

1	Examination of the Placenta	1
1.1	Macroscopic Examination	1
1.2	Storage	1
1.3	Selection	2
1.4	Photography	2
1.5	Examination	2
1.6	Placentas of Multiple Births	6
1.7	Fixation	8
1.8	Stereological Analysis	9
1.9	mRNA and Microarray Analyses	9
1.10	Special Procedures	9
	References	10
2	Macroscopic Features of the Delivered Placenta	13
2.1	Fetal Surface	13
2.2	Maternal Surface	14
2.3	The Terms “Fetal Placenta” and “Maternal Placenta”	14
	References	15
3	Microscopic Survey	17
3.1	Typical Histological Features of the First Trimester Placenta	17
3.2	Typical Histological Features of the Third Trimester Placenta	23
4	Placental Types	27
4.1	Placental Shapes	28
4.2	Types of Maternal-Fetal Interdigitation	29
4.3	Maternal-Fetal Interface	30
4.4	Maternal-Fetal Blood Flow Interrelations	31
4.5	Placental Types and Phylogeny	32
4.6	Genomic Imprinting	35
4.7	Human Placenta	36
4.8	Animal Models	37
	References	37
5	Early Development of the Human Placenta	41
5.1	The Origin of Trophoblast	41
5.2	Prelacunar Stage	41
5.3	Lacunar Stage	44
5.4	Early Villous Stages	45
5.5	Histiotrophic Nutrition	46
5.6	Villus Regression and Formation of the Definitive Placenta	48
5.7	The Amnion and Yolk Sac	50
	References	51

6	Basic Structure of the Villous Trees.	55
6.1	Syncytiotrophoblast	55
6.1.1	Microvillous Surface	55
6.1.2	Basal Surface	61
6.1.3	Organelles	61
6.1.4	Nuclei	63
6.1.5	Cytoskeleton	64
6.1.6	Enzymes	64
6.1.7	Glycogen	65
6.1.8	Specialized Regions of the Villous Surface	66
6.1.9	Syncytial Sprouts and Knots	67
6.1.10	Intervillous Bridges	69
6.1.11	Transtrophoblastic Channels	70
6.2	Villous Cytotrophoblast (Langhans' Cells)	70
6.2.1	Villous Cytotrophoblast Cell Types	71
6.2.2	Cytotrophoblast Fusion	73
6.2.3	Junctional Proteins	74
6.2.4	Endogenous Retroviral Glycoproteins	74
6.2.5	Externalization of Phosphatidylserine	76
6.2.6	Reorganization of the Cytoskeleton	76
6.2.7	Reorganization of the Plasma Membranes	77
6.2.8	Overview	77
6.3	Syncytiotrophoblast Regeneration and Repair	78
6.3.1	Trophoblast Apoptosis	79
6.3.2	Trophoblastic Basement Membrane	80
6.3.3	Connective Tissue	81
6.3.4	Matrix Components of the Villous Stroma	83
6.4	Villous Macrophages (Hofbauer Cells)	84
6.4.1	Origin and Distribution	84
6.4.2	Functions	85
6.5	Other Free Connective Tissue Cells	86
6.5.1	Fetal Vasculature	86
6.5.2	Stem Villous Arteries	86
6.5.3	Fetal Capillaries	87
6.5.4	Vasomotor Control	88
6.5.5	Lymphatics	89
6.6	Fibrinoid of the Villous Trees	89
6.6.1	Perivillous Fibrinoid	89
6.6.2	Intravillous Fibrinoid	89
	References	89
7	Architecture of Normal Villous Trees	101
7.1	Classification of Villous Types	101
7.1.1	Stem Villi	102
7.1.2	Immature Intermediate Villi	104
7.1.3	Mature Intermediate Villi	106
7.1.4	Terminal Villi	106
7.1.5	Mesenchymal Villi	109
7.2	Differentiation and Growth of Villous Types	110
7.2.1	Formation of Mesenchymal Villi	110
7.2.2	Differentiation of Mesenchymal Villi	111
7.2.3	Development of the Terminal Villi	112
7.3	Angioarchitecture of Villi	113
7.3.1	Vascular Arrangement in Immature Villi	113
7.3.2	Larger Vessels of Stem Villi	113

7.3.3	Paravascular Capillary Net of Stem Villi	113
7.3.4	Arrangement of Vessels in Mature Intermediate and Terminal Villi	115
7.3.5	Sinusoids of Terminal Villi	117
7.4	General Aspects of Placental Vasculogenesis and Angiogenesis	117
7.4.1	Vasculogenesis (Day 15–32)	118
7.4.2	Angiogenesis and Vascular Remodeling (Day 32 to Week 40)	121
7.5	Molecular Regulation of Vasculogenesis and Angiogenesis	121
7.5.1	Vascular Endothelial Growth Factor	124
7.5.2	Placental Growth Factor	124
7.5.3	Angiopoietins	125
7.5.4	Fibroblast Growth Factor	125
7.5.5	Homeobox Genes	125
7.6	Oxygen and Oxygen-Controlled Growth Factors as Regulators of Villous and Vascular Development	126
7.6.1	Oxygen Sensing by Placental Tissues	128
7.6.2	Evidence for Oxygen-Controlled Fetoplacental Angiogenesis	130
7.6.3	Oxygen and Villous Trophoblast	131
7.6.4	Oxygen and Villous Stroma	133
7.6.5	Oxygen and Intervillous Circulation	133
7.6.6	The Lobular Arrangement of the Villous Trees	134
7.6.7	The Intervillous Clefts	136
7.7	Histopathological Importance of Inhomogeneity of Villous Trees	137
7.8	Fetomaternal Flow Interrelations	137
	References	138
8	Characterization of the Developmental Stages	145
8.1	Stages of Development	145
	References	155
9	Nonvillous Parts and Trophoblast Invasion	157
9.1	Extravillous Trophoblast	157
9.1.1	Origins of Extravillous Trophoblast and Cell Columns	157
9.1.2	Stages of Extravillous Trophoblast Differentiation Along the Invasive Pathway	160
9.1.3	Proliferative Stem Cells	161
9.1.4	Migratory Cells of the Cell Column	161
9.1.5	Cytotrophoblastic Shell	162
9.1.6	Invasive Interstitial Extravillous Trophoblast Cells	162
9.1.7	Multinucleated Placental-Bed Giant Cells	164
9.1.8	Endovascular Trophoblast	164
9.1.9	Proteinases, Activators, and Inhibitors Involved in Trophoblast Invasion	165
9.1.10	Cytokines and Hormones Controlling Differentiation and Invasion of Extravillous Trophoblast	166
9.1.11	Nitric Oxide, Carbon Monoxide, and Trophoblast Invasion	169
9.1.12	MHC Class I Molecules	171
9.1.13	Oxygen-Mediated Regulation of the Invasive Pathway	172
9.1.14	Failure of Extravillous Trophoblast Invasion in Pathological Pregnancies	174
9.1.15	Endocrine Activities of Extravillous Trophoblast	175
9.2	Decidua	175
9.2.1	Composition of Decidua	176
9.2.2	Endometrial Stromal Cells and Decidual Cells	176
9.2.3	Endocrine and Paracrine Aspects of Decidua	177
9.2.4	Uterine Natural Killer Cells (UNK Cells)	178

9.2.5	Macrophages	179
9.2.6	Dendritic Cells	180
9.2.7	B Cells and T Cells	180
9.2.8	Regulatory T Cells	180
9.2.9	Endometrial Glands	181
9.2.10	Decidual Extracellular Matrix	181
9.3	Fibrinoid.	182
9.3.1	Localization of Fibrinoid Subtypes	182
9.3.2	Functions of Fibrinoid	183
9.4	Calcification	185
9.5	Chorionic Plate.	187
9.5.1	Development	187
9.5.2	Structure at Term	188
9.5.3	Amnion.	188
9.5.4	Spongy Layer.	189
9.5.5	Chorionic Mesoderm	189
9.5.6	Extravillous Cytotrophoblast	189
9.5.7	Langhans' Fibrinoid Layer.	190
9.6	Marginal Zone	190
9.6.1	Subchorial Closing Ring	190
9.6.2	Marginal Sinus	190
9.7	Basal Plate	191
9.7.1	Development of the Basal Plate	191
9.7.2	Layers of the Basal Plate at Term	191
9.8	Uteroplacental Vessels	194
9.8.1	The Anatomy of the Uteroplacental Vasculature	194
9.8.2	Establishment of the Maternal Arterial Circulation	195
9.8.3	Number and Position of the Uteroplacental Vessels	196
9.8.4	Importance of Physiological Changes of Uteroplacental Arteries.	196
9.8.5	Stages of Physiological Changes in Uteroplacental Arteries.	198
9.8.6	Structure of Uteroplacental Veins	200
9.8.7	Septa.	200
9.8.8	Cell Islands.	202
9.9	Pathology of Trophoblast Invasion	204
9.9.1	Placenta Accreta.	204
9.9.2	Placenta Increta and Percreta	207
9.9.3	Uterine Rupture	210
9.9.4	Placenta in Ectopic (Tubal) Pregnancy	211
9.9.5	Placenta in Abdominal Pregnancy	213
9.9.6	Cysts and Breus' Mole.	214
9.9.7	Maternal Floor Infarction.	218
9.9.8	Decidual Degeneration.	222
	References	223
10	Involution of Implantation Site: Retained Placenta.	241
10.1	Involution of the Placental Site	241
10.2	Subinvolution	243
10.3	Placental Polyps.	244
10.4	Involution of a Remaining Placenta.	247
	References	248
11	Anatomy and Pathology of the Placental Membranes.	249
11.1	Overview	249
11.1.1	Development.	250
11.1.2	Amnion.	253

11.2	Amnionic Epithelium: Different Cell Types and Cell Degeneration	254
11.3	Cytological and Functional Aspects of the Amnionic Epithelium.	255
11.3.1	Amnionic Fluid	258
11.3.2	Chromosomal Determinations	259
11.4	Cellular Metaplasia and Glycogen	260
11.5	Amnionic Mesoderm	261
11.5.1	A Medley of Themes	262
11.5.2	Clinical and Research Applications	263
11.6	Chorion Laeve	263
11.7	Intermediate (Spongy) Layer	264
11.8	Chorionic Mesoderm	264
11.9	Trophoblast Layer	265
11.10	Decidua	266
11.11	Tensile Properties of the Membranes	267
11.12	Pathology of the Membranes	268
11.12.1	Preterm Rupture of the Membranes	268
11.12.2	Cysts, Tumors, and Hemorrhage	269
11.12.3	Amnionic Fluid Embolism	272
11.12.4	Meconium	274
11.12.5	Gastroschisis	283
11.12.6	Epidermolysis Bullosa	284
11.12.7	Amnion Nodosum	285
11.12.8	Amnionic Bands	287
11.12.9	Limb-Body Wall Defect	293
11.12.10	Extramembranous Pregnancy	293
	References	295
12	Anatomy and Pathology of the Umbilical Cord	309
12.1	Development	309
12.2	Amnionic Epithelium	311
12.3	Wharton's Jelly	311
12.4	Structure of Umbilical Vessels	312
12.4.1	Innervation	313
12.4.2	Contractility of Umbilical Vessels	314
12.4.3	Hyrtl Anastomosis, False Knots, and Hoboken Nodes	315
12.4.4	Allantois	317
12.4.5	Omphalomesenteric Duct	318
12.5	Spiral Turns of the Cord	321
12.6	Length of the Cord	324
12.6.1	Abnormal Length, Nuchal Cord	325
12.6.2	Site of Cord Insertion	330
12.6.3	Furcate Cord Insertion	331
12.6.4	Velamentous Cord Insertion	331
12.7	Placental Surface Vessels	336
12.8	Nucleated Red Blood Cells (NRBCs)	339
12.9	Cysts and Edema	339
12.10	Single Umbilical Artery	341
12.11	Placental Transfusion	344
12.12	Knots	345
12.13	False Knots	346
12.14	Strictures	346
12.15	Rupture	348
12.16	Hematoma	349
12.17	Varices and Aneurysms	351
12.18	Thrombosis of the Umbilical Vessels	354

12.19	Thrombosis of the Placental Vascular Tree	357
12.20	Tumors of the Umbilical Cord	362
	References	363
13	Placental Shape Aberrations	377
13.1	Site of Placental Attachment	377
13.2	Volumetric Growth	379
13.3	Abnormal Shapes (“Errors in Outline”)	379
13.4	Placenta Previa	382
13.5	Placenta Membranacea	386
13.6	Circumvallate Placenta (Extrachorial, Circummarginate Placentas)	387
	References	390
14	Histopathological Approach to Villous Alterations	395
14.1	Microscopic Evaluation	395
14.1.1	Assessment of Villous Maturation	395
14.1.2	Placental Insufficiency	397
14.1.3	Examination of Fetal Stem Vessels	398
14.1.4	Examination of the Fetal Capillary Bed	399
14.1.5	Villous Architecture and Fibrinoid	399
14.1.6	Intervillous Space, Infarcts	400
14.1.7	Abruptio Placentae	401
14.2	Major Histopathological Findings	401
14.2.1	Syncytiotrophoblast	401
14.2.2	Knotting of the Syncytiotrophoblast	402
14.2.3	Langhans’ Cells	402
14.2.4	Vasculosyncytial Membranes	403
14.2.5	Trophoblastic Basement Membrane	403
14.2.6	Perivillous Fibrinoid	403
14.2.7	Intravillous Fibrinoid	403
14.2.8	Villous Calcification	403
14.2.9	Stem Vessels	404
14.2.10	Nucleated Red Blood Cells	405
14.2.11	Villous Capillarization	405
14.2.12	Stromal Architecture and Stromal Fibrosis	406
14.2.13	Hofbauer Cells (Macrophages)	406
14.2.14	Inflammatory Changes	406
14.2.15	Villous Edema or Immaturity	407
	References	409
15	Villous Maldevelopment	411
15.1	Three-Dimensional Interpretation of Two-Dimensional Sections	411
15.2	Syncytial Knotting: Artifact or Meaningful Pathological Finding?	411
15.3	Classification of Villous Maldevelopment	414
15.4	Cases of Villous Maldevelopment	416
15.4.1	Synchronous Villous Immaturity	416
15.4.2	Persisting Villous Immaturity and Rhesus Incompatibility	417
15.4.3	Normal Mature Placenta	417
15.4.4	Preterm Villous Maturation and Villous Hypermaturation	419
15.4.5	Prolonged Pregnancy	419
15.4.6	Placentas at High Altitude and Maternal Anemia	420
15.4.7	Intrauterine Growth Restriction	421
15.4.8	Maternal Diabetes Mellitus	423
	References	425

16 Erythroblastosis Fetalis and Hydrops Fetalis	429
16.1 Erythroblastosis Fetalis	429
16.2 Placental Pathology in Erythroblastosis	430
16.2.1 Nonimmune Hydrops	436
16.2.2 α -Thalassemia	437
16.3 Fetal Hemorrhage	439
16.3.1 Fetal Tumors	440
16.4 Congenital Anomalies and Hydrops Fetalis	443
16.5 Congenital Heart Disease	444
16.6 Cardiac Arrhythmias	445
16.7 Nephrotic Syndrome	445
16.8 Parvovirus Anemia and Other Causes of Myocarditis	446
16.8.1 Hydrops of Unknown Etiology	450
References	452
17 Transplacental Hemorrhage, Cell Transfer, Trauma	461
17.1 Transplacental Blood and Cell Transfer	461
17.2 Trauma	461
17.3 Placenta in Hemorrhage	466
17.4 Technique for Identification of Fetal Red Blood Cells	467
17.5 Significant Transplacental Hemorrhage	471
17.6 Fetal Consequences of Massive Hemorrhage Across the Placenta	473
17.7 Nucleated Fetal Blood Elements Passing Through the Placenta	477
17.8 Mother to Fetus Transfer of Cells	478
References	479
18 Fetal Storage Disorders	487
References	492
19 Maternal Diseases Complicating Pregnancy: Diabetes, Tumors, Preeclampsia, Lupus Anticoagulant	495
19.1 Maternal Diseases	495
19.1.1 Scleroderma	495
19.1.2 Dermatomyositis	496
19.1.3 Ehlers–Danlos Syndrome	496
19.1.4 Rheumatoid Arthritis	496
19.1.5 Acute Fatty Liver of Pregnancy	497
19.1.6 Hyperemesis Gravidarum	497
19.1.7 Smoking	499
19.1.8 Hodgkin's Disease	500
19.1.9 Irradiation	501
19.1.10 Hypercholesterolemia	501
19.1.11 Pruritus Gravidarum	201
19.1.12 Pheochromocytoma	502
19.1.13 Hematological Disorders	502
19.1.14 Endocrine Disorders	505
19.1.15 Diabetes Mellitus During Pregnancy	506
19.1.16 Maternal Neoplasms	509
19.2 Hypertensive Disorders	513
19.2.1 Preeclampsia	513
19.2.2 Animal Models	514
19.2.3 Placental Pathology of Preeclampsia	514
19.2.4 Decidual Arteriopathy	515

19.2.5	Infarcts	519
19.2.6	Abruptio Placentae	522
19.2.7	Fetal Effects of Abruptio Placentae	526
19.2.8	Other Placental Changes in Preeclampsia	526
19.2.9	Etiology of Toxemia, Pregnancy-Induced Hypertension, or Preeclampsia	529
19.3	Lupus Erythematosus and Lupus Anticoagulant	532
19.3.1	Lupus Erythematosus	532
19.3.2	Lupus Anticoagulant	536
	References	539
20	Infectious Diseases	557
20.1	Chorioamnionitis	557
20.1.1	Macroscopic Appearance	557
20.1.2	Microscopic Appearance	559
20.1.3	General Considerations of Chorioamnionitis	572
20.1.4	Specific Microorganisms	575
20.2	Leprosy	581
20.3	Tuberculosis	582
20.4	Listeriosis	583
20.5	Actinomyces	586
20.6	Mycoplasma Hominis and Ureaplasma Urealyticum	586
20.7	<i>Chlamydia trachomatis</i> and <i>C. psittaci</i>	587
20.8	Bacterial Vaginosis	589
20.9	Syphilis	589
20.10	Necrotizing Funisitis	592
20.11	Other Spirochetal Diseases	595
20.12	Fungus Infections	595
20.13	Virus Infections and Villitides	599
20.13.1	Cytomegalovirus Infection	599
20.13.2	Herpes Simplex Virus Infection	603
20.13.3	Varicella (Chickenpox)	607
20.13.4	Epstein–Barr Virus	608
20.13.5	Smallpox, Vaccinia, Alastrim, and Parvovirus B19	608
20.13.6	Enteroviruses	609
20.13.7	Influenza, Mumps, and Rabies	610
20.13.8	Hepatitis	610
20.13.9	Rubella (German Measles) and Other Viral Infections	612
20.13.10	Rubeola: Measles	612
20.13.11	Human Immunodeficiency Virus (HIV) Infection	613
20.14	Toxoplasmosis	614
20.15	Kala-Azar	618
20.16	Chagas’ Disease	618
20.17	Babesiosis, Trichomoniasis, Rickettsia, and Ehrlichia	619
20.18	Malaria	620
20.19	Other Parasitic Infections	621
20.20	Villitis of Unknown Etiology (VUE)	622
	References	629
21	Abortion, Placentas of Trisomies, and Immunological Considerations of Recurrent Reproductive Failure	657
21.1	Anatomical Findings	659
21.2	Summary of Placental Findings in Chromosomally Defined Abortions	662
21.2.1	Trisomies	662
21.2.2	Polyploidies	664

21.2.3	Monosomy X	665
21.2.4	Induced Abortion	666
21.3	Incomplete Abortion	670
21.4	Placenta in Chorionic Villus Sampling	671
21.5	Trisomic Placentas	674
21.5.1	Chemical Markers and Trisomy	676
21.6	Recurrent or Habitual Abortion	677
	References	679
22	Molar Pregnancies	687
22.1	Incidence	688
22.2	Genetics	690
22.3	Recurrent Hydatidiform Moles	695
22.4	Complete Hydatidiform Moles	696
22.5	Partial Hydatidiform Mole	700
22.6	Other Attributes	703
22.7	Deportation.	705
22.8	Invasive Mole (Chorioadenoma Destruens).	706
22.9	Therapy	708
22.10	Ectopic Moles.	709
22.11	Complete Mole and Coexistent Fetus	709
22.12	PHM with Twin Gestation	711
	References	713
23	Trophoblastic Neoplasms	723
23.1	Choriocarcinoma	723
23.1.1	Intraplacental Choriocarcinoma (Choriocarcinoma “In Situ”) and Choriocarcinoma Coincident with Pregnancy.	728
23.1.2	Chorangiocarcinoma	730
23.2	Lesions of Extravillous Trophoblast: Exaggerated Placental Site, Placental Site Nodule, Placental Site Trophoblastic Tumor (PSTT), and Epithelioid Trophoblastic Tumor (ETT)	731
23.3	Ultrastructure of Trophoblastic Tumors.	735
23.4	Antigenic Studies of Trophoblastic Tumors.	735
23.5	Epidemiology of Choriocarcinoma	736
23.6	Endocrine Aspects of GTN	737
23.7	Ectopic Choriocarcinomas: Tumors in Men	738
23.8	Therapy of GTN.	739
23.9	Choriocarcinoma in Animals	740
23.10	Choriocarcinoma in Cell Lines and Genetics.	740
	References	741
24	Benign Tumors and Chorangiomas	747
24.1	Chorangiomas	747
24.2	Other Benign Tumors.	754
24.3	Chorangiomas and Chorangiomas	754
24.4	Mesenchymal Dysplasia and the Beckwith-Wiedemann Syndrome	756
	References	756
25	Multiple Pregnancies	761
25.1	Zygosity	761
25.2	The Placenta in the Study of Zygosity	764
25.3	Causes of Multiple Births and Incidence	769
25.4	Third Type of Twin	774

25.5	Twinning Incidence	776
25.6	Superfetation and Superfecundation	778
25.7	Vascular Anatomy of Twin Placentas	778
25.8	Monoamniotic Monochorionic Twin Placenta	784
25.9	Diamniotic Monochorionic Twin Placenta	798
25.10	Diamniotic, Dichorionic Twin Placenta	800
25.11	Vanishing Twin Phenomenon	801
25.12	Fetus Papyraceus	805
25.13	Twin-to-Twin Transfusion Syndrome	811
25.14	Amniopatch	825
25.15	Acardiac Twins	826
25.16	Conjoined Twins	835
25.17	Sacrococcygeal Teratoma, Epignathus	838
25.18	Congenital Anomalies	840
25.19	Cytogenetics and “Heterokaryotypic MZ Twins”	842
25.20	Chimerism, Mosaicism	843
25.21	Whole-Body Chimerism	845
25.22	Triplets and Higher Multiple Births	846
25.23	Twins in Abortion and Ectopic Pregnancy	851
25.24	Morbidity and Mortality	853
25.25	Hormones in Twin Pregnancy	855
	References	855
26	Legal Considerations	883
26.1	Twinning Problems	886
26.2	Inflammation	888
26.3	The Green Placenta	889
26.4	Vascular Abnormalities	890
26.5	Umbilical Cord	891
26.6	Placental Villous Color	892
26.7	Other Types of Pathology	893
	References	895
27	Artificial Reproductive Technology (ART)	897
27.1	Placental Pathology with ART	899
27.2	Monozygosity and Monochorionicity Following ART	900
27.3	Chimerism	901
27.4	Confined Placental Mosaicism	901
27.5	Imprinting	901
27.6	Immunology	902
	References	902
	Appendix	907
	Index	925