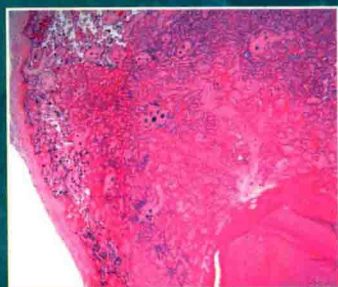


Handbook of
**PLACENTAL
PATHOLOGY**

Second Edition



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Handbook of Placental Pathology

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Preface to the Second Edition

It has been estimated that about 20% of placentas from deliveries are submitted to pathology departments in the United States. Hence, pathologists in all types of practice receive large numbers of these specimens. Training in pathology often does not address this organ in great detail, and many pathologists who do not have a special interest in the placenta are at a loss. However, the importance of placental findings is indisputable. The placenta can shed light on conditions relating to the current pregnancy outcome, as well as be predictive of future pregnancies. The placenta has a major role to play in medicolegal litigation as well. The few texts that are currently available are greatly detailed, and do not take the needs of the busy surgical pathologist into account. This book was designed to fill that need,

while also being of interest to placental pathologists, obstetricians, neonatologists, as well as trainees in these specialties. As such, the original format was retained, aiming at being easy to read and follow. Furthermore, we wanted to give updated data, introduce recent concepts and expand on aspects of etiopathogenesis and clinical features relevant to placental pathology, and hence new sections were added as well. The original photographs have been entirely replaced by a new set of digitized images and diagrams. The number of gross and microscopic photographs has been increased. It is our hope that this book will find an equal home on the workbench of the practicing pathologist, the desk of the trainee, and the reference shelf of all practitioners who deal with aspects of the delivery of a healthy newborn.

Ona Faye-Petersen
Debra S Heller
Vijay Joshi

Preface to the First Edition

The seeds of this book were sown when, about 4 years ago, I started signing out placentas in large numbers for the first time in my career. In order to prepare for the task and approach it in a systematic manner, I started reading monographs, book chapters, and articles on the subject. I prepared a short write-up on placental pathology for my surgical pathologist colleagues. As I continued signing out placentas at the rate of about 1400 per year, and began seeing variants of common placental lesions and different types of uncommon and rare placental lesions, I felt the need to organize the process of signing out in a more systematic way. That led to the preparation of this handbook, which should serve as a concise yet comprehensive guide for general surgical pathologists in carrying out gross and microscopic examination of placentas and preparing reports systematically, expeditiously, and with better understanding of placental pathology. I believe that it should also be useful to trainees in pathology, obstetrics and gynecology, and neonatology, as well as to practicing clinicians in these specialties.

It is estimated that about 20% of the placentas from about 5 million births occurring every year in the United States are submitted to the surgical pathology laboratory. (It appears that in some countries, many of the placentas that are not sent to the surgical pathology laboratory are used for preparation of albumin, immunoglobulins, and collagen.) Thus pathologists working in all types of hospitals

are likely to get placentas in their laboratories. The single-author and multiauthor monographs on placental pathology published in the past several years are excellent and comprehensive. However, they are not oriented to the needs of busy surgical pathologists, clinicians, and trainees in various specialties. On the other hand, the chapters on placental pathology in various textbooks of pathology and its subspecialties are not sufficiently comprehensive for their needs. This handbook occupies an intermediate position. In the opening section of the book, the normal structure of the placenta is briefly described. Common gross and microscopic lesions of the placenta are briefly discussed and adequately illustrated. These sections will help both the trainee and the practicing physician to develop a better understanding of and a systematic approach to placental pathology. The subsequent sections describe and illustrate the primary disorders. Besides the pathologic features, pathogenesis and clinical significance are described in every section for better understanding of various lesions. Tables that summarize the features of various lesions are suited for quick reference by the side of the microscope while one is signing out a case. In addition, pertinent original and recent references are cited at the end of the book. These references should serve as the source of more detailed discussion of various topics. Those who wish to keep up with the literature on the placenta need to review not only pathology journals but also obstetrics

journals and the journal *Placenta*. This book, which represents an attempt to fulfil the practical needs of practicing and trainee physicians, is largely based on material that has been published by various

investigators. However, wherever indicated, I have given my own views and related my own experience. I hope that the readers will find the book helpful.

Vijay V Joshi
Greenville, NC

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First, we would like to thank Ms Veronica Owens, Ms Linda Plunkett, Ms Lee Ann Brown, Ms Tara Allen, Mr James ('Bo') Moreno, and Mr E. Scott Young of the University of Alabama (UAB) Surgical Pathology service and Mr Thurman Richardson and Mr David Stephens of the UAB Autopsy Pathology service for the overwhelming majority of the gross photographs used in this manual. Their efforts are truly appreciated since the gross examination is so critical to a meaningful evaluation of the placental specimen.

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Ona Faye-Petersen
Debra Heller
Vijay Joshi

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Vijay Joshi

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Introduction

The placenta (derived from the Latin word translating as ‘flat cake’) provides oxygen, nourishment, and protection to the fetus. It also has excretory and endocrine functions. Numerous hormones such as human chorionic gonadotropin, progesterone, estrone, estradiol, estriol, and human placental lactogen are secreted by the placenta. Thus, the trophoblast contributes significantly to the hormonal milieu during pregnancy. Examination of the placenta in cases of poor pregnancy outcome and certain maternal disorders provides documentation and information useful to the obstetrician and neonatologist. Pathologic lesions of the placenta can be broadly classified into four types depending on their clinical relevance:

- (1) Lesions responsible for fetal or neonatal morbidity and/or mortality (infarction, infection, abruption, etc.);
- (2) Lesions related to premature delivery (chorioamnionitis, abruption, etc.);
- (3) Lesions that are likely to modify immediate management of the mother (e.g. hydatidiform mole);
- (4) Lesions that may recur in future pregnancies (thrombi, villitis of unknown etiology, maternal floor infarction, etc.).

The placenta has not been a particularly favorite subject of surgical pathologists for a variety of reasons. There seem to be too many of them, the terminology is different from other surgical pathology terminology, the yield of information is low for the volume of specimens, and information obtained is less likely to have a one-to-one correlation with that particular newborn’s situation than is a usual surgical specimen. There are also issues of cost to consider. On the other hand, the placenta can sometimes provide exceedingly useful information relating to perinatal morbidity and mortality, or subsequent pregnancy outcome. With the increase in medical malpractice suits against obstetricians, the placenta is often an important component of the defense. A placental finding that indicates significant prior compromise will be supportive in defending against a suit for failure to intervene appropriately during labor.

Both the American College of Obstetricians and Gynecologists, and the College of American Pathologists, are supportive of the value of placental examination^{1,2}. The purpose of this handbook is to make placental pathology comprehensible to the practicing surgical pathologist, trainee, and obstetrician who deal with placentas, and would like to be more comfortable with their interpretation.

2

Development of the placenta

After repeated mitotic divisions, the zygote, composed of the fused male and female pronuclei, transforms into a 32-cell ball of blastomeres or a *morula* (from Latin word *morum*, mulberry) by day 4 post-fertilization. The morula then begins to take on fluid, blastomeric segregation and compaction occur, and a fluid-filled cavity develops within the morula, changing it to a *blastocyst*. The blastomeres of the blastocyst form an outer shell of cells, now called *trophoblast* (from the Greek, *trophe*, meaning nutrition), and a localized, inner cell mass, the *embryoblast*. The side of the blastocyst with the inner cell mass is called the embryonic pole. The blastocyst emerges from its covering of zona pellucida, and is thereby enabled to attach tightly to the endometrium on about day 6. The site of attachment is at the embryonic pole, and, upon implantation, the trophoblast cells at the embryonic pole rapidly proliferate and differentiate into an outer, leading layer of *syncytiotrophoblast* and an inner, proliferating mass of *cytotrophoblasts*. These broad solid trophoblast columns invade the endometrium, which, due to progesterone from the corpus luteum, has become decidualized, and additional cytotrophoblast differentiation into an intermediate type occurs. Invasion (implantation) enables the conceptus to derive nourishment from the endometrium. Before implantation is completed, the embryoblast differentiates into a bilaminar embryo, composed of *epiblast* and *hypoblast*. On about day 6–7, epiblasts nearest to the site of implantation (i.e.

the dorsal epiblast) differentiate into *amnioblasts*. The amnioblasts proliferate, become decohesive, and fluid collects between them; the amnioblast is split and forms a small space, the amniotic cavity, by about the end of day 7. Thus, amnioblasts cover the epiblast, line the newly formed amniotic cavity, and separate the embryo from the trophoblast. Simultaneously, the trophoblasts invade the decidual interstitium and its blood vessels (capillaries and spiral arterial vessels); this vascular invasion results in blood extravasation and the formation of decidual blood lakes. At about day 9, the invading trophoblast also develops *internal* sites of cellular decohesion that progress to form lacunae; these become filled by maternal blood of the lakes. These lacunae then progressively enlarge and coalesce to form a network of blood-filled channels, the early intervillous spaces. These, the lacunar-lake formations, represent the beginning of the uteroplacental circulation as the maternal blood drains back into the maternal circulation via maternal veins. In addition, during the second week of development, the bilaminar embryonic disk exhibits an *extraembryonic* extension at its lateral aspects, the *extraembryonic mesenchyme*. Also, the invading fingers of syncytiotrophoblast have formed a radiating but spherical shell around the embryo and the amnion. The invasive syncytiotrophoblast projections gain a central, conical component of cytotrophoblast between days 11 and 13 and become the primary stem villi. The primary villi, which lie

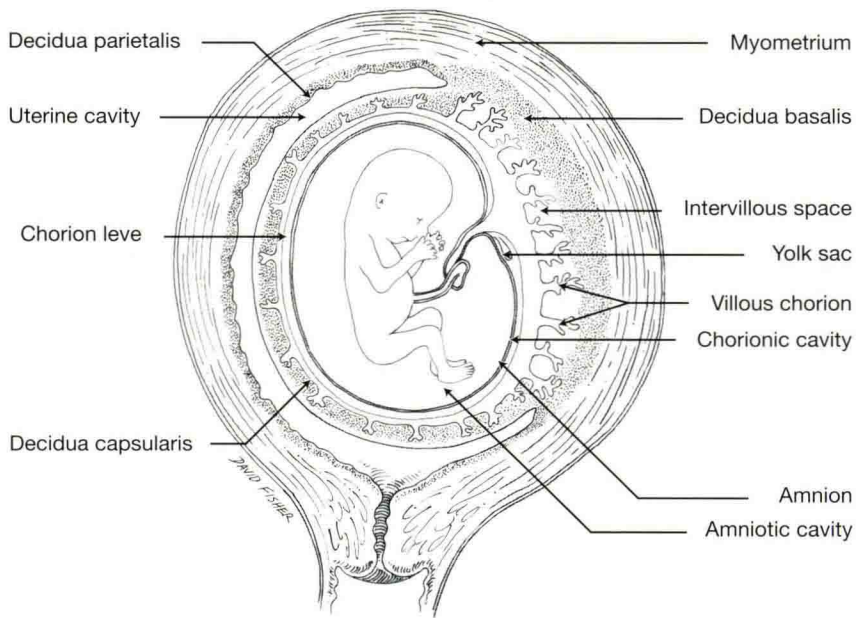


Figure 1 Diagram of fetus *in utero*. Representation of an intrauterine singleton pregnancy at about 16 weeks of gestation. In this illustration, some license is taken, since the amnion is shown as still *separate* from the chorion; this is done to illustrate the process of apposition of the amniotic sac to the chorion and to accentuate the interposition of the yolk sac between the amnion and the chorion. (Normally, the amnion and chorion are fully apposed by 12 weeks.) However, as is true at this stage of gestation, the chorion is shown fused to the decidua capsularis, and the fetal sac is not yet large enough to obliterate the uterine cavity

within blood-filled lacunae, in turn become infiltrated by protrusions of the extraembryonic mesenchyme, which has come to line the shell of the radiating trophoblast villous projections, and become secondary villi. The innermost core of extraembryonic mesenchyme within each secondary villus then gives rise to villous blood vessels, changing them to tertiary villi. By the end of the third week, the vessels of the tertiary villi become connected through channels in the extraembryonic chorionic plate and root of a connecting stalk to those vessels of the *intraembryonic* mesenchyme of the embryo proper. Thus, the extraembryonic mesenchyme develops into the vascular chorion plate of the placenta and the vascular cores of the chorionic villous tree. Due to the folding of the embryo during the 4th week, the chorion forms a sac whose projections vascularize the villous cytotrophoblast and its syncytiotrophoblast covering. The embryo and its

amniotic sac thereby lie suspended within this chorionic sac via the connecting stalk of vessels; this connecting stalk develops into the umbilical cord and contains the allantois (a ventral, tubular extension of the developing cloaca in the embryo), the yolk sac (the ventral extension of the primitive endodermal canal) and its tiny vascular supply, and two umbilical arteries and two veins. Later, the right umbilical vein disappears and the umbilical cord begins to lengthen. Up to about 8 weeks, chorionic villi cover the entire chorionic sac, but with growth of the sac, there is compression atrophy of the villi along the decidua capsularis. This compressed and atrophic chorion is called the chorion leve, or smooth chorion, and constitutes the free membranes. The villi along the decidua basalis rapidly proliferate, forming the chorionic plate and villous chorion (chorion frondosum), which constitute the placental disk. The amniotic sac enlarges faster than the chorionic sac, resulting in

fusion of the amnion with the chorion leve, by about 12 weeks of gestation. The chorioamnion, in turn, fuses with the decidua capsularis (Figure 1). By about 18–20 weeks of gestation, progressive enlargement of the fetal sac results in obliteration of the uterine cavity as the decidua capsularis fuses with the decidua

parietalis of the opposite uterine wall. At 20 weeks of gestation, the dome of the uterus is typically palpable at the level of the maternal umbilicus; thereafter, uterine size, as measured by fundal height above the umbilicus, increases by about 1 cm/gestational week.

3

Structure of the placenta

The placenta consists of the placental disk, the extraplacental free membranes, and the umbilical cord. The fetal surface of the disk is the chorionic plate (Figure 2), and the cotyledons and basal plate constitute the maternal surface (Figure 3). The fetal surface, the chorionic plate, is covered by amnion, and normally the cord is inserted here. The free membranes are normally inserted at the margins of the disk. On microscopic examination, the following structures are noted:

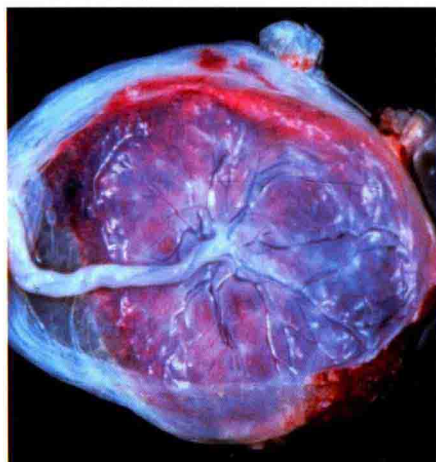


Figure 2 This placental specimen is from a spontaneous, uninfected, previable delivery at 20 weeks of gestation. The fetal surface of the placenta has a normal bluish tinge, is translucent, and shiny, the vessels of the umbilical cord split and ramify evenly over it, and the membranes attach at the placental margin

- (1) Placental disk: from the fetal to the maternal surface (Figure 4);
 - (a) Chorionic plate (fetal surface) (Figure 5): amnion, chorion, subchorionic fibrin, larger branches of umbilical blood vessels in the chorion, and smaller branches in the stem villi;
 - (b) Placental parenchyma (Figure 6): stem villi with smaller branches of the umbilical



Figure 3 The maternal surface of this trimmed placenta shows numerous demarcating cotyledons. (The upper left margin of the placenta also shows cut ends of velamentous segments of an abnormal umbilical cord insertion; velamentous cord insertion is discussed in a later section in this manual)