

### Activity 2 - What is the placenta and which species have one?

All biologists have an idea of what the placenta is, but it is actually quite hard to define. Its structure varies dramatically between different species, many of its functions are unclear, and not all species which give birth to live offspring actually have one.

It is perhaps easiest to define what it *does* – here is a definition from the 1930s, which still works quite well today:

# 'An apposition of parental and fetal tissue for the purposes of physiological exchange'.

Note the word 'parental'. Obviously, it is usually the mother who forms the placenta with the developing embryo/fetus.

Can you find any vertebrate species in which the placenta forms between the father and fetus?

Difficult, and irritating question: what is the difference between an embryo and a fetus? How many people do you think know this?

#### What does the placenta do?

The placenta does at least four different things, and possibly more.

<u>1. Exchange of molecules</u> – nutrients and oxygen from mother to fetus, and waste products and carbon dioxide from fetus to mother.

This exchange can be via diffusion, facilitation diffusion, active transport, or even fetal cells ingesting large molecules or even maternal cell fragments.

For example, if you've ever seen kittens or puppies being born, you may have noticed the green/brown staining caused by maternal blood cells broken down in the 'haemophagous zone' of the carnivore placenta. However if you watch the Youtube video you'll see that there's actually almost no blood visible during birth in the domestic animals:

www.youtube.com/watch?v=V2ND055kYns

http://biology.about.com/od/cellularprocesses/ss/diffusion.htm

From your knowledge of Chemistry, why is the staining often green, but turns brown on exposure to the air?

<u>2. Barrier to molecules.</u> The placenta stops many toxic molecules getting through to the fetus. However, sometimes this process fails, and the fetus's developmental processes are damaged, a process called 'teratogenesis'. For example, this is an image of a 'cyclops' lamb born to a ewe which ate the toxic plant *Veratrum californicum* during pregnancy.





(Public domain: https://en.wikipedia.org/wiki/Cyclopamine#/media/File:Cyclopelamb2.jpg)

Do you know of any teratogenic medicines which should not be used in pregnant women or animals?

<u>3. Production of hormones.</u> The placenta makes hormones which (a) tell the mother's endocrine system a fetus is present, (b) induce the uterus to support a pregnancy, (c) prepare the mammary glands for lactation, and (c) initiate birth. The following is a human-focused webpage, and some of the details differ in different species of animal:

http://www.embryology.ch/anglais/fplacenta/physio07.html

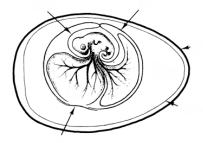
4. Immune protection of the fetus. That's what this entire resource is about!

#### What forms the placenta?

The placenta is formed by maternal AND fetal tissues – the uterine lining epithelium, and the 'fetal membranes'.

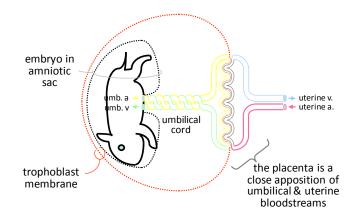
Many people do not realise the two-sided nature of the placenta, probably because you learn about humans in school, and humans are unusual because most of the maternal tissue in the placenta is destroyed.

All developing vertebrates are surrounded by fetal membranes, and the membranes present inside a hen's egg...





...have direct equivalents in a developing mammal. The only different is that a patch of membrane has become specialised for exchange of nutrients and wastes. That patch is called a 'placenta'.



Notice two very important things:

1. The outer layer of the fetal membranes, in contact with the mother is called the 'trophoblast'.

2. The blood in the fetal umbilical blood vessels never mixes with the blood in the maternal uterine blood vessels.

#### What vertebrates have placentas?

We all know that eutherian 'placental' mammals have placentas. Marsupials have them, too, although often they do not function for as long. Monotremes (egg laying mammals) also have them – sometimes they form, function and then disappear all before the egg shell forms – how confusing!



(Public domain: https://en.wikipedia.org/wiki/Platypus#/media/File:Australianstamp\_1551.jpg)



No birds give birth to live young, so they do not form placentas, and neither do any turtles or crocodiles. However, all the other groups of vertebrates contain species which give birth to live young – many lizards and snakes, amphibians, bony fish and cartilaginous fish.

Many of these form complex placentas. For example, the European skink forms a placenta very like the structure of a mammal's...



(Creative Commons:

https://en.wikipedia.org/wiki/Ablepharus\_kitaibelii#/media/File:Ablepharus\_kitaibelii\_01.jpg)

...and if you follow these links, you'll see a pregnancy ultrasound of a tiger shark, and even an invertebrate – a scorpion – giving birth:

http://www.discovery.com/tv-shows/shark-week/videos/first-ever-tiger-shark-sonogramreveals-pups/

https://www.youtube.com/watch?v=AYz\_ZLT2I2g

In other words, placentas are not a purely mammalian invention. Almost everything we know about the immunology of pregnancy was learnt from mammals, but presumably all these other vertebrate and invertebrate species face the same immunological challenges.

## Why is the placenta, and the trophoblast in particular, important in the immunology of pregnancy?

When we are trying to work out why the developing fetus is not rejected like a tissue transplant by its mother's immune system, we mainly think about the interactions between the outer trophoblast layer of the placenta and the mother's immune cells. Why is this?

Below is a photomicrograph of a mammalian embryo at an early stage of development – probably less than one week after fertilisation.

It consists of a sense little clump of cells (the inner cell mass) inside a hollow outer sphere of cells called the trophoblast. Obviously many complicated changes lie ahead, but in most species the trophoblast remains the outermost layer of the embryonic/fetal 'unit' until birth.





(Public domain: https://en.wikipedia.org/wiki/Blastocyst#/media/File:Human\_blastocyst.jpg)

http://www.wisegeek.com/what-is-trophoblast.htm

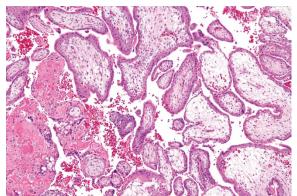
The differentiation between inner cell mass and trophoblast is the first time cells in the developing embryo commit themselves to entirely different fates, so this process has been intensively studied:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2874917/

From the point of view of the maternal immune system, the trophoblast is what the mother 'sees' – it is what she is exposed to.

This is why pregnancy immunologists are so interested in trophoblast cells, because if these outer cells can evade the mother's immune attack, then probably the rest of the embryo can, too.

The following image shows fronds of trophoblast cells from a later stage of pregnancy, bathed in little red specks – maternal blood cells – demonstrating just how 'exposed' to the mother's immune system the fetal trophoblast cells are.



(Creative Commons: https://en.wikipedia.org/wiki/Chorionic\_villi#/media/File:Chorionic\_villi\_ \_intermed\_mag.jpg)