Functions of the placenta

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Abstract
The placenta is an ephemeral materno-fetal organ with chorionic (fetal) villi bathed in maternal blood spaces, which allows restricted transfer of metabolites and drugs across specialized transfer areas. The placenta develops respiratory, nutritive and excretory functions while the fetal organs mature, and is also an important endocrine organ.

Keywords Function; physiology; placenta

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Learning objectives

After reading this article, you should be able to describe:

- the structure and development of the placenta and the relationship between structure and function
- how adequate gas exchange, supplies of nutrients and mineral salts, water balance and removal of waste products are achieved by the placenta
- the endocrine role of the placenta during pregnancy and the kinds of drug that are counter-indicated for the mother during this time.

Structure of the placenta

The hemichorial placenta forms at the interface of the maternal uterine tissues and those of the implanted embryo, specifically that part of the modified endometrium apposed to the chorionic vesicle, the *decidua basalis*, and the associated part of the fetal trophoblast, which eventually develops leafy villi and is known as the *chorion frondosum*.

The trophoblast rapidly differentiates into two layers: the syncytiotrophoblast and the cytotrophoblast. The multinucleated syncytiotrophoblast develops lacunae, between which the cytotrophoblastic layer projects villi. The syncytiotrophoblast becomes progressively compressed into a layer covering each villus and separating the cytotrophoblastic layer (which itself becomes discontinuous) from the lacunae, which merge to form intervillous spaces. Trophoblastic enzymes erode about 100 spiral arteries and veins of the uterine wall, and so the branched villi become bathed in approximately 150 ml of maternal blood (Figure 1a), which is replaced three to four times a minute. Fetal mesenchymal cells invade the villi and generate vascular networks connecting the umbilical arteries and vein. The fetal and maternal circulations, therefore, come to be separated, in specialized transfer areas between cytotrophoblastic cells, by only the endothelial cells lining the microvessels of the fetal villi, associated basement membrane, and thin areas of syncytiotrophoblast (Figure 1b). These areas may constitute 5–10% of the 16 m^2 surface area within the term placenta.

The apices of the villi tend not to develop a mesenchymal core, but remain as solid cytotrophoblastic cell columns. While others remain free-floating in the intervillous space, some villi take on an anchoring function by abutting onto the maternal decidual cells. Moreover, the cytotrophoblastic cells spread over the *decidua basalis* to form a complete layer – the cytotrophoblastic shell. Specialized cytotrophoblastic cells further invade the spiral arteries and cause them to become remodelled.[1,2] so that blood enters the intervillous space at a lower than normal arterial pressure. In this way, the placenta progressively and temporarily assumes the eventual functions of the fetal lungs (gaseous exchange), gastrointestinal tract (uptake of nutrients), and kidneys (regulation of fluid volume and elimination of waste metabolites) while these organs are developing. It also acts as an endocrine organ in its own right, releasing steroid and peptide hormones into both circulations.

Transfer of a substance across the materno–fetal barrier depends on the thickness and extent of the barrier as well as the concentration gradient of the substance, or the presence of active transfer mechanisms, as detailed below.

Gas exchange across the placenta

Respiratory gases are relatively small molecules, which cross the materno-fetal barrier by flow-limited passive diffusion. This placental blood–blood barrier, however, is much thicker than the blood–gas barrier of the lung (3.5 μm versus 0.5 μm) and has a much smaller surface area (about 16 m^2 versus 50–60 m^2).

The fetus compensates by:

- having an increased concentration of fetal haemoglobin (HbF; 170 g/litre versus 120 g/litre in the mother, an increase of about 40%)
- HbF having a higher affinity for oxygen, resulting in 50% saturation (P_{50}) at a lower partial pressure of oxygen (PO_2). This represents an arterial oxygen tension of 18–20 mmHg in the fetus versus 26.6 mm Hg in the adult. The end result of all this is a higher oxygen content in fetal blood at any given PO_2 (Figure 2). This left shift in the oxyhaemoglobin dissociation curve occurs because HbF is a tetramer of α and γ subunits ($\alpha_2\ \gamma_2$) and does not contain β subunits found in adult haemoglobin (HbA; $\alpha_2\ \beta_2$). The β subunits of HbA (especially deoxyHbA) bind strongly to 2,3-diphosphoglycerate (a by-product of glycolysis, which approaches similar molar concentrations to HbA in the vicinity of respiring tissues, and displaces oxygen)
- a double Bohr effect (i.e. the direct effect of pH on haemoglobin's affinity for oxygen). Carbon dioxide is very soluble and, within red blood cells, the majority (60%) combines with water to form carbonic acid, which then dissociates into protons and bicarbonate ions:

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Diagram of mature chorionic villus (a) and villus in cross section (b)

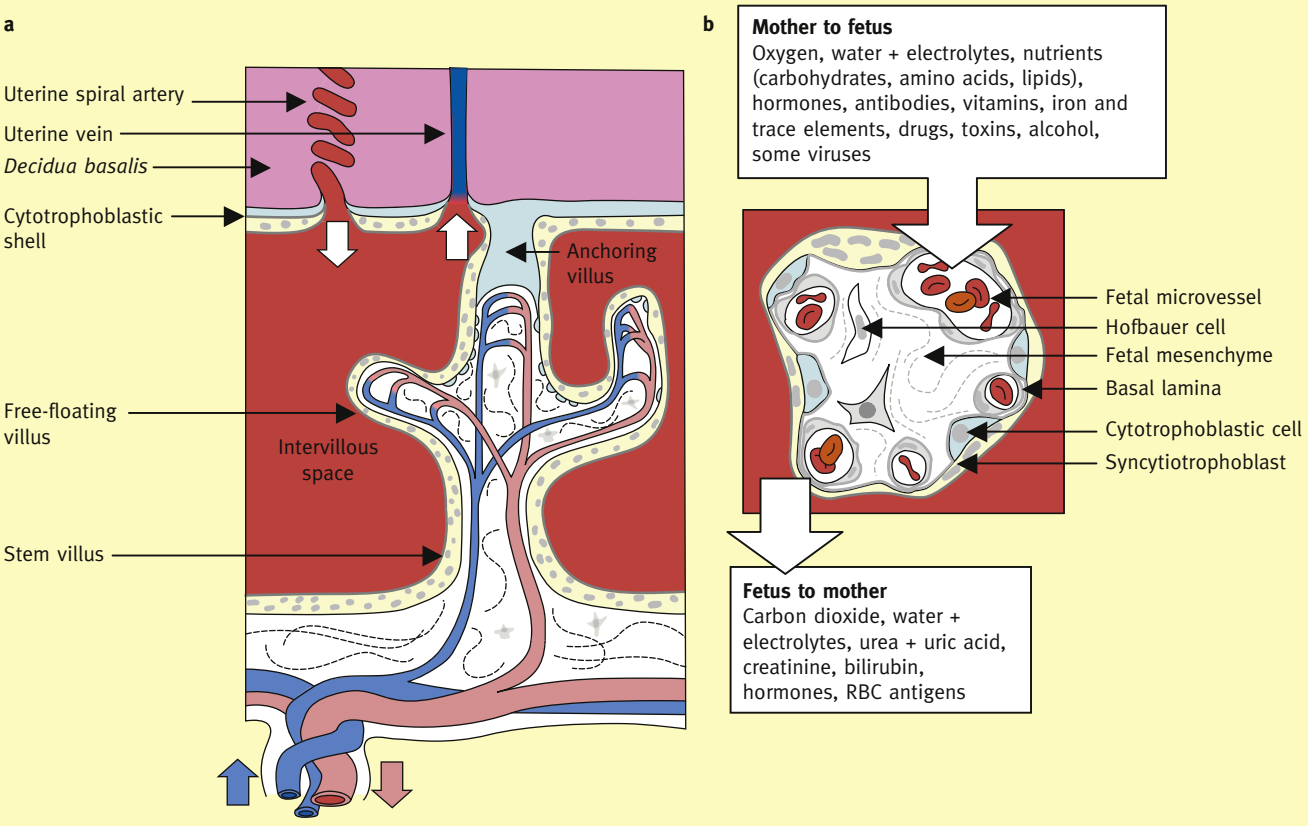

Figure 1

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

(only 30% of carbon dioxide combines with haemoglobin and 10% remains in physical solution). The fetal microcirculation has a high partial pressure of carbon dioxide (PCO_2) and a relatively low pH (44 mmHg and 7.33 in the umbilical artery) compared with the uterine artery (28 mmHg and 7.45). Protons and bicarbonate ions will diffuse along concentration gradients from the fetal microcirculation to the intervillous space, lowering the pH and causing oxygen to dissociate from the maternal HbA. With the removal of protons, the pH will simultaneously increase within the fetal microvessels, facilitating uptake of oxygen by HbF. This double Bohr effect means that the oxygen dissociation curves for HbA and HbF move apart (Figure 2)

- a double Haldane effect (i.e. the increased ability of deoxyhaemoglobin to accept protons and carry carbon dioxide). As maternal blood unloads oxygen, its deoxygenated HbA accepts protons with greater avidity, shifting the above equation to the right, and facilitating the formation of carboxyhaemoglobin. The uptake of oxygen by HbF simultaneously reduces its capacity to accept protons, allowing them to combine with bicarbonate ions and so shifting the equation to the left.

Nutrient uptake by the placenta

The fetus obtains the nutrients required to support its growth from the maternal blood via the placenta – principally glucose, amino acids, fatty acids, vitamins and minerals. Nutrient transport is influenced by concentration gradients as well as placental blood flow and metabolism.[3]

Glucose

Transport of glucose occurs by facilitated diffusion along a concentration gradient across the placenta from mother to fetus. The process is mediated by the GLUT family of transporters, principally the GLUT-1 isoform, which occurs within the maternal ('microvillous') and fetal ('basal') membranes of the syncytiotrophoblast.[4] The latter site is populated less densely and GLUT-1 at this locale acts as a rate-limiting step. Other isoforms occur variably at different times of gestation.

Amino acids

The high rate of protein synthesis needed for growth and development means that fetal concentrations of amino acids are generally higher than the maternal, and some 15 to 20 specific active transport mechanisms have been identified in the microvillous or basal syncytiotrophoblast membranes.[3,5] These mechanisms include Na^+-dependent as well as Na^+/Cl^--dependent,