Doppler Velocimetry of the Uteroplacental Circulation During Early Pregnancy

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Throughout pregnancy marked changes in uterine blood flow are observed that are related to a decrease in the resistance to flow in uterine vessels and to an increase in their diameter. Fetal growth is directly related to the incremental increase in uterine blood flow, and any long-term alteration in normal flow patterns could disrupt the oxygen and nutrient supply to the growing conceptus and result in an adverse pregnancy outcome.

Early normal pregnancy is characterized by profound morphologic changes in uterine vessels destined to supply the developing placenta. The trophoblast invades the inner third of the myometrium as early as 8 weeks’ gestation and migrates through the entire length of the spiral arteries, a process completed by approximately 20 weeks. During these “physiologic changes” the spiral arteries lose their musculoelastic tissue and are transformed into markedly dilated uteroplacental arteries. These changes are probably responsible for the marked reduction in the resistance to flow in the uterine arteries during the first half of gestation and determine the large increase in uterine blood flow that is evident throughout pregnancy. The developing uteroplacental circulation is also regulated by systemic and local vasoactive substances. Of particular interest are the endothelium-derived relaxing and contracting substances.

In the event that the physiologic processes are absent or incomplete, the course of pregnancy may be abnormal, and such complications as pregnancy-induced hypertension and fetal growth restriction could arise. That has become evident is that abnormal conditions during late pregnancy that could adversely affect both the mother and her fetus may reflect abnormal morphologic processes that have occurred at early stages of gestation. Under such circumstances it is theoretically possible to predict such conditions by detecting abnormal blood flow patterns during early pregnancy. Obviously we first have to know the normal characteristics of uteroplacental perfusion.

With the development of sophisticated Doppler ultrasonographic techniques, including color flow imaging, it has become possible to study the uteroplacental vascular bed more accurately and in greater detail than ever before. In this chapter we focus on the morphologic and physiologic changes of the uteroplacental circulation during the first half of pregnancy and on systemic and local factors that regulate uterine blood flow. Methodologic and anatomic aspects related to Doppler flow measurements of the uteroplacental circulation are highlighted, and patterns of uterine blood flow in normal and abnormal gestations are described. Finally, the use of Doppler sonography to predict pregnancy-induced hypertension, preeclamptic toxemia, and intrauterine growth restriction are discussed.

Maternal Vascular Response to Placentaion

The human placenta is hemochorial. Its maternal arterial blood supply is derived from the paired uterine arteries and, to some extent, from the ovarian arteries. The uterine arteries branch in the myometrium, giving rise to the arcuate arteries that encircle the uterus. The arcuate arteries have multiple branches called the radial arteries, which are directed centripetally. As the radial arteries enter the endometrium and approach the uterine cavity, they become the spiral arteries. During early pregnancy, as the maternalplacental circulation is established, profound morphologic and histologic changes take place in the spiral arteries. These morphologic changes are essential during normal pregnancy, as they provide for the ever-increasing demand imposed on the maternoplacental circulation by the advancing gestation. These “physiologic changes” are the result of retrograde intraluminal endovascular trophoblastic growth [1]. The endovascular trophoblasts invade the walls of the spiral arteries, converting them into funnel-shaped, dilated uteroplacental arteries. This transformation occurs in two steps: In the first step, the internal elastic lamina of the spiral arteries disintegrates, so a thin layer of basement membrane is all that remains between the endothelium and the smooth muscle. Next the trophoblast penetrates the arteries, and the media is replaced by a matrix containing cytotrophoblast and fibrin fibers. These morphologic changes
are limited to the decidual portion of the spiral arteries during the first trimester. During the early second trimester a new wave of endovascular trophoblast migration penetrates as far as the myometrial portion of the spiral arteries [2]. The second wave of trophoblastic migration is present in most women by 20 weeks’ gestation [3]. Normal uterine blood supply to the placenta is shown in Fig. 17.1. The physiological changes are functionally complete by 17 weeks as was demonstrated by measuring spiral artery blood flow using color Doppler ultrasound in the second trimester [4].

By 19 weeks’ gestation the coiling of the spiral arteries disappears [5]. This event is probably due to stretching of the uterine wall, as the shape of the uterus changes from spheroidal to cylindrical as it grows [6].

The disappearance of musculoelastic tissue from the decidual and myometrial spiral arteries allows them to attain a substantial increase in diameter. A 30-fold increase in diameter, compared to that of the nonpregnant state, has been described [7]. The physiological correlate of these structural alterations is a reduction in vascular resistance in the spiral arteries and increased uteroplacental flow rates throughout gestation [8]. This change has also been verified by radioisotopic techniques [9–11] and Doppler flow studies [12–14].

In normal pregnancy the trophoblast invades all spiral arteries in both the decidual endometrium and the myometrium. A defective maternal vascular response at the time of placentation is found in pregnancies complicated by preeclampsia and in a proportion of those with small-for-gestational-age (SGA) fetuses [15, 16]. In those pregnancies the vascular changes in the spiral arteries are restricted to the decidual segments or are totally absent. The arterial vascular response may be partial, so only a portion of the spiral arteries undergo normal “physiologic changes”, whereas others are not affected by endovascular trophoblast and remain in the same state as in the nonpregnant uterus. It is believed that a defective maternal response to placentation is due to failure of the second wave of intravascular trophoblastic migration [17]. The myometrial segments of the spiral arteries are unaltered in their musculoelastic architecture and are responsive to vasomotor influences (e.g., vasoactive peptides). Figure 17.2 demonstrates abnormal uterine blood supply to the placenta secondary to abnormal placentation.

Intraluminal trophoblast is a normal finding, then, during the first and second trimesters of normal pregnancy, where it plays a role in establishing placentation [18]. A defective interaction of trophoblast and uterine tissue, well established in preeclampsia and some forms of fetal growth restriction, may be due to immunologic maladaptation [18, 19]. Disturbance of trophoblastic invasion during early pregnancy is frequently associated with renewed trophoblastic migration during the third trimester [16, 20]. The luminal lining in the uteroplacental arteries remains trophoblastic and not endothelial [20]. The disrupted endothelium may be responsible for endothelial cell dysfunction, thought to be of pathogenetic importance in preeclampsia [21]. In addition, many of the affected vessels demonstrate necrotizing vascular lesions – deposition of fibrinoid material and adjacent foam cell invasion – a process also termed atherosclerosis [22].

Hemodynamic studies using radioisotope clearance values [10, 11], dynamic placental scintigraphy [23],

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**Fig. 17.1.** Normal blood supply to the placenta. Note the termination of radial arteries each into two spiral arteries that have been physiologically converted to uteroplacental arteries (dotted areas). (Reprinted from [16] with permission)