Functions of the placenta

Sarah Vause
Daljit K Saroya

The placenta is an interface for the exchange of gases, nutrients and waste products and therefore has respiratory, nutritive and excretory functions. It is also a partial barrier to the transfer of drugs, bacteria and cells between mother and fetus. It is an important site of hormone production and, as an integral part of the fetomaternoplacental unit, has a profound influence on the endocrinology of pregnancy.

Placental blood flow

The fetal and maternal circulations interface in the placenta. The maternal circulation through the intervillous space of the placental bed is almost wholly pressure dependent, with little or no autoregulation. This is unusual because control of blood flow in the arterial tree of most organs depends on vasomotor activity in the arterioles. However, in the pregnant uterus the muscular walls of the spiral arterioles are destroyed by trophoblasts and become passive channels in the uterine circulation.

Blood flow to the uterus is difficult to quantify because the uterus is supplied by a number of arterial channels that anastomose with the ovarian and vaginal blood supplies. Blood flow to the uterus increases throughout pregnancy, reaching about 500 ml/min at term.

The fetal circulation through the placenta is altered by the resistance of the placenta. Usually there is forward flow in the umbilical artery throughout the cardiac cycle of the fetus. However, if placental resistance is increased, for example in pre-eclampsia, flow in the umbilical artery may be absent during diastole. Umbilical artery Doppler measurements are useful in monitoring high-risk pregnancies, because they reflect placental resistance.

Placental transfer

In a healthy human pregnancy the transfer of a substance from mother to fetus depends on:

- maternal uteroplacental blood flow
- fetal umbilical blood flow
- surface area (gross and functional)
- placental metabolism
- concentration in maternal circulation
- concentration in fetal circulation
- mechanism of transfer
- availability of carrier proteins and relative affinities (e.g. fetal haemoglobin).

The materials are transported across the placental membrane by simple diffusion, facilitated diffusion, active transport or pinocytosis. Transfer of a substance may be influenced by its molecular weight, ionization, lipid solubility and protein binding.

Gases

Respiratory gases cross the placenta by diffusion. The rate and quantity of gas transferred depends on the concentration of each on either side of the placenta, the dissociation curves in both maternal and fetal blood and the supply of blood to each side of the placenta.

Fetal haemoglobin has a greater affinity for oxygen than maternal haemoglobin. The fetal oxygen dissociation curve is shifted to the left of the maternal curve (Figure 1). The partial pressure of oxygen of fetal haemoglobin 50% saturated (P_{50}) is lower (20 mm Hg) than that of maternal haemoglobin (27 mm Hg). This is because the γ chains in fetal haemoglobin bind 2,3-diphosphoglycerate (2,3-DPG) less avidly than the β chains in adult haemoglobin. If the following equation is considered:

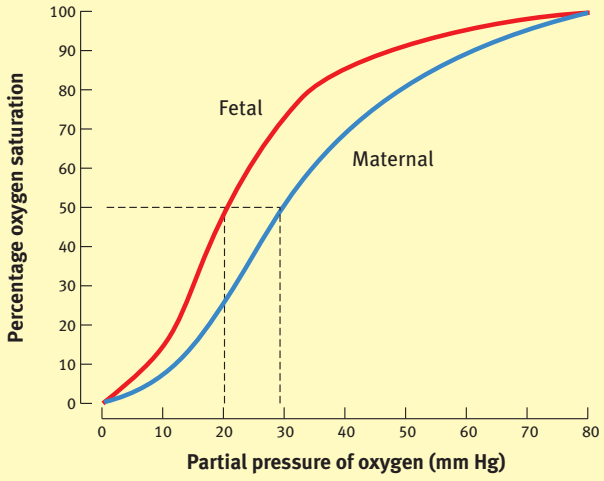
$$HbO_2 + 2,3\text{-DPG} = Hb - 2,3\text{-DPG} + O_2$$

it can be seen that in maternal blood, where 2,3-DPG binds to haemoglobin, the equation is tipped to the right and oxygen is liberated. However, in fetal blood where the binding of 2,3-DPG is less, the equation is tipped to the left, and more oxygen is bound to the fetal haemoglobin.

The increased haemoglobin concentration (17 g/dl) in the term fetus compared with the maternal haemoglobin concentration also favours oxygen transfer to the fetus. Therefore, at term, the amount of oxygen carried per ml of fetal blood is greater than that of maternal blood.

The decrease in oxygen affinity of haemoglobin when the pH of blood falls is called the Bohr effect. As fetal blood passes through the placenta, carbon dioxide is excreted into the maternal

Oxygen–haemoglobin dissociation curves for fetal and maternal haemoglobin



1

Sarah Vause *is Consultant in Fetomaternal Medicine at St Mary's Hospital, Manchester, UK. She qualified from Manchester University and trained in obstetrics in Yorkshire and Manchester.*

Daljit K Saroya *is Consultant Anaesthetist at Stepping Hill Hospital, Stockport, UK. Her interest is obstetric anaesthesia.*

circulation. Consequently, maternal blood becomes more acidic and the oxygen affinity of the maternal haemoglobin decreases. Fetal blood becomes less acidic as it passes through the placenta and its oxygen affinity increases. There is therefore a double Bohr effect in the placenta. Figure 2 shows mechanisms that facilitate oxygen transfer to the fetus.

Carbon dioxide is very soluble and once in the blood soon passes into the red cells. There, about 30% combines with haemoglobin, about 10% is in physical solution, and 60% combines with water to make H_2CO_3 which ionizes almost immediately. The H^+ is buffered by fetal haemoglobin so there is only a slight drop in pH and the fetus is able to carry more carbon dioxide. The HCO_3^- passes out of the red cell. Because of the high haemoglobin content of fetal blood, there are smaller pH changes for any given increase in the partial pressure of carbon dioxide.

Deoxygenated haemoglobin binds more H^+ than oxygenated haemoglobin and forms carbamino compounds more readily. Therefore venous blood can carry more carbon dioxide than arterial – the Haldane effect. At the placental surface, maternal blood releases oxygen and so its deoxygenated haemoglobin is free to bind to H^+ and carbon dioxide. At the same time in fetal blood, oxygen binds to the fetal haemoglobin molecule and carbon dioxide is released, facilitating the excretion of carbon dioxide into the maternal circulation. This is a double Haldane effect and occurs in the placenta only because of the relative positions of the fetal and maternal oxygen dissociation curves.

Fetal haemoglobin is a major buffer and in acidosis the oxygen dissociation curve shifts to the right so that for any given partial pressure of oxygen the oxygen saturation falls. This releases oxygen for use in the tissues and makes more fetal deoxyhaemoglobin available for buffering (deoxygenated haemoglobin is a better buffer than oxygenated haemoglobin).

Excretion

Excretion of carbon dioxide is discussed above. Urea and uric acid pass through the placental membrane by simple diffusion and bilirubin is cleared quickly.

Nutrients

Glucose passes through the placenta at a faster rate than might be expected on the basis of simple diffusion alone because there is a carrier system (intramembrane protein carrier molecules) that selectively binds glucose molecules. This facilitated diffusion mechanism can be saturated, but only with extreme hyperglycaemia. Placental glucose carriers are insulin independent.

Amino acids cross the placenta against a concentration gradient – the concentrations in fetal blood are higher than in maternal blood. An energy-dependent, active-transport mechanism is employed. Transfer of amino acids is limited by the capacity of the placental membrane proteins to transfer amino acids, rather than by placental blood supply. Alcohol and nicotine inhibit placental amino acid transfer.

Essential fatty acids – linoleic and linolenic acids cannot be synthesized by the fetus and must be obtained transplacentally. Lipid transport across the placenta is less in humans than in some other mammals and appears to be non-selective.

Calcium is transferred across the placenta by active transport against a concentration gradient.

Maternal antibodies

Maternal antibodies, such as immunoglobulin G, are transferred across the placenta to the fetus by pinocytosis. Immunoglobulins are mainly protective and confer passive immunity to the immunologically immature fetus. However, in some situations transplacental transfer of maternal immunoglobulin can cause problems, for example in haemolytic disease of the newborn.

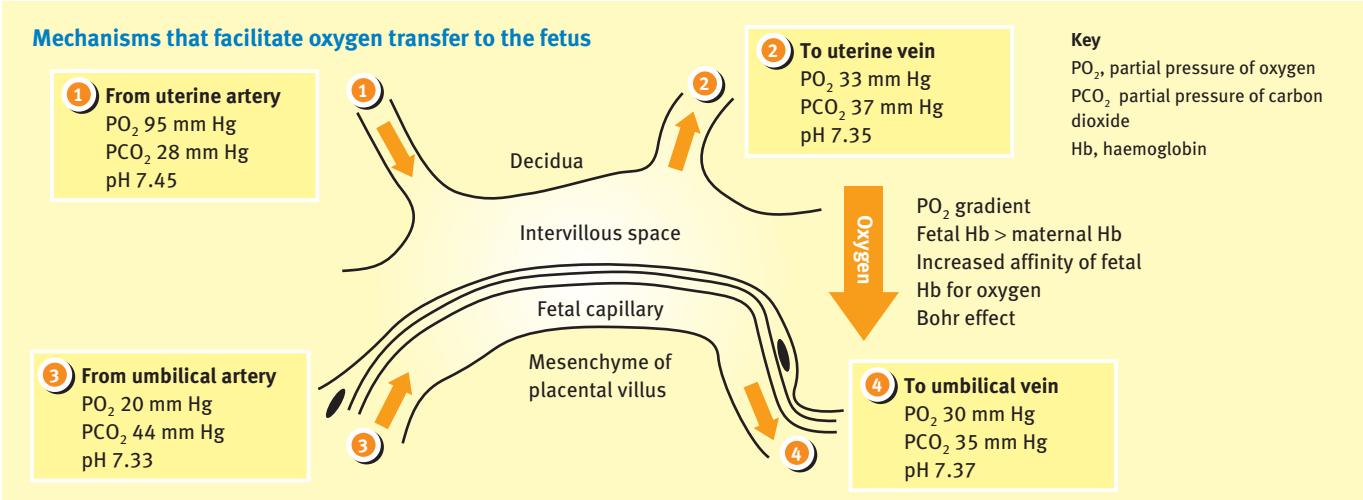
Drugs

Many drugs cross the placenta; some benefit the fetus (e.g. prophylactic corticosteroids) but others may be teratogenic. The drugs most relevant to the obstetric anaesthetist are discussed below.

Anaesthetic agents: non-ionized lipophilic molecules cross the placenta more readily than ionized molecules. The structures of some of these drugs are illustrated in Figure 3.

Inhalational anaesthetic agents cross the placenta rapidly even with relatively short induction to delivery times because of their lipid solubility. Nitrous oxide concentrations may reach 80% of that in the mother within 3 min and may cause diffusion hypoxia during prolonged delivery.

Induction agents cross the placenta rapidly. Thiopental can be detected in fetal blood as soon as 1 min after injection at a con-



2