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The Uterine Spiral Arteries In Human Pregnancy: Facts and Controversies

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Abstract

Uterine spiral arteries play a vital role in supplying nutrients to the placenta and fetus, and for this purpose they are remodelled into highly dilated vessels by the action of invading trophoblast (physiological change). Knowledge of the mechanisms of these changes is relevant for a better understanding of pre-eclampsia and other pregnancy complications which show incomplete spiral artery remodelling. Controversies still abound concerning different steps in these physiological changes, and several of these disagreements are highlighted in this review, thereby suggesting directions for further research. First, a better definition of the degree of decidua- versus trophoblast-associated remodelling may help to devise a more adequate terminology. Other contestable issues are the vascular plugging and its relation with oxygen, trophoblast invasion from the outside or the inside of the vessels (intravasation versus extravasation), the impact of haemodynamics on endovascular migration, the replacement of arterial components by trophoblast, maternal tissue repair mechanisms and the role of uterine natural killer (NK) cells. Several of these features may be disturbed in complicated pregnancies, including the early decidua-associated vascular remodelling, vascular plugging and haemodynamics. The hyperinflammatory condition of pre-eclampsia may be responsible for vasculopathies such as acute atherosis, although the overall impact of such lesions on placental function is far from clear. Several features of the human placental bed are mirrored by processes in other species with haemochorial placentation, and studying such models may help to illuminate poorly understood aspects of human placentation.

Keywords: Spiral arteries; Trophoblast invasion; Vascular remodelling; Human; Pre-eclampsia; Decidualization; Uterine NK cells

1. Introduction

The interrelationship between maternal and fetal circulations enabling physiological exchange within the placenta is still not fully understood. Probably the most significant breakthrough was achieved in the 18th century when William and John Hunter demonstrated by injection experiments that maternal and fetal vascular structures remain separate, thus refuting the previously held opinion of a continuous mother-to-fetus circulation. This might have been a chance observation, since injecting blood vessels with coloured wax was becoming a routine procedure for anatomical demonstrations at that time. Most probably it was the younger brother John, who actually did the dissections, who quickly grasped the physiological implications of this observation, which in later years led to a quarrel concerning priority [1,2]. Nevertheless, it was William who illustrated for the first time spiral arteries in his famous "*Anatomia uteri humani gravidi tabulis illustrata – The anatomy of the human gravid uterus exhibited in figures*" (1774) [3], in a series of superb engravings based on careful dissections of several pregnant uteri. The spiral arteries were then described as "*arteriae convolutae/convoluted arteries*" which are "*passing between the womb and placenta*". These vessels were most clearly visible in drawings of the inside of the uterus after separation of the placenta, "*which we broke through in separating these two parts*". This short passage reveals their ignorance about the factual arrangement of maternal blood supply to the placenta. In spite of the ingenuity of

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the Hunter brothers, they could not have envisioned at that time how the uteroplacental circulation is established by the action of invading cells from the placenta. Since this review deals a lot with placental–uterine interactions, it may be relevant that it was also William Hunter who introduced the term ''decidua'' for the thickened inner lining of the pregnant uterus which is discarded at parturition. The term is etymologically significant since the Latin word ''decidere'' means ''to fall off'', which also applies to the expulsion of the decidualizing uterine mucosa at menstruation.

After these pioneering observations it took more than a century to clarify the detailed anatomy of the uterine vasculature [4–6]. The matter is basically settled now, although some confusion arose concerning terminology, i.e. whether the arteries in the inner myometrium should be considered as spiral [7] or radial arteries [8] (Fig. 1). Part of the argument was due to a disagreement about the level where the basal arteries are branching off in the decidua or in the myometrium, as this point is considered to form the demarcation line between radial and spiral arteries. Meanwhile observations on placental bed biopsies have confirmed the deep myometrial origin of basal arteries, which nourish both the inner myometrium and basal endometrium. Therefore the designation of the inner myometrial arteries as spiral arteries has subsequently been followed. A precise terminology – although it may look like a rather insignificant issue – is important regarding the depth over which pregnancy-associated changes in spiral arteries are reported to occur.

Studies on the endometrial spiral arteries of the non-pregnant uterus indicated the remarkable sensitivity of these vessels to stimuli by hormones or growth factors, while the basal arteries are thought to be more stable non-hormone responsive structures [4,8,9]. The convoluted course of the spiral arteries obviously results from arterial growth exceeding the increase in endometrial thickness during the cycle and during pregnancy. There can be no doubt that this spiral shape has haemodynamical repercussions. John Hunter already noted that ''*The intention of these spiral turns would appear to be that of diminishing the force of the circulation as it approaches the spongy substance of the placenta … where quick motion of the blood is not wanted*'' (quoted by Ramsey [6]). Their peculiar shape would not only lead to a progressive decrease in blood pressure along their length, but would also dampen the pulse, which is important for maintaining a steady blood flow to the intervillous space of the placenta. Ramsey found that the coiling of the spiral arteries still increased in early pregnancy, but that uncoiling started around midpregnancy [6,10]. The reserve length of the convoluted vessels obviously allows easy stretching during pregnancy-associated uterine growth.

Reynolds [4] made the interesting point that coiled or spiral arteries are not seen in the endometria of most non-pregnant animals, and therefore he speculated that their peculiar shape in primates may be related to menstruation. In fact, increased coiling of endometrial arteries is related to decidualization of the endometrium which in primates is started off spontaneously during the luteal phase of each cycle. In non-menstruating animals such as rats, mice and hamsters, spiral outgrowth of uteroplacental arteries definitely occurs during pregnancy and is also associated with the decidualization process, which in these animals does not occur spontaneously during their estrous cycle, but is induced by blastocyst implantation [11].

2. Basic histological observations on spiral arteries during pregnancy: a historical overview

The earliest histological observations on uterine spiral arteries in human pregnancy were reported by German investigators in the last third of the 19th century. This early research was summarized and extensively discussed by Grosser, and his monograph should be consulted for detailed references [12]. He quoted Friedländer (1870) as the first to have

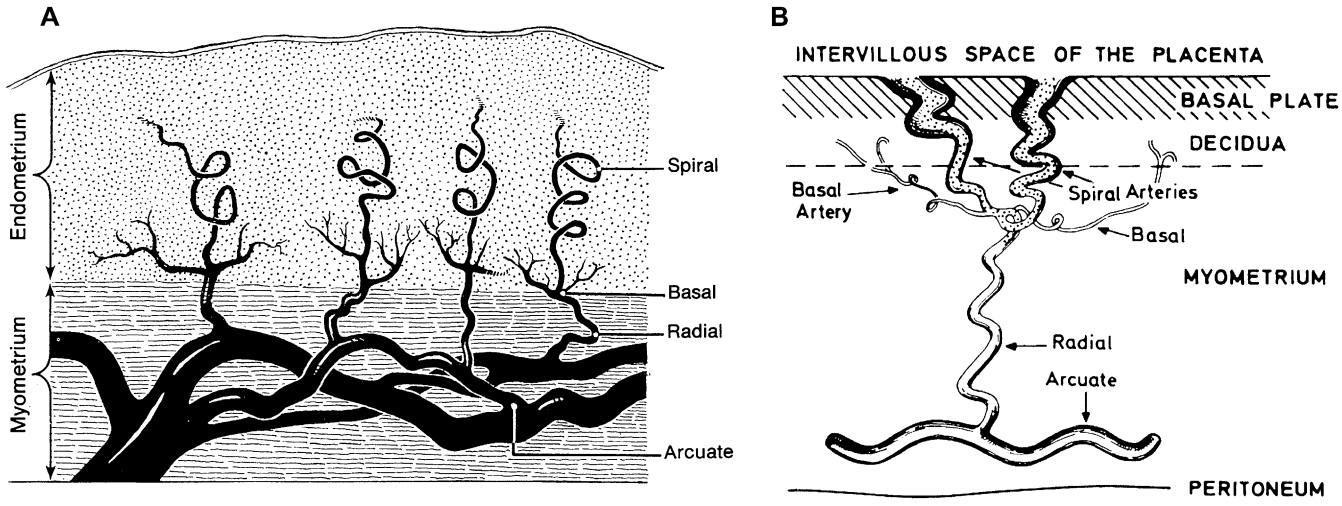

Fig. 1. Vascular anatomy of the pregnant uterus according to (A) Ramsey and Donner [8] and (B) Brosens et al. [7]. Because of initial uncertainties about the location of the branching points of basal arteries from the main arteries, Ramsey considered the whole myometrial segments as radial arteries (A). Following later confirmation of deep basal artery branching points, spiral arteries were recognized as having myometrial as well as decidual segments (B).