The placenta

Kirsty McIntyre

The placenta is a temporary organ that develops inside the uterus alongside the growing fetus. Reproductive scientist Kirsty McIntyre explores how nutrients reach the fetus via the placenta during pregnancy, and highlights the need to understand this fascinating organ

Exam links

AQA Transport across cell membranes; Surface area to volume ratio
Edexcel A Properties of exchange surfaces
Edexcel B Development of the embryo to blastocyst stage
OCR A Biological membranes; Exchange surfaces
OCR B Growth and development of the fetus; Mammalian reproduction
WJEC Eduqas The role of the placenta

Key words

Placenta
Fetal growth restriction
Stillbirth

The placenta is a unique and important organ. It is the essential link between mother and fetus during pregnancy. It performs all the functions that the unborn baby cannot yet do for itself, such as delivering a steady supply of nutrients and oxygen to the developing fetus throughout pregnancy.

Problems with the placenta (placental dysfunction) can have serious consequences. Pregnancy complications such as pre-eclampsia and fetal growth restriction (FGR) — when the baby doesn't grow to the size that it should (see Biological Sciences Review, Vol. 31, No. 4, pp. 26–29) — can both be caused

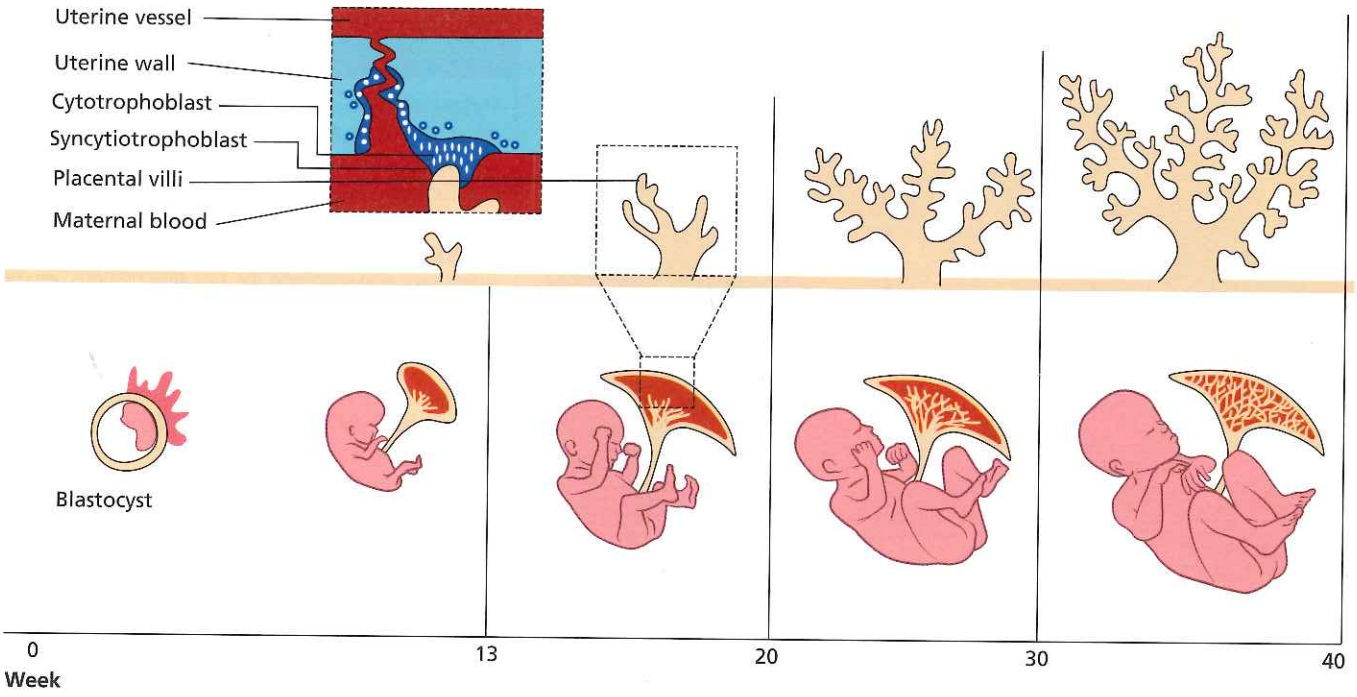


Figure 1 Placental development, fertilisation to full term

by placental dysfunction. Signs of pre-eclampsia include high blood pressure and protein in the mother's urine.

Understanding how the placenta works normally and what happens when things go wrong is one of the big challenges facing research scientists in the field today. Currently, there are no tests that can accurately predict pregnancy complications such as FGR, nor are there any treatment options to help babies that aren't growing well inside the womb.

Placental development

Around 4 days after an egg has been fertilised, the **blastocyst** embeds into the lining of the mother's uterus. During early pregnancy, before the placenta has fully developed, secretions from the uterine glands called histotroph are a vital nutrient source for the fetus. The placenta begins to develop a complex network of finger-like projections called villi, which allow nutrients and waste products to be exchanged between mother and fetus.

From approximately 12 weeks of pregnancy, nutrients and oxygen are passed from the maternal circulation into the space surrounding these villi in the placenta, and then to the fetus via the umbilical cord. The umbilical cord has one large vein and two smaller arteries. The vein carries oxygenated blood from the mother towards the fetus's heart, and the arteries deliver deoxygenated blood, and waste, including carbon dioxide, away from the fetus to the mother. Importantly, maternal and fetal blood never mix, which ensures that the fetus is not attacked by the mother's immune system. However, the placenta is not a perfect barrier and alcohol, nicotine from smoking and other drugs can all cross the placenta and affect the development and growth of the fetus.

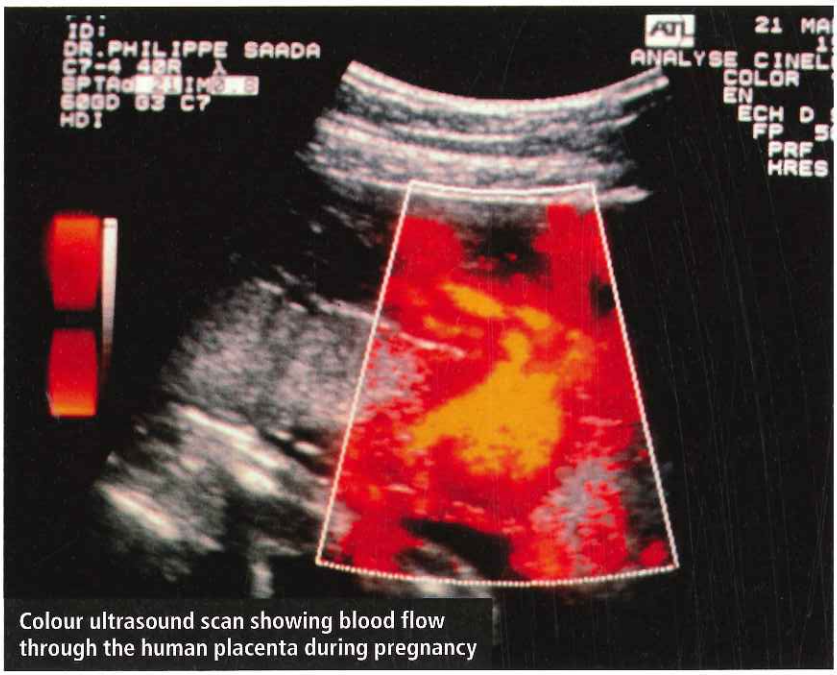
Another function of the placenta is to secrete hormones including oestrogen and human chorionic gonadotrophin, the hormone that positive pregnancy tests detect. Human chorionic gonadotrophin stimulates the **corpus luteum** to continue secretion of the hormone progesterone, which maintains the thick lining of the uterus. As pregnancy progresses, the blood vessels in the placenta become increasingly branched and compact, thus increasing their surface area to meet the demands of the developing fetus (see Figure 1). If you were to stretch out the fetal capillaries in a fully developed placenta, they would be about 320 km long.

The placenta develops alongside the fetus over the course of pregnancy. Towards term, the placenta does not increase significantly in size. Instead it increases the branching and complexity of the villi, so increasing the surface area available for nutrient exchange. This enables the placenta to support the growing fetus.

An average placenta at the end of pregnancy weighs 400–650 g, is about 3 cm thick and the size and shape of a dinner plate — the word placenta means 'flat cake'. Over the course of pregnancy the uterus will also have grown, from just 7 cm long by 5 cm wide before pregnancy to the size of a watermelon at the time of delivery (see Figure 2).

Contractions during labour are caused by the shortening and tightening of the uterine muscles. The placenta is delivered after the birth of the baby, which is why it is often called the 'afterbirth'. This can happen naturally, as more contractions help the placenta come away from the wall of the uterus and push it out of the vagina, or contractions can be induced by an injection into the mother's thigh.

The placenta's vital role in determining the growth and subsequent health of the developing fetus means that researchers are keen to understand more



Colour ultrasound scan showing blood flow through the human placenta during pregnancy

about the placenta in normal healthy pregnancies and in pregnancies where the placenta is not working as it should.

Placental dysfunction

Placental dysfunction is the primary cause of FGR, which occurs in approximately 5–10% of pregnancies in the UK. Fetuses with FGR grow poorly in the uterus and therefore do not reach the size that they should. Furthermore, FGR infants are at an increased risk of **stillbirth** and of chronic diseases such as type 2 diabetes, and cardiovascular disease as adults. We know that several factors — including smoking, high or low maternal body mass index, high blood pressure (hypertension) and poorly controlled diabetes — increase the risk of placental dysfunction during pregnancy. However, in many cases, placental dysfunction has no known cause.

One of the major challenges in placental biology is detecting and treating placental dysfunction. Despite the prevalence of FGR, and other pregnancy complications such as pre-eclampsia, there are currently no treatments available to intervene in these pregnancies. The only option is early delivery of the fetus, which is less than ideal given the risks of premature delivery. To address this need,

Box 1 Should you eat your placenta?

Placentophagy — eating your placenta — is a growing trend in Western society. The practice has been endorsed by celebrities such as the Kardashians. But are there benefits? Supporters say that placentophagy is a way to tackle **postpartum** depression, boost milk production and improve mood. Advocates also highlight the fact that humans are the only mammal not to eat their placenta after they have given birth, though it is thought that other animals do this to avoid attracting predators. However, unlike animals, which have been eating their placentas for centuries, the first reports of placentophagy in humans date to the 1960s.

The recent boost in popularity comes with a rise in companies promoting services to dehydrate and encapsulate placental tissue for consumption. Since these practices often take place at home, preparation of placental tissue for consumption is unregulated. In light of recent reports of infection following maternal placentophagy, more needs to be done to investigate this risk.

Hormones, iron and protein are all present in the placenta after delivery but the amount of other potentially harmful substances that the placenta prevented from reaching the fetus is not well understood. However, scientific studies to date indicate that placentophagy has negligible nutritional benefit and does not influence rate of depression, energy levels or ease of breastfeeding.

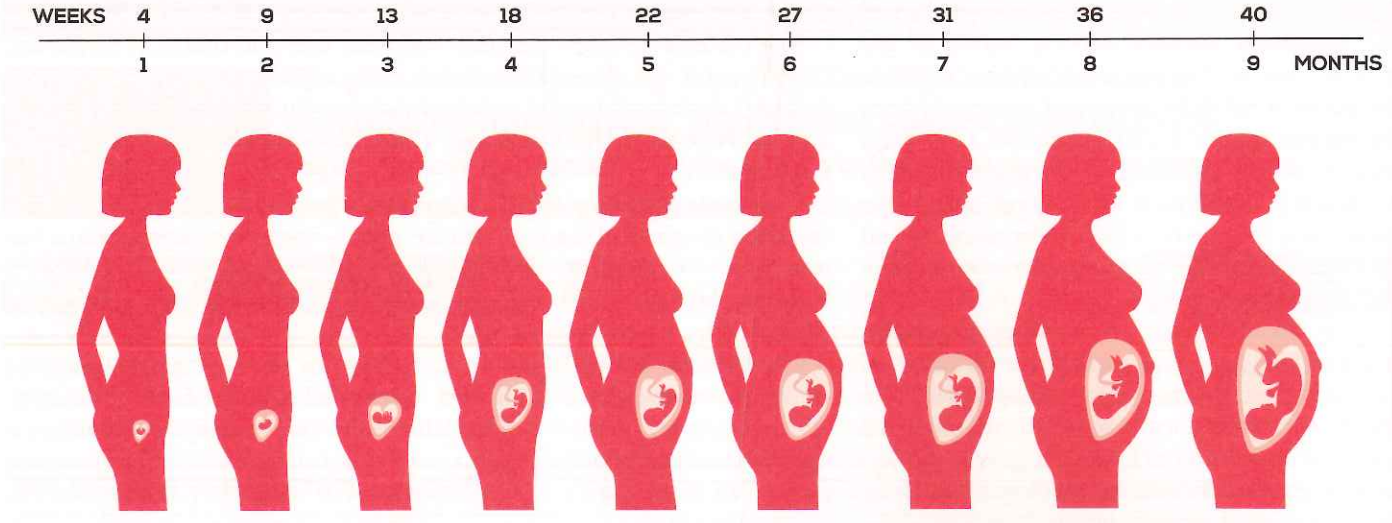


Figure 2 The uterus must increase dramatically in size over the course of pregnancy to accommodate the growing fetus and placenta

Further reading and viewing

Watch 'A day in the life of a placenta scientist': **https://goo.gl/1HNTa7**

Visit Tommy's charity website to find out more about pregnancy research: **www.tommys.org**

Go to the Anthony Nolan website to read about the collection of stem cells from umbilical cord blood: **https://tinyurl.com/y2khd4l4**

scientists and doctors are working together to come up with new strategies and design therapies for pregnant women and their babies.

A rare benefit of studying the placenta is that it is an organ that is usually discarded after delivery. This means that at hospitals such as St Mary's Hospital in Manchester, research can be carried out using human placental tissue, provided written informed consent is given by the mother. However, when looking to develop new treatments, studying pregnancy and the placenta poses a challenge, owing to a lack of available drug safety data about pregnant women as well as anxiety from women and pharmaceutical companies about causing harm to the fetus. To tackle this, one approach is to repurpose drugs that are already licensed for other uses outside of pregnancy. For example, the StAmP (pravastatin to ameliorate early onset pre-eclampsia) trial — a double-blind, randomised placebo-controlled trial — is currently investigating whether the drug pravastatin, usually prescribed for those with heart disease, could help to tackle the effects of pre-eclampsia early in pregnancy.

Another new strategy that is being tested in the laboratory is to use drug-targeting techniques, currently used for chemotherapy to treat cancer, to target drugs specifically to the placenta. Tiny (~100 nm) spheres called **liposomes** are coated in a layer of peptides that are chosen so that they bind

Terms explained

Blastocyst After an egg has been fertilised by a sperm, rapid cell division occurs. Four days after fertilisation there are around 200 cells and the structure is called a blastocyst.

Corpus luteum The corpus luteum develops in the ovary after an egg has been released. If an egg is fertilised, the corpus luteum will remain for the duration of pregnancy.

Liposome A fluid-filled sac that can be used to house a drug for delivery to a target organ, such as the placenta.

Postpartum After the birth of a child.

Stillbirth The death of a baby after 24 weeks of pregnancy before or during birth.

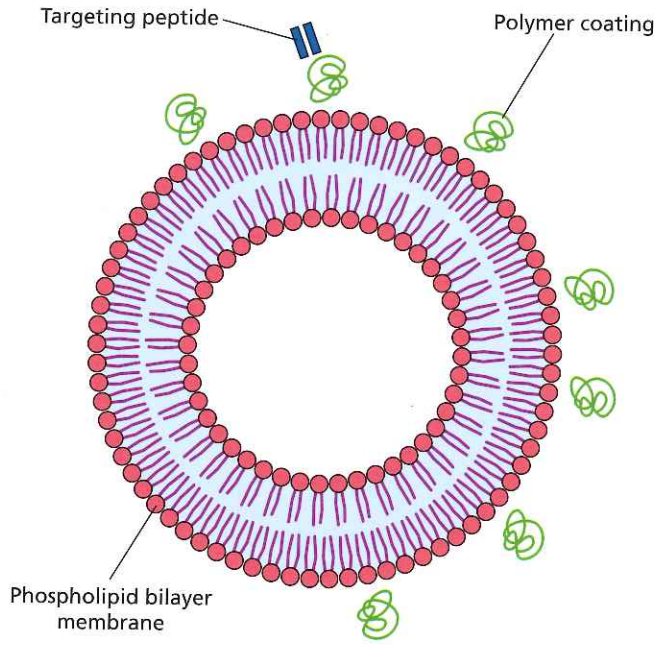


Figure 3 Unique peptides can be attached to the outer lipid bilayer of a liposome, enabling the drug to be delivered and released once it has reached its target

only to target proteins in the placenta. These liposomes are then filled with the chosen drug (see Figure 3). When the liposome reaches its target protein in the placenta, the drug is released. While still in the development stages, this exciting technology would enable delivery of a drug only to where it is needed (the placenta). This strategy would allow potential side effects that may occur if the drug was given as an injection or pill given to the mother to be avoided.

Research is also underway to investigate dietary interventions that may improve placental function during pregnancy. Nitric oxide is a vasodilator — it widens blood vessels — that can be derived from nitrate in the diet. Supplementation with dietary nitrate, present in green leafy vegetables and beetroot, has been shown to lower blood pressure in non-pregnant people with hypertension. Whether nitrate supplementation using concentrated beetroot juice could be a way of reducing blood pressure in pregnant women with hypertension is currently being investigated.

In conclusion, the success of pregnancy relies on a healthy placenta. There is an unmet need for effective therapies to treat pregnancy complications. Understanding how the placenta works in normal pregnancies and the development of new strategies as discussed in this article provide hope of developing treatment options for women who suffer complications during their pregnancy.

Dr Kirsty McIntyre is a lecturer at the University of Glasgow Medical School. Her PhD research at The University of Manchester focused on understanding the nutrient demands of the growing baby and how this relates to placental transport.

Key points

- The placenta is an essential organ during pregnancy that produces hormones, provides immune protection and delivers oxygen and nutrients to the growing baby.
- Pregnancy complications such as fetal growth restriction, pre-eclampsia and stillbirth are often caused by placental dysfunction.
- Understanding how the placenta works in normal pregnancies can help researchers develop ways of detecting and treating pregnancy complications.