

Contents

Preface	v
1. Examination of the Placenta	1
Macroscopic Examination	1
Storage	1
Selection	2
Photography	2
Examination	2
Placentas of Multiple Births	7
Fixation	8
Special Procedures	10
References	11
2. Macroscopic Features of the Delivered Placenta	13
Fetal Surface	13
Maternal Surface	13
The Terms Fetal Placenta and Maternal Placenta	15
References	15
3. Microscopic Survey	16
Typical Histologic Features of the First Trimester Placenta	16
Typical Histologic Features of the Third Trimester Placenta	20
Immunohistochemical Markers	24
4. Placental Types	30
Placental Shapes	32
Types of Maternofetal Interdigitation	34
Maternofetal Barrier	35
Maternofetal Blood Flow Interrelations	37
Placental Types and Phylogeny	37
Human Placenta	38
References	40

5. Early Development of the Human Placenta	42
Prelacunar Stage	42
Lacunar Stage	44
Early Villous Stages	46
References	48
6. Basic Structure of the Villous Trees	50
<i>M. Castellucci and P. Kaufmann</i>	
Syncytiotrophoblast	50
Syncytium or Multinucleated Giant Cells?	50
Syncytial Plasmalemmas and Microvilli	54
Syncytiotrophoblastic Cytoskeleton	55
Specialized Regions of the Villous Surface	55
Syncytiotrophoblast with Prevailing Rough Endoplasmic Reticulum	55
Syncytiotrophoblast with Prevailing Smooth Endoplasmic Reticulum	57
Vasculosyncytial Membranes	59
Syncytial Lamellae Covering Langhans' Cells	61
Syncytial Knots, Sprouts, and Bridges	61
Transtrophoblastic Channels	64
Trophoblastic Blebbing	64
Villous Cytotrophoblast (Langhans' Cells)	65
Cytotrophoblast Cell Types	66
Nematosomes	70
Endocrine Activities of the Villous Cytotrophoblast	70
Trophoblast Turnover and Syncytial Fusion	72
Quantitation of Trophoblast Turnover	72
Why Does Syncytiotrophoblast Survival Depend on Syncytial Fusion?	72
Trophoblastic Differentiation and Apoptosis Cascade	73
Molecular Mechanisms of Syncytial Fusion	76
Phosphatidylserine Flip as Fusion Signal	76
Junctional and Adhesion Molecules as Fusion Mediators	76
The ADAM Family of Fusogenic Proteins	76
Endogenous Retroviral Envelope Proteins of the HERV Family (Syncytins) and Their Receptors	77
Molecular Control of Syncytial Fusion	78
The Role of Oxygen and Cytokines in Trophoblast Proliferation and Fusion	79
The Impact of Trophoblast Turnover on Syncytiotrophoblast Specialization	81
Trophoblastic Basement Membrane	82
Connective Tissue	82
Mesenchymal Cells (V Cells)	82
Fibroblasts (VD Cells and VDA Cells)	83
Myofibroblasts (VDAG Cells and VDAGM Cells)	84
Matrix Components of the Villous Stroma	86
Hofbauer Cells (Villous Macrophages)	87
First Descriptions	87
Morphology	87
Occurrence and Distribution	90
Origin	90

Immunologic Aspects	91
Other Free Connective Tissue Cells	93
Basic Structure of the Vessel Walls	93
Fetal Capillaries	94
Large Fetal Vessels	94
Vasomotor Control	96
Fibrinoid of the Villous Trees	96
Perivillous Fibrinoid	96
Intravillous Fibrinoid	98
References	99
7. Architecture of Normal Villous Trees	121
Classification of Villous Types	121
Stem Villi	121
Immature Intermediate Villi	126
Mature Intermediate Villi	128
Terminal Villi	129
Mesenchymal Villi	133
Immunohistochemistry of Villous Types	134
Differentiation and Maturation of Villous Types	137
Development of the Mesenchymal Villi	137
Development and Fate of Immature Intermediate Villi	138
Development of Stem Villi	138
Development of the Mature Intermediate Villi	140
Development of the Terminal Villi	140
Angioarchitecture of Villi	140
Vascular Arrangement in Immature Villi	140
Larger Vessels of Stem Villi	141
Paravascular Capillary Net of Stem Villi	141
Arrangement of Vessels in Mature Intermediate and Terminal Villi	143
Sinusoids of Terminal Villi	145
Fetoplacental Angiogenesis as the Driving Force for Villous Development	146
General Aspects of Placental Vasculogenesis and Angiogenesis	147
Vasculogenesis 1: Origin of Hemangiogenic Progenitor Cells (Days 15 to 21)	148
Vasculogenesis 2: Formation of Endothelial Tubes (Days 21 to 32)	148
Angiogenesis 1: Branching Angiogenesis (Day 32 to Week 25)	153
Angiogenesis 2: Formation of Stem Vessels and Regression of Capillaries in Stem Villi (Weeks 15 to 32)	153
Angiogenesis 3: Prevailing Nonbranching Angiogenesis (Week 25 to Term)	154
Oxygen and Oxygen-Controlled Growth Factors as Regulators of Villous and Vascular Development	155
The Special Role of Oxygen in the Placenta	155
Types of Hypoxia and Its Effects on Villous Development	155
Evidence for Oxygen-Controlled Fetoplacental Angiogenesis	157
Oxygen-Controlled Angiogenic Growth Factors	157
The Timing Mismatch Between Changes in Oxygenation and Morphologic Changes	158
Oxygen and Villous Trophoblast	159

Oxygen and Villous Stroma	159
Oxygen and Intervillous Circulation	159
Hormones as Regulators of Villous Development	160
Intervillous Space as Related to the Villous Trees	160
Width of the Intervillous Space	161
Organization of Villous Trees	161
Histopathologic Importance of Inhomogeneity of Villous Trees	164
Fetomaternal Flow Interrelations	164
References	165
8. Characterization of the Developmental Stages	174
Stages of Development	174
Nucleated Red Blood Cells	185
References	189
9. Nonvillous Parts and Trophoblast Invasion	191
<i>H.G. Frank and P. Kaufmann</i>	
Extravillous Trophoblast	191
Historical Aspects and Nomenclature	191
Extravillous Trophoblast Is a Tissue of Its Own	193
Proliferation Patterns of Extravillous Trophoblast and the Invasive Pathway	194
Stages of Extravillous Trophoblast Differentiation Within the Invasive Pathway	196
One Stem Cell Origin for Villous Syncytiotrophoblast and the Extravillous Trophoblast?	200
Cytokines and Hormones Controlling Differentiation of Extravillous Trophoblast	201
Extracellular Matrix Secretion Along the Invasive Pathway	204
Extracellular Matrix Receptors (Integrins)	204
Other Cell Adhesion Molecules and Gap Junction Molecules	206
Proteinases, Activators, and Inhibitors Involved in Trophoblast Invasion	207
Nitric Oxide and Trophoblast Invasion	209
Major Basic Protein	209
Cell Surface Carbohydrates	211
MHC Class I Molecules	212
Normal Extravillous Trophoblast Cells Are Never Proliferative and Invasive at One Time	213
Oxygen-Mediated Regulation of the Invasive Pathway	214
Extracellular pH as Trigger of Trophoblast Invasion	215
Trophoblastic Mechanisms Limiting Trophoblast Invasion	215
Endocrine Activities of Extravillous Trophoblast	216
Does Extravillous Trophoblast Differ from One Nonvillous Part to the Other?	217
Decidua	217
Composition of Decidua	217
Endometrial Stromal Cells and Decidual Cells	218
Endocrine and Paracrine Aspects of Decidua	220
Functional Considerations of Decidualization	221
B Cells and T Cells	222

Endometrial Large Granular Lymphocytes (Endometrial NK Cells and uNK Cells)	223
Macrophages	224
Glandular Residues	225
Decidual Extracellular Matrix	225
Fibrinoid	226
Definition and Historical Remarks	226
Types of Fibrinoid	227
Origin of Fibrinoids	230
Interactions Between Matrix-Type and Fibrin-Type Fibrinoid	231
Functions of Fibrinoid	231
Trophoblast Invasion as a Result of Deciduo-Trophoblastic Interactions	233
Calcification	236
Chorionic Plate	239
Development	239
Structure at Term	239
Amnion	239
Spongy Layer	240
Chorionic Mesoderm	241
Extravillous Cytotrophoblast	241
Langhans' Fibrinoid Layer	242
Marginal Zone	243
Subchorial Closing Ring	243
Trabeculae	244
Marginal Sinus	244
Basal Plate	244
Trophoblastic Shell and Development of the Basal Plate	244
Layers of the Basal Plate at Term	246
Uteroplacental Vessels	249
Development	249
Number and Position of the Uteroplacental Vessels	251
Importance of Physiologic Changes of Uteroplacental Arteries	252
Stages of Physiologic Changes in Uteroplacental Arteries	252
Sites and Routes of Endovascular Trophoblast Invasion	254
Trophoblast-Endothelial Adhesion Mechanisms	255
The Role of Macrophages in the Control of Endovascular Trophoblast Invasion	256
Incompetent Trophoblast Invasion or Exaggerated Maternal Defense as Causes for Maladaptation of Uteroplacental Arteries	257
Structure of Uteroplacental Veins	258
Intramural Fibrinoid of Uteroplacental Arteries and Veins	260
Functional Aspects of Uteroplacental Vessels	260
Septa, Cell Islands, and Cell Columns	261
Septa	261
Cell Islands	264
Cell Columns	265
Pathology of Trophoblast Invasion	268
Placenta Accreta	268
Placenta Increta and Percreta	271
Uterine Rupture	273
Placenta in Ectopic (Tubal) Pregnancy	275
Placenta in Abdominal Pregnancy	276
Cysts and Breus' Mole	277

Maternal Floor Infarction	281
Decidual Degeneration	284
References	287
10. Involution of Placental Site; Retained Placenta	313
Involution of the Placental Site	313
Subinvolution	316
Placental Polyps	316
Involution of a Remaining Placenta	319
References	319
11. Anatomy and Pathology of the Placental Membranes	321
Overview	321
Development	323
Amnion	326
Amnionic Epithelium: Different Cell Types or Cell Degeneration	327
Cytologic and Functional Aspects of the Amnionic Epithelium	327
Amnionic Fluid	330
Chromosomal Determinations	331
Cellular Metaplasia and Glycogen	331
Amnionic Mesoderm	333
A Medley of Themes	334
Clinical and Research Applications	334
Chorion Laeve	335
Intermediate (Spongy) Layer	335
Chorionic Mesoderm	335
Trophoblast Layer	336
Decidua	337
Tensile Properties of the Membranes	338
Pathology of the Membranes	338
Preterm Rupture of the Membranes	338
Cysts, Tumors, and Hemorrhage	340
Amniotic Fluid Embolism	342
Meconium	345
Gastroschisis	354
Epidermolysis Bullosa	354
Amnion Nodosum	355
Amnionic Bands	358
Extramembranous Pregnancy	364
References	366
12. Anatomy and Pathology of the Umbilical Cord	380
Development	380
Amnionic Epithelium	380
Wharton's Jelly	381
Structure of Umbilical Vessels	383
Innervation	384
Contractility of Umbilical Vessels	385
Hyrtil's Anastomosis, False Knots, and Hoboken Nodes	386
Allantois	388
Omphalomesenteric Duct	389
Spiral Turns of the Cord	392

Length of the Cord	394
Abnormal Length, Nuchal Cord	395
Site of Cord Insertion	401
Furcate Cord Insertion	402
Velamentous Cord Insertion	403
Placental Surface Vessels	407
Nucleated Red Blood Cells (NRBCs)	410
Cysts and Edema	411
Single Umbilical Artery	413
Placental Transfusion	415
Knots	416
False Knots	418
Strictures	419
Rupture	420
Hematoma	421
Varices and Aneurysms	423
Thrombosis of the Umbilical Vessels	426
Thrombosis of the Placental Vascular Tree	428
Tumors of the Umbilical Cord	434
References	435
13. Placental Shape Aberrations	452
Site of Placental Attachment	452
Volumetric Growth	454
Abnormal Shapes (“Errors in Outline”)	454
Placenta Previa	457
Placenta Membranacea	462
Circumvallate Placenta (Extrachorial, Circummarginate Placentas)	464
References	468
14. Histopathologic Approach to Villous Alterations	473
How to Assess Villous Histopathology	473
Assessment of Villous Maturation	473
Placental Insufficiency	476
Examination of Fetal Stem Vessels	477
Examination of the Fetal Capillary Bed	477
Villous Architecture and Fibrinoid	478
Intervillous Space, Infarcts	479
Abruptio Placentae	480
Major Histopathologic Findings	480
Syncytiotrophoblast	480
Knotting of the Syncytiotrophoblast	480
Langhans’ Cells	482
Vasculosyncytial Membranes	482
Trophoblastic Basement Membrane	482
Perivillous Fibrinoid	482
Intravillous Fibrinoid	483
Villous Calcification	483
Stem Vessels	483
Nucleated Red Blood Cells	484
Villous Capillarization	484
Stromal Architecture and Stromal Fibrosis	485

Hofbauer Cells (Macrophages)	486
Inflammatory Changes	486
Villous Edema or Immaturity	486
References	488
15. Classification of Villous Maldevelopment	491
Three-Dimensional Interpretation of Two-Dimensional Sections	491
Syncytial Knotting: Artifact or Meaningful Pathologic Finding	491
Interpretation of Syncytial Knotting	491
Artificial Knotting as Related to Villous Shapes in Paraffin Sections	494
Conclusions Concerning Knotting	497
Classification of Villous Maldevelopment	497
Summarizing Diagram of Villous Maldevelopment	497
Villous Maturation Score	500
Cases of Villous Maldevelopment	502
Synchronous Villous Immaturity	502
Persisting Villous Immaturity and Rhesus Incompatibility	502
Normal Mature Placenta	504
Preterm Villous Maturation and Villous Hypermaturation	506
Prolonged Pregnancy	507
Placentas at High Altitude and Maternal Anemia (Preplacental Hypoxia)	508
Intrauterine Growth Restriction with Preserved End-Diastolic Umbilical Flow in the Third Trimester, with or Without Late-Onset Preeclampsia (Uteroplacental Hypoxia)	509
Intrauterine Growth Restriction Combined with Absent or Reverse End-Diastolic Umbilical Blood Flow in the Second Trimester, with or Without Early-Onset Preeclampsia (Postplacental Hypoxia)	511
Preeclampsia	512
HELLP Syndrome (Postplacental Hypoxia)	513
Maternal Diabetes Mellitus	515
References	516
16. Erythroblastosis Fetalis and Hydrops Fetalis	519
Erythroblastosis Fetalis	519
Placental Pathology in Erythroblastosis	520
Nonimmune Hydrops	526
α -Thalassemia	527
Fetal Hemorrhage	529
Fetal Tumors	530
Congenital Anomalies and Hydrops Fetalis	532
Congenital Heart Disease	533
Cardiac Arrhythmias	534
Nephrotic Syndrome	534
Parvovirus Anemia	535
Hydrops of Unknown Etiology	540
References	541
17. Transplacental Hemorrhage, Cell Transfer, Trauma	552
Transplacental Blood and Cell Transfer	552
Trauma	552

Placenta in Hemorrhage	558
Technique for Identification of Fetal Red Blood Cells	559
Significant Transplacental Hemorrhage	561
Fetal Consequences of Massive Hemorrhage Across the Placenta ...	563
Other Fetal Blood Elements Passing Through the Placenta	568
Mother-to-Fetus Transfer of Cells	569
References	569
18. Fetal Storage Disorders	577
References	582
19. Maternal Diseases Complicating Pregnancy: Diabetes, Tumors, Preeclampsia, Lupus Anticoagulant	584
Maternal Diseases	584
Hematologic Disorders	592
Endocrine Disorders	596
Diabetes Mellitus During Pregnancy	596
Maternal Neoplasms	600
Hypertensive Disorders	604
Preeclampsia	604
Animal Models	605
Placental Pathology of Preeclampsia	605
Decidual Arteriopathy	606
Infarcts	612
Abruptio Placentae	615
Fetal Effects of Abruptio Placentae	620
Other Placental Changes in Preeclampsia	620
Etiology of Toxemia, Pregnancy-Induced Hypertension, or Preeclampsia	623
Lupus Erythematosus and Lupus Anticoagulant	625
Lupus Erythematosus	625
Lupus Anticoagulant	630
References	634
20. Infectious Diseases	657
Chorioamnionitis	657
Macroscopic Appearance	657
Microscopic Appearance	660
General Considerations of Chorioamnionitis	674
Specific Microorganisms	676
Mycoplasma Hominis and Ureaplasma	687
Chlamydia Trachomatis and C Psittaci	689
Bacterial Vaginosis	690
Syphilis	690
Necrotizing Funisitis	694
Other Spirochetal Diseases	696
Fungus Infections	696
Virus Infections and Villitides	700
Cytomegalovirus Infection	700
Herpes Simplex Virus Infection	706
Varicella (Chickenpox)	709
Epstein-Barr Virus	710

Smallpox, Vaccinia, Alastrim, and Parvovirus B19	710
Enteroviruses	712
Influenza, Mumps, Rabies	712
Hepatitis	712
Rubella (German Measles) and Other Viral Infections	713
Rubeola (Measles)	714
Human Immunodeficiency Virus Infection	715
Toxoplasmosis	716
Kala-Azar	720
Chagas' Disease	720
Babesiosis, Trichomoniasis, Rickettsia, and Ehrlichia	722
Malaria	722
Other Parasitic Infections	724
Villitis of Unknown Etiology	724
References	732
21. Abortion, Placentas of Trisomies, and Immunologic Considerations of Recurrent Reproductive Failure	762
Anatomic Findings	764
Summary of Placental Findings in Chromosomally Defined Abortions	768
Trisomies	768
Polyploidies	770
Monosomy X	772
Induced Abortions	772
Incomplete Abortion	777
Placenta in Chorionic Villus Sampling	778
Trisomic Placentas	781
Chemical Markers and Trisomy	782
Recurrent or Habitual Abortion	784
References	787
22. Molar Pregnancies	797
Hydatidiform Moles and Partial Moles	797
Hydatidiform Moles	797
Other Attributes	811
Therapy	815
Partial Hydatidiform Mole	817
References	825
23. Trophoblastic Neoplasms	837
Choriocarcinoma	837
Choriocarcinoma In Situ and Choriocarcinoma Coincident with Pregnancy	843
Chorangiocarcinoma	846
Exaggerated Placental Site: Placental Site Nodule, Placental Site Trophoblastic Tumor, and Epithelioid Trophoblastic Tumor	846
Ultrastructure of Trophoblastic Tumors	851
Antigenic Studies of Trophoblastic Tumors	851
Epidemiology of Choriocarcinoma	852
Endocrine Aspects of Gestational Trophoblastic Neoplasia	852

Ectopic Choriocarcinomas; Tumors in Men	853
Therapy of Gestational Trophoblastic Neoplasia	854
Choriocarcinoma in Anamils	855
Choriocarcinoma in Cell Lines and Genetics	855
References	856
24. Benign Tumors and Chorangiomas	863
Angiomas	863
Other Benign Tumors	870
Chorangiomas and Chorangiomas	871
Mesenchymal Dysplasia and the Beckwith-Wiedemann Syndrome	873
References	873
25. Multiple Pregnancies	877
Zygosity	877
The Placenta in the Study of Zygosity	879
Causes and Incidence of Multiple Births	885
Third Type of Twin	890
Twinning Incidence	891
Superfetation and Superfecundation	893
Vascular Anatomy of Twin Placentas	893
Monoamniotic/Monochorionic Twin Placenta	902
Diamniotic/Monochorionic Twin Placenta	915
Diamniotic/Dichorionic Twin Placenta	917
Vanishing Twin Phenomenon	919
Fetus Papyraceus	923
Twin-to-Twin Transfusion Syndrome	928
Acardiac Twins	941
Conjoined Twins	950
Sacrococcygeal Teratoma and Epignathus	953
Congenital Anomalies	955
Cytogenetics and Heterokaryotypic Monozygotic Twins	956
Chimerism and Mosaicism	957
Whole-Body Chimerism	959
Triplets and Higher Multiple Births	960
Twins in Abortion and Ectopic Pregnancy	967
Morbidity and Mortality	968
Hormones in Twin Pregnancy	971
References	971
26. Legal Considerations	1001
Twinning Problems	1004
Inflammation	1005
The Green Placenta	1007
Vascular Abnormalities	1008
Umbilical Cord	1009
Placental Villous Color	1009
Other Types of Pathology	1010
References	1013

27. Glossary 1016

28. Normative Values and Tables 1019

Index 1027