JOGNN

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The Placenta as a Research Biospecimen

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Keywords
placenta
National Children's Study
cytokines
biospecimens
pregnancy
maternal fetal exposures
fetal development
developmental biology
biomarkers

ABSTRACT

The placenta provides a unique opportunity to study the prenatal environment of the fetus to better understand subsequent infant and child health and illness. In this article we describe the role of the placenta as a research biospecimen, including placental morphology and cytokine biomarkers. Because of the role of the placenta in contemporary research, members of the perinatal health care team involved in birth have an important role in advancing science.

JOGNN, 41, 834-845; 2012. DOI: 10.1111/j.1552-6909.2012.01420.x

Accepted May 2012

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The authors report no conflict of interest or relevant financial relationships.

The health of the placenta is crucial for the health of the developing fetus, and the health of the fetus is crucial for the health of the developing infant and child. Thus, understanding the placenta provides a critical link to identifying key physiological processes in subsequent infant and child health and illness. The study of the placenta includes clinical, sonographic, laboratory, and anatomic data. The placenta (Salafia et al., 2008) as well as other birth specimens including maternal serum, cord blood, meconium, and breast milk (Barr, Wang, & Needham, 2005) provide invaluable scientific and clinical information about the health of the mother and fetus during gestation. Because of its ability to store biochemical information about events during gestation, the placenta has been referred to as the diary of pregnancy (Aagaard-Tillery, Thornburg, Bernstein, & Washburn, 2011; Baergen, 2007). Examination of the placenta provides a unique window into the prenatal environment of the fetus and may predict the future life course of the child (Burton, Barker, Moffett, & Thornburg, 2011).

In this article, we provide an overview of how the placenta is studied as a biospecimen by researchers seeking to understand the relationship between in-utero exposures and subsequent infant and child health outcomes. We provide background information and describe the morphologic examination of the placenta. The study of molecular biomarkers is an active area of perinatal and infant health research. Therefore, we describe cytokine biomarkers identified in specimens retrieved during birth. Although we only present a synopsis, this article frames some of the key components that may be studied in large-scale studies requiring the collection of birth specimens such as the National Children's Study (NCS) (Kent, Mancini, Pacholski, & Janisak, 2012).

The Placenta

Overview

The placenta is a very complex organ responsible for three major functions during pregnancy: metabolism, interfacing between the mother and fetus, and serving as an endocrine organ. The placenta, a unique repository or holding place of biochemical and genetic information, begins developing during the first 2 weeks of gestation. Early placental development occurs during the pre-embryonic period when the fertilized egg begins forming the placenta, the fetal membranes, and an interconnecting vascular space between the mother and fetus known as the intervillous network (Evain-Brion & Malassine, 2003; Maltepe, Bakardjiev, & Fisher, 2010).

The placental barrier separating the mother's blood from that of the fetus is composed of one layer of multinucleated cells, the syncytiotrophoblasts. The two sides (maternal and fetal)

of this single-layered barrier, the sycytium, are structurally and functionally different. On the maternal-facing side of the syncytium, a brush border membrane comes into direct contact with the mother's blood. Conversely, on the fetal-facing side, a basal membrane containing microvillous protrusions faces the fetal blood but does not come into direct contact. Interface between maternal blood and fetal trophoblastic cells takes place at this single-cell layer barrier (Prouillac & Lecoeur, 2010).

The placenta is able to adapt to its own growth needs and those of the fetus based on available maternal resources (Burton et al., 2011). The composition of the placenta is fluid, and changes throughout pregnancy. At one point of gestation, a placenta may be considerably different in size and molecular composition than at a different point in gestation (Burton et al.; Salafia et al., 2008).

The weights of the placenta and the infant at birth are often used to determine the health of the intrauterine milieu. Specifically, low birth weight has been linked to increased lifetime risks of cardiovascular disease and diabetes (Barker, 2007; Landrigan et al., 2006). Accordingly, Salafia et al. (2008) suggested that the characteristics of the placenta might be used as indicators of the fetal experience. These researchers analyzed data collected between 1959 and 1965 on 24,061 singleton infants born between 34 and 42 weeks gestation. They measured six placental characteristics: (a) distance from the umbilical cord insertion to the margin of the placental disc, (b) size of the smallest placental disc diameter, (c) size of the largest placental disc diameter, (d) thickness of the placental disc, (e) length of the umbilical cord, and (f) weight of the placenta. They proposed that measurements of the placenta reflect placental development during gestation and may indicate placental function, including most importantly the ability of the placenta to carry fetal blood to and from the maternal villious interface. Furthermore, they suggested that without adequate placental disc surface area and disc thickness, the placenta may not be able to adequately provide the nutrition and waste removal necessary for the fetus to grow and flourish (Baptiste-Roberts et al., 2008; Salafia et al., 2008). Salafia and colleagues suggested comprehensive and in-depth research of the placenta is needed to advance the current understanding of the intricate interactions between the fetus, mother, and placenta.

Understanding the placenta provides a critical link to identifying key physiological processes in subsequent infant and child health and illness.

Importance of Placenta Research

The study of the placenta is multifaceted and contributes significantly to understanding the in-utero experience of the developing fetus. Placenta research has been conducted internationally since at least the mid-1800s. The unusual interface between maternal-fetal circulation was reported in the *Journal of the British Royal Society of Medicine* in 1841 when Dalrymple published an article describing microscopic examination of placental tissue. The article included a series of three sketches depicting the vascular structure of the umbilical arteries and vein and the segments of the placenta (Dalrymple). Research of placenta morphology and function continues to this day. The International Federation of Placenta Associations is devoted to the scientific study of the placenta. The official scientific journal of this organization, *Placenta,* has been published since 1980.

To conduct research on the placenta, scientists need access to tissue specimens. Clinicians, including nurses, are the most common bridge between scientists conducting biological research and patients whose placentas would otherwise be discarded. Maternal/child health clinicians, educators, and researchers need to understand their critically important roles in retrieving specified birth biospecimens, such as the placenta, according to specific study protocols.

Researchers are currently studying the extent to which maternal exposure to environmental chemicals influences fetal development and childhood health via placental transfer. Environmental exposures that adversely affect the developing fetus include air pollution (Chalupka & Chalupka, 2010; Myren, Mose, Mathiesen, & Knudsen, 2007), metals such as lead and mercury (Chalupka & Chalupka; Dietrich et al., 2005), and pesticides (Dietrich et al.; Fenske, Bradman, Whyatt, Wolff, & Barr, 2005). Furthermore, a growing number of researchers are examining the adverse effects of maternal exposures to asbestos, pesticides, and leaded gasoline on long-term childhood illness (Landrigan et al., 2006; Swanson, Entringer, Buss, & Wadhwa, 2009; Wang, Needham, & Barr, 2005). Scientific examination of birth biospecimens is an established method to measure perinatal exposure (Evain-Brion & Malassine, 2003; Myren