 46–47
 - OT regulation of, 6, 23–26
 - Ucn regulation of, 4–5
- myometrial invasion, estrogen role in, 42–44
- myometrial relaxation
 - hCG role in, 17
 - OT role in, 21–23
 - progesterone role in, 17, 23, 54–55
- myometrium, placental signals to, 17
- NAFLD. *See* non-alcoholic fatty liver disease
- natriuretic factors, in PE, 157
- NCD. *See* non-communicable disease
- neonatal death (NND)
 - maternal obesity association with, 113–115
 - PTB impact on, 124
- neuroendocrinology of pregnancy, 1–9. *See also specific topics*
- neuroestrogens, 45
- neuropeptide Y (NPY), 7
- neurosteroids, 8–9
- nitric oxide (NO)
 - estrogen effects on, 45, 64–65
 - progesterone effects on, 65–67
 - prolactin family role in, 67
 - relaxin effects on, 68–69
- NND. *See* neonatal death
- NO. *See* nitric oxide
- non-alcoholic fatty liver disease (NAFLD), 113–115
- non-communicable disease (NCD)
 - developmental programming theory of, 189, 194
 - early background of, 189–190
 - human studies of, 190
 - maternal microbiome role in, 194
 - placenta role in, 189–191
 - reproductive health effects, 193–194
 - stress and glucocorticoid role in, 191–193
 - obesity role in, 107
 - noradrenaline, 167–168
 - NPY. *See* neuropeptide Y
 - nutritional deprivation. *See* malnutrition
 - obesity. *See also* maternal obesity
 - in GDM offspring, 100–101
 - maternal obesity role in offspring, 108–109, 113–115
 - octreotide, 88–89
 - opioids, 8
 - OT. *See* oxytocin
 - ovarian stimulation, 87
 - ovary, progesterone production by, 51, 53
 - ovum
 - DNA demethylation in, 14
 - placental signaling of fertilized, 13–14
 - oxytocin (OT), 20–30
 - clinical applications of
 - autism, maternal depression, and mental disorders, 26–27
 - breast-feeding facilitation, 25–26
 - food intake regulation, 29
 - labor induction, 25–26
 - male infertility, 29
 - pain relief, 29
 - PPH prevention, 26
 - maternal, fetal, and placental, 6
 - receptor for, 21
 - reproductive physiology roles of, 21
 - breast-feeding, 24
 - conception and initiation of pregnancy, 22
 - infant care, parenting, and motherhood, 6, 24–25
 - maintenance of pregnancy, 22–23
 - parturition, 6, 23–24
 - postpartum, 23–24
 - secretion of
 - pulsatile nature of, 21, 23–24
 - regulation of, 20–21
 - synthesis of, 20–21
 - oxytocin (OT) receptor antagonists, 27–28
 - PTL prevention with, 27–29
 - spontaneous abortion prevention with, 27
 - P4. *See* progesterone
 - P4 receptorss (PRs), 51–57, 66–67, 125–126
 - PA. *See* primary aldosteronism
 - pain relief, OT administration for, 29
 - paraganglioma (PPGL), 176
 - delivery in patients with, 177–178
 - diagnosis of, 176–177
 - genetic considerations of, 177
 - management of, 177
 - parathyroid hormone-related protein (PTHrP), 8
 - parenting, OT role in, 6, 24–25
 - parturition. *See* labor
 - pasireotide, 88–89
 - PCOS. *See* polycystic ovarian syndrome
 - PE. *See* preeclampsia
 - Pedersen’s hypothesis, 97–98
 - pegvisomant, 88–89
 - PGF. *See* placental growth hormone
 - phaeochromocytoma, 176
 - delivery in patients with, 177–178
 - diagnosis of, 176–177
 - genetic considerations of, 177
 - management of, 177
 - phenoxybenzamine, 177
 - physical activity
 - for GDM, 101–103
 - for maternal obesity, 112, 115–117
 - PIH. *See* pregnancy-induced hypertension
 - pituitary. *See also* hypothalamus–pituitary–adrenal axis; hypothalamus–pituitary–gonadal axis; hypothalamus–pituitary–thyroid axis
 - apoplexy, 79–80
 - pregnancy effects on, 74
 - pituitary tumors
 - ACTH-secreting, 164–174
 - GH-producing, 87–89
 - PRL-secreting, 73–83
 - during breast-feeding, 80–82
 - gonadotropic axis and fertility effects of, 75–76
 - before pregnancy, 76–77
 - during pregnancy, 77–80
 - after pregnancy and breast-feeding, 82–83
 - safety of DA treatment for, 80–81
 - placenta, 13, 18
 - chronic disease risk in later life and, 189–191
 - cytotrophoblast, 14, 42–44
 - development of, 42–45
 - estrogen ratios and, 16
 - estrogen synthesis by, 14–16, 42–43
 - expulsion of, 23–24
 - GH production by, 5, 17–18, 87, 92–93
 - hCG production by, 16, 33
 - insulin resistance and, 92–93
 - maternal targets for signals by
 - breast, 18
 - endometrium, 17

Index

- placenta (cont.)
 maternal brain, 18
 maternal metabolism, 17–18, 92–93
 myometrium, 17
 maturational trajectory of, 13–14
 neuroendocrine system of, 1–2, 9
 HPA axis, 1–5
 hypothalamus–growth hormone axis, 5
 hypothalamus–pituitary–gonadal axis, 5
 hypothalamus–pituitary–thyroid axis, 5–6
 neurosteroids, 8–9
 NPY, 7
 opioids, 8
 OT, 6
 PRL and hPL, 6–7
 PTHrP, 8
 relaxin, 7–8
 in PE, 45–46, 151–152
 cortisol production, 154
 estrogen production, 152–153
 peptide hormone production, 154–155
 progesterone production, 153–154
 steroid hormone production, 152–154
 testosterone production, 152–153
 peptide hormone production by regulation of, 16
 release of, 17
 pregnancy presence signaling by, 14
 fertilized ovum presence signaling, 13–14
 syncytin expression and trophoblast formation, 14
 progesterone production by, 53
 progesterone synthesis by, 14–16
 syncytiotrophoblast
 estrogen synthesis by, 42–43
 formation of, 14, 42–44
 hormone secretion by, 13, 16–17
 stress of, 151–152
 thrombosis of, 43
 trophoblast, 14, 42–44
 placental growth factor (PLGF), 92–93, 154–155
 placental growth hormone (PGF), 5, 17–18, 87, 92–93
 placental lactogen. *See* human placental lactogen
 Placental System A amino acid transporter, 190–191
 plasma volume
 maternal, 61–62
 in PE, 152
 PLGF. *See* placental growth factor
 polycystic ovarian syndrome (PCOS)
 androgens in, 127–128
 GDM association with, 94–95, 98–99, 103
 POMC. *See* pro-opiomelanocortin
 postpartum cardiomyopathy (PPCM), 67–68
 postpartum depression, 8–9, 26–27
 postpartum hemorrhage (PPH), 23–24, 26
 postpartum thyroiditis (PPT), 148–149
 post-term pregnancies
 CRH levels in, 2–4
 GnRH levels in, 5
 poverty, PTB association with, 123
 PPCM. *See* postpartum cardiomyopathy
 PPGL. *See* paraganglioma
 PPH. *See* postpartum hemorrhage
 PPT. *See* postpartum thyroiditis
 prednisolone, 164–169, 172–173
 preeclampsia (PE), 151
 aldosterone levels in, 69
 allopregnanolone levels in, 8–9
 CRH expression in, 4
 discriminatory clinical features of, 173
 estrogen effects in, 45–46
 GDM association with, 98–99
 “hormonal origin” of, 151–152
 maternal cardiovascular involvement in, 63–64
 maternal hormones in, 155, 158
 AVP and copeptin, 157–158
 CL and, 155
 natriuretic factors and corin, 157
 RAAS, 156–157
 relaxin, 7–8, 155
 thyroid hormones, 155–156
 normal metabolic and cardiovascular adaptations compared with, 152, 158–159
 NPY expression in, 7
 placenta role in, 45–46, 151–152
 cortisol metabolism, 154
 estrogen production, 152–153
 peptide hormone production, 154–155
 progesterone production, 153–154
 steroid hormone production, 152–154
 testosterone production, 152–153
 Ucn expression in, 5
 pregnancy of unknown location, 37
 pregnancy tests, 37–38
 pregnancy-induced hypertension (PIH)
 CRH expression in, 4
 NPY expression in, 7
 Ucn expression in, 5
 preterm birth (PTB), 120–138
 corticosteroid therapy for, 192
 CRH and stress roles in, 128–129
 CRH expression in, 4
 definitions and clinical presentation of, 120–121
 epidemiology and demographics of, 120
 GnRH levels in, 5
 hormonal roles in
 androgens, 126–128
 estrogens, 126–127
 progesterone, 125–126
 thyroid hormones, 128
 infection and, 123, 129–135
 inflammation role in, 129, 135–136
 inflammatory load trajectory role in, 56–57
 management: of morbidity and mortality of
 antibiotics, 130–133
 corticosteroid therapy, 132–133, 192
 magnesium sulphate, 133
 models and future interventions of, 134
 animal, 135–136
 infectious, 134–135
 non-infectious (sterile), 134
 morbidity and mortality of
 maternal, 124–125
 neonatal, 124
 in multiple pregnancy
 epidemiology and pathophysiology of, 185–186
 hormonal profiles and, 186
 OT receptor antagonists for prevention of, 27–29
 prediction of, 130
 cervical length, 130
 fetal fibronectin and other biomarkers, 130–131
 prevent and delay of, 131
 cervical cerclage, 132
 cervical pessary, 132
 progesterone therapy, 56–57, 131–132, 135–136
 tocolysis, 132
 relaxin levels in, 7–8
 risk factors associated with, 121
 current pregnancy risks, 121–124
 demographic, social and environmental, 121–123
 obstetric and gynecological, 121–123
 Ucn expression in, 5

- preterm labor (PTL), 121
 primary aldosteronism (PA), 173, 175–176
 PRL. *See* prolactin
 PRLR. *See* prolactin receptor
 progesterone (P4), 8–9, 50, 57–58
 CRH regulation of, 3
 decidualization promotion by, 17
 endometrial receptivity
 stimulation by, 42–44, 54
 evolutionary perspective of, 51–52
 historical discovery of, 52–53
 insulin resistance role of, 92–93
 maternal cardiovascular system
 effects of, 65–67
 mechanism of action of, 53–54
 in multiple pregnancies, 183–184
 myometrial relaxation promotion
 by, 17, 23, 54–55
 parturition and withdrawal of,
 46–47, 55–57, 125–126
 in PE, 153–154
 placental maturational trajectory
 effects on, 13
 placental synthesis of, 14–16
 pregnancy establishment roles of,
 54
 pregnancy maintenance roles of,
 54–55
 in PTB, 125–126
 PTB prevention with, 56–57,
 131–132, 135–136
 structure of, 50
 progestins. *See also* progesterone
 historical discovery of, 52
 for PTB prevention, 56–57,
 135–136
 prolactin (PRL), 6–7, 18, 73–83. *See also* hyperprolactinemia
 insulin resistance role of, 93
 maternal cardiovascular system
 effects of, 67–68
 during normal pregnancy and
 breastfeeding, 73–74
 prolactin receptor (PRLR), 67
 prolactinoma, 73–83
 gonadotropic axis and fertility
 effects of
 in men, 76
 in women, 75
 management of
 during breast-feeding, 80–82
 before pregnancy, 76–77
 during pregnancy, 77–80
 after pregnancy and breast-
 feeding, 82–83
 safety of DA treatment for,
 80–81
 pro-opiomelanocortin (POMC), 8,
 15, 191–192
 propylthiouracil, 143–144
 prolrenin, 156–157
 prostacyclin, 45, 64–65
 prostaglandins, 17, 23
 PRs. *See* P4 receptors
 psychological stress, PTB
 association with, 123,
 128–129
 PTB. *See* preterm birth
 PTHrP. *See* parathyroid hormone-
 related protein
 PTL. *See* preterm labor
 quinagolide, 80
 RAAS. *See* renin-angiotensin-
 aldosterone system
 race, PTB association with, 122
 radioactive iodine (RAI), 143–144
 relaxin, 7–8
 hCG promotion of secretion of,
 37
 maternal cardiovascular system
 effects of, 68–69
 in PE, 7–8, 155
 relaxin peptide receptors (RXFP), 68
 renin-angiotensin-aldosterone
 system (RAAS), 69
 normal pregnancy changes in,
 152, 167
 in PA, 175–176
 in PE, 156–157
 reproductive behavior, OT role in,
 22
 reproductive health, developmental
 programming theory of,
 193–194
 respiratory distress syndrome,
 132–133
 retosiban, 27–29
 RU-486, 50, 53–55
 RXFP. *See* relaxin peptide receptors
 RXFP1, 7–8
 SBGM. *See* self blood glucose
 monitoring
 selective PR modulators (SPRMs),
 50, 53–55
 self blood glucose monitoring
 (SBGM), 101–102
 semen quality, 76
 s-endoglin, 154–155
 sex hormone-binding globulin
 (SHBG), 93
 sexual behavior, OT role in, 22
 sexual differentiation, hCG role in,
 35–36
 sexual maturity, of fetus, 13–14
 sFlt-1. *See* soluble fms-like tyrosine
 kinase - 1
 SHBG. *See* sex hormone-binding
 globulin
 shoulder dystocia, 97–98
 smoking, 123
 social deprivation, PTB association
 with, 123
 soluble fms-like tyrosine kinase -1
 (sFlt-1), 154–155
 somatostatin (SST), 5
 somatostatin (SST) analogs, 88–89
 sperm, DNA demethylation in, 14
 spironolactone, 175–176
 spontaneous abortion
 CRH expression in, 4
 hCG levels after, 38–39
 OT receptor antagonist
 administration to prevent, 27
 SPRMs. *See* selective PR modulators
 SST. *See* somatostatin
 ST. *See* syncytiotrophoblast
 stillbirth
 of GDM offspring, 98
 maternal obesity association with,
 113–115
 stress
 AI management during, 169–170
 maternal
 chronic disease risk in later life
 and, 189–193
 placental response to, 190–191
 parturition as state of, 54–57
 PTB association with, 123, 128–129
 syncytiotrophoblast, 151–152
 stress response
 catecholamine role in, 167–168
 HPA axis role in, 1–5
 OT role in, 6, 26–27
 PRL and hPL role in, 7
 stroke volume (SV), 62
 subclinical hyperthyroidism,
 140–142, 147
 subclinical hypothyroidism,
 144–147
 sulfated estrogens, 43
 SV. *See* stroke volume
 SVR. *See* systemic vascular resistance
 syncytins, 14
 syncytiotrophoblast (ST)
 estrogen synthesis by, 42–43
 formation of, 14, 42–44
 hormone secretion by, 13, 16–17
 stress of, 151–152
 systemic vascular resistance (SVR).
 See also vasodilation
 maternal, 61–62
 in PE, 152
 relaxin effects on, 68–69
 T2DM. *See* type 2 diabetes
 T3. *See* triiodothyronine
 T4. *See* thyroxine
 testis, fetal, hCG stimulation of,
 35–36
 testosterone
 hCG stimulation of secretion of,
 35–36

Index

- testosterone (cont.)
 - hyperprolactinemia effects on, 76
 - in multiple pregnancies, 184
 - normal pregnancy changes in, 166–167
 - in PE, 152–153
 - in PTB, 126–128
 - thionamide antithyroid drugs, 143–144
 - thrombosis, placental, 43
 - thyroid
 - fetal brain development and, 36–37
 - hCG stimulation of, 5–6, 36–37, 140–141
 - normal pregnancy physiology of, 140
 - thyroid dysfunction, 140. *See also* hyperthyroidism; hypothyroidism
 - euthyroid autoimmune thyroid disease, 147–148
 - in PE, 155–156
 - PPT, 148–149
 - universal screening for, 147
- thyroid hormones
- normal pregnancy demand for, 140
 - in PTB, 128
- thyroidectomy, 143–144
- thyroid-stimulating hormone (TSH), 5–6
- hCG and, 36, 140
 - in PE, 155–156
 - universal screening of, 147
- thyrotoxicosis
- clinical features and diagnosis of, 141–142
 - definition, epidemiology and etiology of, 140–141
 - maternal-fetal consequences of, 142–143
 - PPT, 148–149
- thyrotropin-releasing hormone (TRH), 5–6
- thyroxine (T4), 140, 155–156
- TNF- α . *See* tumor necrosis factor alpha
- tobacco use, 123
- tocolysis
- OT receptor antagonists, 27–29
 - progestin therapy, 56–57
 - PTB prevention with, 132
- transsphenoidal selective adenomectomy
- for acromegaly, 88
 - for prolactinoma, 77, 79
- TRH. *See* thyrotropin-releasing hormone
- triiodothyronine (T3), 140, 155–156
- trophectoderm, 14, 42–44
- trophoblast
- development of, 42–44
 - hCG production by, 33
- trophoblastic disease, 38
- TSH. *See* thyroid-stimulating hormone
- tubal pregnancy, 37–39
- tumor necrosis factor alpha (TNF- α), 93
- twin pregnancy, 183–187 . *See also* multiple pregnancy
- type 2 diabetes (T2DM)
- GDM association with maternal risk for, 99–100
 - in GDM offspring, 100–101
 - prevalence of, 107–108
- Ucn. *See* urocortin
- undernutrition. *See* malnutrition
- urocortin (Ucn), 3–5
- uterine artery remodeling, 42–44
- uterine blood flow, 45
- uterine contraction. *See* myometrial contractility
- uterine curettage, 123
- uterine peristalsis, 22
- uterine quiescence
- hCG role in, 17
 - OT role in, 21–23
 - progesterone role in, 17, 23, 54–55
- uterotonic drugs, 26
- vaginal infection, 123, 129–131
- vascular endothelial growth factor (VEGF), 44–45
- vascular resistance. *See also* systemic vascular resistance
- uterine, 45
- vasodilation, systemic, 61–62
- estrogen role in, 45, 64–65
 - progesterone role in, 65–67
 - prolactin family role in, 67
 - relaxin role in, 68–69
- vasoinhibin, 67–68
- vasopressin, 157–158, 165–167
- VEGF. *See* vascular endothelial growth factor
- viviparity, progesterone role in, 51–52
- weight management
- for GDM, 101–103
 - for maternal obesity, 112
 - metabolic adaptations to, 110–112