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<p>Birthweight is a well-known predictor of adult-onset chronic disease. The placenta plays a necessary role in regulating fetal growth and determining birth size. Maternal stressors that affect placental function and prenatal growth include maternal overnutrition and undernutrition, toxic social stress, and exposure to toxic chemicals. These stressors lead to increased vulnerability to disease within any population. This vulnerability arises from placental and fetal exposure to stressors during fetal life. The biological drivers linking various social determinants of health to compromised placental function and fetal development have been little studied.</p>	
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<p>Cardiovascular disease remains the leading killer of women, with sex-specific manifestation, mechanisms, and morbidity. Preeclampsia, fetal growth restriction, and a subset of preterm births demonstrate aberrancies in the maternal vessels supplying the placenta and damage to the placental parenchyma consistent with hypoxic/ischemic or oxidative injury. This constellation of findings, maternal vascular malperfusion (MVM) lesions, may hold the key to understanding and identifying the elevated risk for early cardiovascular disease in women who experience adverse pregnancy outcomes. This intriguing possibility has only begun to be examined, but accumulating evidence is compelling and is reviewed here.</p>	
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<p>The placenta can serve as a valuable source of information about maternal and fetal conditions during the pregnancy; however, the abilities to perform a preliminary gross examination and interpret a placental pathology report are variable among obstetricians. This article discusses the indications for placental submission to pathology; the essentials of gross examination, including elements that should be performed in the delivery suite; and the most common and clinically relevant histologic findings that may be encountered in the report.</p>	

Immunology of the Placenta

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Mancy Tong and Vikki M. Abrahams

In this article, the authors provide a general overview of the major immune cells present at the maternal-fetal interface, describe the key mechanisms used by the placenta to promote maternal immune regulation, tolerance, and adaptation, and discuss how dysregulation of these pathways could lead to obstetric complications such as pregnancy loss and preeclampsia. Finally, they conclude with a description of the innate immune properties of the human placenta that not only serve to protect the pregnancy from infection but also contribute to pregnancy complications such as preterm birth.

Diabetes Mellitus, Obesity, and the Placenta

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Gernot Desoye and Mila Cervar-Zivkovic

The placenta is exposed to metabolic derangements in the maternal and fetal circulation. The effects of the early placental “exposome” determine further trajectories. Overstimulation of the fetal pancreas in early gestation results in fetal hyperinsulinemia, augmenting glucose transfer with adverse effects on the fetus. The manifold placental changes at the end of pregnancy can be regarded as adaptive responses to protect the fetus from diabetes and obesity. The causal role of the placenta, if any, in mediating long-term effects on offspring development is an important area of current and future research.

The Placental Basis of Fetal Growth Restriction

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Rebecca L. Zur, John C. Kingdom, W. Tony Parks, and Sebastian R. Hobson

Placental dysfunction is a major contributing factor to fetal growth restriction. Placenta-mediated fetal growth restriction occurs through chronic fetal hypoxia owing to poor placental perfusion through a variety of mechanisms. Maternal vascular malperfusion is the most common placental disease contributing to fetal growth restriction; however, the role of rare placental diseases should not be overlooked. Although the features of maternal vascular malperfusion are identifiable on placental pathology, antepartum diagnostic methods are evolving. Placental imaging and uterine artery Doppler, used in conjunction with angiogenic growth factors (specifically placenta growth factor and soluble fms-like tyrosine kinase-1), play an increasingly important role.

Placental Anatomy and Function in Twin Gestations

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Matthew A. Shanahan and Michael W. Bebbington

With an increasing incidence of twin gestations, understanding the inherent risks associated with these pregnancies is essential in modern obstetrics. The unique differences in placentation in twins contribute to the increased risks. Monochorionic twins are susceptible to complications because of their unique placental architecture, including twin-to-twin transfusion syndrome, the twin anemia-polycythemia sequence, selective intrauterine growth restriction, and the twin reversed arterial perfusion sequence. Knowing the clinical correlations of placental anatomy in these

gestations helps perinatal pathologists perform a more informed placental evaluation, allowing for better care for the mother and her children.

Placental Implantation Disorders

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Eric Jauniaux, Ashley Moffett, and Graham J. Burton

Primary disorders of placental implantation have immediate consequences for the outcome of a pregnancy. These disorders have been known to clinical science for more than a century, but have been relatively rare. Recent epidemiologic obstetric data have indicated that the rise in their incidence over the last 2 decades has been iatrogenic in origin. In particular, the rising numbers of pregnancies resulting from in vitro fertilization (IVF) and the increased use of caesarean section for delivery have been associated with higher frequencies of previa implantation, accreta placental implantation, abnormal placental shapes, and velamentous cord insertion. These disorders often occur together.

Key Infections in the Placenta

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Maria Laura Costa, Guilherme de Moraes Nobrega, and Arthur Antolini-Tavares

Congenital infections are an important cause of morbidity and mortality worldwide, especially in low-income settings. This review discusses the main pathways of infections and associated adverse maternal and fetal outcomes, considering the TORCH pathogens, including Zika virus; the acronym stands for *Toxoplasma gondii* infection, other (*Listeria monocytogenes*, *Treponema pallidum*, and parvovirus B19, among others, including Zika virus), rubella virus, cytomegalovirus, and herpes simplex viruses type 1 and type 2.

Fetal Membranes, Not a Mere Appendage of the Placenta, but a Critical Part of the Fetal-Maternal Interface Controlling Parturition

147

Ramkumar Menon and John J. Moore

Fetal membranes (FMs) play a role in pregnancy maintenance and promoting parturition at term. The FMs are not just part of the placenta, structurally or functionally. Although attached to the placenta, the amnion has a separate embryologic origin, and the chorion deviates from the placenta by the first month of pregnancy. Other than immune protection, these FM functions are not those of the placenta. FM dysfunction is associated with and may cause adverse pregnancy outcomes. Ongoing research may identify biomarkers for pending preterm premature rupture of the FMs as well as therapeutic agents, to prevent it and resulting preterm birth.

Evidence for Corpus Luteal and Endometrial Origins of Adverse Pregnancy Outcomes in Women Conceiving with or Without Assisted Reproduction

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Kirk P. Conrad

Preeclampsia may arise from impaired decidualization in some women. Transcriptomics of mid-secretory biopsy endometrial stromal cells decidualized in vitro and of early gestation choriondecidua from women who experienced preeclampsia with severe features overlapped significantly with the classical endometrial disorders giving rise to the concept of

“endometrium spectrum disorders”. That is, recurrent implantation failure and miscarriage, endometriosis, normotensive intrauterine growth restriction, preeclampsia and preterm birth may all lie on a continuum of decidual dysregulation, in which phenotypic expression is determined by the specific molecular pathway(s) disrupted and severity of disruption. Women conceiving by programmed IVF protocols showed widespread dysregulation of cardiovascular function and increased rates of adverse pregnancy outcomes including preeclampsia. Programmed cycles preclude development of a corpus luteum (CL), a major regulator of endometrial function. Lack of circulating CL product(s) that are not replaced in programmed cycles (eg, relaxin) could adversely impact the maternal cardiovascular system directly and/or compromise decidualization, thereby increasing preeclampsia risk.

When the Fetus Goes Still and the Birth Is Tragic: The Role of the Placenta in Stillbirths

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Nicole Graham and Alexander E.P. Heazell

Because of the critical role that placental structure and function plays during pregnancy, abnormal placental structure and function is closely related to stillbirth: when an infant dies before birth. However, understanding the role of the placental and specific lesions is incomplete, in part because of the variation in definitions of lesions and in classifying causes of stillbirths. Nevertheless, placental abnormalities are seen more frequently in stillbirths than live births, with placental abruption, chorioamnionitis, and maternal vascular malperfusion most commonly reported. Critically, some placental lesions affect the management of subsequent pregnancies. Histopathological examination of the placenta is recommended following stillbirth.

Placental Magnetic Resonance Imaging: A Method to Evaluate Placental Function In Vivo

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Anne Sørensen and Marianne Sinding

This article describes the use of placental magnetic resonance imaging (MRI) relaxation times in the in vivo assessment of placental function. It focuses on T2*-weighted placental MRI, the main area of the authors' research over the past decade. The rationale behind T2*-weighted placental MRI, the main findings reported in the literature, and directions for future research and clinical applications of this method are discussed. The article concludes that placental T2* relaxation time is an easily obtained and robust measurement, which can discriminate between normal and dysfunctional placenta. Placenta T2* is a promising tool for in vivo assessment of placental function.