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Deep placentation

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Deep placentation in human pregnancy is realised by deep invasion of the placental bed by the extravillous trophoblast, involving the decidua and the inner (junctional zone) myometrium. Interstitial invasion of the stroma and endovascular trophoblast invasion of the spiral arteries both occur. Deep endovascular trophoblast invasion into the myometrial segments of spiral arteries is important for proper placental functioning. Before this extended vascular invasion begins, decidua-associated vascular remodelling, which includes swelling and disorganisation of the vascular smooth muscle, occurs during a period of rising placental oxygen. This early remodelling step may accommodate the progressively increasing maternal blood flow to the developing placenta. The subsequent trophoblast-associated remodelling step enhances and stabilises the widening of the vessels, whereas the vascular smooth muscle and elastic lamina are replaced by a fibrinoid matrix with embedded trophoblast. Defective deep remodelling contributes to placental malfunctioning in complications of pregnancy.

According to Mossman's[1] definition, the placenta is an apposition of fetal and parental tissues for physiological exchange. This process has led to the elaboration of a variety of modifications of maternal–fetal tissue contacts and interaction during the evolution of the different mammalian orders. The haemochorial placenta represents the closest apposition of the maternal and fetal circulations, in which optimization of maternal blood supply is at least partly affected by the invasive activity of a subcategory of fetal trophoblasts. In humans, this 'extravillous' trophoblast invasion reaches greater depth than in most mammalian species, including most non-human primates. This invasion is associated with extensive vascular remodelling of myometrial and decidual segments of spiral arteries. Apart from this

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extended vascular remodelling, humans also differ in other features from primates with shallow placentation, such as interstitial blastocyst implantation, a high degree of decidual erosion, causing a shift of spiral artery outlets into the intervillous space, and possibly in the haemodynamical characteristics of intraplacental maternal flow. It should be evident that trophoblast invasion, with its associated spiral artery remodelling, is not an isolated phenomenon but forms an integrated part of the total placental development, which has been shaped in the course of our evolutionary history.

Invasion of the uterine wall begins with the implantation of the blastocyst. This initiating event proceeds to a deeper level in the human endometrium than in most other primates. This is because implantation is interstitial instead of superficial and results in the formation of a decidua capsularis. This feature is shared with the great apes, but not with Old World and New World monkeys.[2] In all primates, implantation is initiated by the appearance of syncytial trophoblast in the blastocyst wall.[3] Once interstitial implantation is complete, the blastocyst is completely surrounded by this 'primitive' syncytium.[4] For some time, syncytial cells were regarded as primordial invasive trophoblasts in humans.[5]

Villous trees and intervillous flow in primate placentae

The first step in maternal–fetal exchange in the developing placenta is the formation of maternal blood-filled lacunae within the thickening syncytial wall of the implanted human blastocyst. It is not clear whether this primordial 'intervillous space' merely represents extravasated maternal blood or is derived from engulfed parts of the subepithelial capillary network that have lost their endothelial lining. During the first weeks, these maternal blood spaces only communicate with decidual venules,[6] but, at 8 weeks, connecting channels develop between the lacunae and spiral arteries.[7] At this point, the anatomical basis for 'intervillous' maternal blood flow is established, but is contingent upon connecting channels and corresponding spiral artery outlets being clear of intravascular trophoblastic plugs.[7,8]

Meanwhile, strands of mononuclear cytotrophoblast start to proliferate at the inner (fetal) side of the implanted blastocyst wall. The resulting cytotrophoblastic columns push themselves into the primitive syncytial mass, forming primary, secondary and, after the formation of fetal capillaries, tertiary villi. The most distal cytotrophoblasts subsequently break through the syncytium and spread laterally to form a shell of extravillous cytotrophoblasts, separating the placenta from the superficial decidua. In humans, this continuous shell is only a temporary structure, and begins to disintegrate early in pregnancy. Extravillous trophoblasts are still generated from the cell columns at the tips of anchoring villi, but most cells immediately start to migrate deeper into the maternal tissues. Fetal circulation starts at around 6 weeks as soon as the fetal capillary network has been connected with the fetal heart. Maternal flow starts somewhat later and gradually increases from ~8 to 12 weeks,[9] while intravascular plugs are dissolved and endovascular trophoblast migration into the spiral arteries begins.[8] Only then can the placenta be considered as fully functional, with both fetal and maternal circulations being established. It has been argued[11] that, because intra-arterial trophoblast invasion (and plugging) begins at the centre of the placental bed,[12] maternal flow into the placenta will start from the most lateral non-plugged spiral arteries. Therefore, increasing oxidative stress in these lateral regions is responsible for the progressive regression of the 'chorion frondosum' to a 'chorion laeve'.

During further placental development, intermediate and terminal villi branch off from the main stem villi, forming a system of villous trees, each consisting of a villous stem and side branches. Consequently, the placenta subdivides into functional units, the placental lobules. In casts of young placentae, each lobule seems to contain a relatively empty centre within the denser villous tissue. It was originally thought that the central open spaces would be created by the force of the incoming maternal blood, entering the intervillous space in the intralobular regions of the placental floor.[13,14] In the human placenta at term, however, most spiral artery outlets tend to be distributed to interlobular areas.[15] This contrasts sharply with monkey (i.e., rhesus monkey and baboon) placentae, in which spiral artery outlets are nearly always located in intralobular regions of the basal plate.[16] This difference is likely to be caused by the more extensive decidual erosion occurring in human pregnancy, as a result of more intensive and deeper trophoblast invasion.

Intervillous maternal flow patterns also need to be considered. There is general agreement[17] that, in most placentae, maternal and fetal gross flow directions are countercurrent, providing the most