Abdominal circumference (AC)
  - delivery risks 280, 281
  - ultrasound 235
Acarbose, safety in pregnancy 210
Adherens junctions, placental vasculogenesis 113, 116
Adiponectin, deficiency and gestational diabetes role 24–26
Advanced glycation end products (AGEs), fetoplacental effects 120
Alcohol, avoidance in pregnancy 177
Amino acid metabolism, gestational diabetes 37, 38, 156
Amniocentesis
  - chromosome anomaly screening 169
  - fetal monitoring 170, 227, 281
Ammiotic fluid, insulin levels 156–158
Anencephaly, fetal ultrasound 242
Angiopoietins, placental vasculogenesis 112, 116, 121
Angiotensin-converting enzyme (ACE) inhibitors, diabetic nephropathy management in pregnancy 165, 263, 264
Angiotensin II receptor blockers, diabetic nephropathy management 263, 264
Apoptosis, blastocysts 61
Aspart, insulin therapy in pregnancy 207–209
Autoantibodies, see Diabetes-related antibodies

Beta cell
  - fetal growth 86, 87
  - glucocorticoids and development effects 89, 91
  - insulin secretion in pregnancy and gestational diabetes 26–29
  - islet amyloid pancreatic polypeptide secretion in pregnancy and gestational diabetes 29–31
  - maternal nutrition effects on fetal development
    - bilateral uterine artery ligation 88
    - generally food-restricted rat model 89, 91
    - hyperplasia 132, 133
    - low-protein rat model 88, 89
    - mild hyperglycemia 87, 88
    - severe hyperglycemia 88

Biparietal diameter (BPD), ultrasound 233, 235
Body mass index (BMI), maternal weight gain recommendations 186
Brachial plexus injury, macrosomic infant delivery 226, 297

Carbohydrate metabolism
  - gestational diabetes 36, 37
  - glucose metabolism in blastocysts 62
Caudal regression sequence
  - fetal ultrasound 248
  - gestational diabetes association 129
Cesarean section
  diabetic mother approach 285
  frequency in diabetic patients 170, 171
  hyperinsulinemic infants 153
  indications 226, 281
Crown-rump length, ultrasound 233

Delivery
  analgesia 284
  cesarean section, see Cesarean section
  fetal monitoring 284
  induction of labor 283, 284
  instrumental deliveries 285
  insulin therapy 171, 282, 283
  macrosomia prediction and complications 280, 281
  postpartum care 285
  preterm labor
    incidence in diabetes 278, 279
    tocolytic drugs 279, 280
  timing 281, 282
Diabetes-related antibodies (DRA)
  morbidity in pregnancy
    fetal diabetes risks 200, 201
    maternal abnormal glucose tolerance 201
    perinatal outcome 199, 200
    placental transfer 199
  pregnancy effects on levels 198
  prevalence in pregnancy
    control mothers 197, 198
    gestational diabetes mellitus 195–197
    type 1 diabetes 197, 198
Diabetes type 1
  autoantibodies, see Diabetes-related antibodies
  complications in pregnancy, see specific complications
  congenital malformations 162, 223, 241, 242
  embryopathy 289, 290
  epidemiology 222, 223, 254
  fetal monitoring 170
  gestational diabetes mellitus and maternal risks 5
  maternal care
  completion of pregnancy 170, 171
diet, see Nutrition
  first trimester 166–168
  preconception 166, 255–258
  puerperium 171
  second trimester 168, 169
  third trimester 169, 170
  maternal risks following gestational diabetes 310, 311
  mortality in perinatal period 161, 162, 222, 223, 294
  offspring risks later in life following diabetic pregnancy 299, 300
Diabetes type 2
  complications in pregnancy, see specific complications
  embryopathy 290
  fetal monitoring 170
  global distribution 1
  maternal care
    completion of pregnancy 170, 171
diet, see Nutrition
    first trimester 166–168
    preconception 166
    puerperium 171
    second trimester 168, 169
    third trimester 169, 170
  maternal risks following gestational diabetes 310, 311, 317
  mortality in perinatal period 294
  offspring of diabetic pregnancies
    risk reduction in subsequent pregnancies 189
    risks later in life 300, 301
trends 1, 2
Diabetic ketoacidosis (DKA)
  clinical features 268
  diagnosis 268, 269
  fetal mortality 224
  frequency in pregnancy 166
  management 269
  pathophysiology 268
Diabetic nephropathy
  clinical features 261, 262
  detection and screening 262, 263
  fetal outcomes 264
  frequency in pregnancy 165, 263
management in pregnancy 165, 263, 264
pregnancy effects on progression 264
Diabetic neuropathy
clinical features 264, 265
management in pregnancy 165, 166
Diabetic retinopathy
epidemiology in pregnancy 260, 261
grading 259
management in pregnancy 165, 260
pathophysiology 258
screening 260
Diet, see Nutrition
Doppler ultrasound, see Ultrasound
Duodenal atresia, fetal ultrasound 247, 248
Erythropoietin, fetal effects 119, 120
Estrogen, gestational diabetes role 23
Evidence-based medicine
decision making 144
definition 146
origins 145
process
application in clinical practice 151, 152
best evidence tracking for question answering 147–149
critical appraisal of evidence
absolute risk reduction 149, 150
levels of evidence 149, 150
odds ratio 149
relative risk 149
need for information conversion to focused questions 146, 147
performance evaluation 152
Exercise
diabetes prevention in later life after gestational diabetes 189
pregnant diabetics 167
weight management in pregnancy 188, 189
Facial defects, fetal ultrasound 243, 244
Fetal effects, gestational diabetes
arachidonic acid and prostaglandin metabolism 64, 65
beta cells
hyperplasia 132, 133
mild hyperglycemia effects 87, 88
severe hyperglycemia effects 88
diabetes risks later in life 289, 299
functional teratogenesis
development of theory 9, 10
insulin-treated rat neonate studies 11, 12
neuropeptide Y system
‘malorganization’ 13, 14
overfeeding of neonatal rats 12, 13
primary prevention 15, 16
streptozotocin rat studies 10, 11
ventromedial nucleus 11, 12
genetic and environmental factors
290–294
glucose gradient 154–156
hyperglycemia-induced tissue damage 35, 36
insulin resistance 4
macrosomia, see Fetal growth
malformations 4, 58, 127–129, 162, 290
mortality 127, 161, 162
myocardial ischemic necrosis 131, 132
myo-inositol depletion 64
neonatal metabolic abnormalities 297–299
obesity 4, 10, 13, 153
peri-implantation phase 63
preimplantation development
animal models 59, 60
apoptosis of blastocysts 61
blastocyst growth 60, 61
fibroblast growth factor-4 deficiency and inner cell mass development 62, 63
glucose metabolism 62
overview 59
oxidative stress role 61, 62
tumor necrosis factor alpha effects 61
teratogenic period in diabetic pregnancy 291
unifying hypothesis of diabetes-induced embryopathy 65–69
Fetal growth
adiposity and birth weight 72, 73
animal models for nutrition impact studies
Fetal growth (continued)
- generally food-restricted rat model of maternal undernutrition 86, 89, 91
- intrauterine growth retardation 83, 84
- low-protein rat model of maternal malnutrition 85, 88, 89
- streptozotocin diabetic rats 84, 85
- beta cell growth 86, 87
- birth weight
distribution in diabetic pregnancy 225, 226, 295
recommendations 187
body composition evaluation 78, 79
critical period 288
evaluation 78, 79
fetal nutrition determinants 73–75
gestational diabetes effects
fat mass 75, 76
monitoring of diabetic pregnancies 79, 80
nutrient availability 76–78
hyperinsulinemia and macrosomia 163, 164
macrosomia features 130, 131, 214
maternal anthropometric factors 73
maternal metabolic changes and fetal growth effects 34–36, 42, 43
restraining factors 296
ultrasound findings
intrauterine growth restriction 238
macrosomia 236–238, 280, 281
Fetal hypoxia
clinical features 224
fetal factors 224–226
maternal factors 224
monitoring 226, 227
mortality rates 222, 223
prevention 227
ultrasound evaluation 170
vascular endothelial growth factor induction 121
α-Fetoprotein (AFP), screening 249, 250
Fibroblast growth factor-2 (FGF-2), expression in pregnancy 120, 121
Fibroblast growth factor-4 (FGF-4), deficiency and inner cell mass development 62, 63
Fish oil, preconception nutrition 178, 179
Folic acid, preconception nutrition 176, 177, 257
Free fatty acids (FFAs)
insulin response in gestational diabetes 21, 22
placental transfer 40–42
Functional teratogenesis, see Fetal effects, gestational diabetes
Gestational diabetes mellitus (GDM)
definition 2, 214, 289
diet, see Nutrition
epidemiology
incidence 3, 214
problems in estimates 2, 3
risk factors 3, 4
fetal risks, see Fetal effects, gestational diabetes
maternal risks 4, 5
mortality in perinatal period 127, 161, 162, 294, 295
screening 5
Glucocorticoids, beta cell development effects 89, 91
Glucose monitoring
continuous glucose monitoring
advantages in pregnancy monitoring 219, 220
adverse fetal outcome prevention 219
clinical use not in pregnancy 215–217
HbA1c comparison 219
hypoglycemia detection 218, 219
overview 215
pregnancy studies 217, 218
self-monitoring of blood glucose 167, 214, 215, 219
Glucose tolerance tests
insulin resistance in pregnancy 19, 20
maternal diabetes risks following gestational diabetes 310–314
villous maturation correlation 139, 140
GLUT1, placental expression in gestational diabetes 77, 78, 155, 156
GLUT4
concentrations in gestational diabetes 19
pregnancy effects on muscle expression 21
Glyburide
fetal effects 209, 210
placental transfer 209
Goldenhar’s syndrome, gestational
diabetes association 129

HbA1c
continuous glucose monitoring
comparison 219
pregnant diabetic monitoring 166, 214
Heart, fetal ultrasound 245–247
Human chorionic gonadotropin (hCG),
screening 249, 250
Human placental lactogen (hPL),
gestational diabetes levels 22, 95
Hypertension, frequency in diabetic
pregnancy 164
Hypoglycemia
classification 265
clinical features 265, 266
continuous glucose monitoring 218, 219
definition 265
driving precautions 267, 268
management 266, 267
meal planning and avoidance 185
neonatal hypoglycemia 298, 299
nocturnal hypoglycemia 267, 268
Hypoxia, see Fetal hypoxia

Infection, frequency in diabetic pregnancy
164
Inositol, embryopathy role 292, 293
Insulin
amniotic fluid levels 156–158
placental transfer 206, 207
receptor autophosphorylation impairment
in pregnancy 21
secretion in pregnancy and gestational
diabetes 26–29
therapy for pregnant diabetics
analogs 207–209
first trimester 167
goals 207
pharmacokinetics 207
preconception period in type 1
diabetes 256, 257
puerperium 171, 282, 283
second trimester 168
third trimester 169
Insulin receptor substrate-1 (IRS-1),
concentrations in gestational diabetes
21
Insulin resistance
fetal programming 153
pregnancy-associated 18–26
Intramyocellular lipid content (IMCL),
gestational diabetes 21, 22
Islet amyloid pancreatic polypeptide
(IAPP), secretion in pregnancy and
gestational diabetes 29–31
JAK-STAT pathways, leptin receptor
signaling 52
Kidneys, fetal ultrasound 248
Labor, see Delivery
Lactation, nutrition requirements 189
Leptin
adiposity signal in pregnancy 23, 24
fetal leptin
consequences 53, 54
functions 49, 50, 53
origins 53
functional overview 46
gestational diabetes levels and role 24,
50, 51
maternal functions 48
placental leptin
function 49
gene expression regulation 51, 52
inflammation correlation 52
receptor signaling 52, 53
synthesis 48
pregnancy changes 24, 47, 48
Lipid metabolism, gestational diabetes
adipose tissue 38, 39
hyperlipidemia 39, 40
placental transfer of lipid metabolites
40–42
Lipid peroxidation, placenta in gestational
diabetes 103
Lipoprotein lipase (LPL), gestational
diabetes activity 39, 40, 42
Lispro, insulin therapy in pregnancy
207–209
Macrosomia, see Fetal growth
Metabolic syndrome, maternal risks following gestational diabetes 315–317
Metformin, fetal effects 209, 210
Mitogen-activated protein kinase (MAPK), leptin receptor signaling 52, 53
Myocardial ischemic necrosis, gestational diabetes 131, 132
Myo-inositol, fetal depletion 64
Neuropeptide Y (NPY), hypothalamic system ‘malorganization’ in functional teratogenesis 13, 14
Neuropsychological development, diabetic pregnancy effects 300
Nitrate stress, placenta in gestational diabetes 101, 104
Nutrition
diabetes prevention in later life after gestational diabetes 189
gestational diabetes risk reduction 174, 175
lactation 189
preconception dietary advice
alcohol avoidance 177
fish oil 178, 179
folic acid 176, 177
foods to avoid 179
overview 175, 176
vitamin supplements 177, 178
pregnant diabetics
carbohydrate 182, 183
energy requirements 180, 181
fat 184, 185
meal planning and hypoglycemia avoidance 185
overview 167
protein 182
weight management in pregnancy exercise 188, 189
extreme caloric restriction 188
maternal weight gain recommendations 186, 187
modest caloric restriction 187, 188
Obesity
gestational diabetes mellitus risks 3
maternal diabetes risks following gestational diabetes 311–315
offspring risks after gestational diabetes 4, 10, 13, 153, 300, 301
weight management in pregnancy exercise 188, 189
extreme caloric restriction 188
maternal weight gain recommendations 186, 187
modest caloric restriction 187, 188
Oxidative stress
fetal effects in gestational diabetes 65, 130, 293
placenta in gestational diabetes antioxidant capacity 102
lipid peroxidation 103
overview 101
superoxide 104
preimplantation development effects in gestational diabetes 61, 62
Pax-3, downregulation in neural tube defects 291, 292
Placenta
amino acid transport 156
angiogenesis and vascular remodeling 114–118
diabetes mellitus effects
chorangiosis type II 138
histological findings 133–138
history of studies 133
morphology 133, 134
staging 137, 138
ultrastructure studies 136, 137
villi changes 134–137
fetal vascular resistance 118, 119
gestational diabetes effects
advanced glycation end products 120
fetoplacental angiogenesis 119, 120
first trimester 95
term placenta
antioxidant capacity 102
lipid peroxidation 103
morphology and development 95–101
oxidative and nitrate stress 101–104
villi features 97–100, 138–140
Subject Index

Transcerebellar diameter, ultrasound 235
Tumor necrosis factor-alpha (TNF-α) blastocyst effects 61
gestational diabetes role 23

Ultrasound
biophysical profile 249
birth weight estimation 169, 170
congenital malformations
anencephaly 242
cardiac anomalies 245–247
caudal regression syndrome 248
duodenal atresia 247, 248
facial defects 243, 244
incidence in diabetes 241, 242
kidneys 248
polyhydramnios 248, 249
spina bifida 242, 243
Doppler imaging of blood flow
238–241, 247
fetal hypoxia evaluation 170
first trimester 231–233
gestational age estimation 230, 231
intrauterine growth restriction findings 238
long bone measures 236
macrosomia findings 236–238, 280, 281
preimplantation period 231
second trimester 168, 169, 235, 236

VACTERL, gestational diabetes association 128, 129
Vascular endothelial cadherin
diabetic perturbations 116, 118
placental vasculogenesis 113, 116
Vascular endothelial growth factor (VEGF)
diabetic perturbations 117, 118, 120, 121
embryopathy role 292
gestational changes in expression 115, 116
hypoxia induction 121
placental vasculogenesis 112–114
receptors 112
Ventricular septal defect, gestational diabetes association 128
Villi, see Placenta
Vitamins, supplements 177, 178

---

glucose transport 77, 78, 154, 155, 156
leptin
  function 49
gene expression regulation 51, 52
inflammation correlation 52
receptor signaling 52, 53
synthesis 48
lipid metabolite transfer 40–42
nutrient transfer capacity in gestational diabetes 77
placenta growth factor expression in pregnancy 112, 115, 116
vasculogenesis 111–114
Polyhydramnios, fetal ultrasound 248, 249
Preeclampsia
definition 271, 272
frequency in diabetic pregnancy 164, 276
hypertension and risks 272
management 275, 276
metabolic control in prevention 272–274
microalbuminuria and risks 272
pathogenesis 274, 275
Pregnancy-associated plasma protein-A (PAPP-A), screening 250
Preterm labor
incidence in diabetes 278, 279
tocolytic drugs 279, 280
Progesterone, gestational diabetes role 22
Prolactin, gestational diabetes role 23
Prostaglandins
  embryopathy role 292
  metabolism in gestational diabetes 64, 65
Resistin, gestational diabetes role 26
Shoulder dystocia, macrosomic infant
delivery 226, 280, 297
Smoking, cessation 257, 258
Spina bifida, fetal ultrasound 242, 243
Sulfonylureas
  fetal effects 209, 210
  placental transfer 209
Syndrome X, see Metabolic syndrome
Thyroid disease, autoimmunity in type 1 diabetes 258
Tight junctions, placental vasculogenesis 113