Role of Placenta in Nutrient Transfer

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Introduction

During intrauterine life, the developing fetus effectively receives all of its nutrition across the placenta, which, in the human, has a chorionic villus structure in which maternal blood directly superfuses the external surface, the trophoblast of the placenta. This trophoblast forms an unusual epithelium separating the maternal plasma from the fetal extracellular space of the villus core through which the fetal capillary circulation flows. For the fetus, the trophoblast is thus equivalent to the epithelium lining the small intestine of the newborn, since, from a nutritional perspective, it must absorb those molecules required for both growth and maintenance of the organism. The trophoblast also has an important role in acting as the lung for the fetus (since all gas exchange between mother and baby must occur across this surface), as the fetus's kidney (since excretion from the conceptus to the mother occurs across this structure), as well as being an important endocrine tissue secreting peptide and steroid hormones into the mother. The placenta itself also plays a very substantial role in intermediary metabolism, so that it cannot be assumed that there is no metabolism of absorbed nutrients during solute movement from mother to fetus.

As an epithelium, the trophoblast has two surfaces, the one facing the mother and the other facing the fetus. These surfaces differ structurally; for example, microvilli are found projecting into the maternal bloodstream at the apical surface, where they form a brush border, whereas the basal surface facing the fetus does not have this surface specialization. From the functional point of view, it is the differences in the distribution of transport membrane proteins (channels, carriers, and pumps) that determine the overall transport of nutrients from mother to baby, at least as far as water-soluble molecules are concerned. In the placenta, all transport appears to be across the trophoblast since, uniquely, the cells that compose this structure are fused to form a syncytium; this is in contrast to other epithelia where transport between adjacent epithelial cells allows a functional paracellular route to lie in parallel to the route through the epithelial cells themselves (the transcellular route). The question in the human as to whether there is a special route available for the transport of large molecules (MW 5000) is not yet resolved: certainly, at term, the human placenta does appear to be able to permit the transport of larger molecules at a slow rate from baby to mother. This route is unlikely to be of nutritional significance, since the rate of transport is low, but it may be important with regard, for example, to immunological sensitization.

The placenta, together with the growing fetus, has a very substantial metabolic energy requirement, and in the human, ATP synthesis appears to be met by the very substantial rate of glucose delivery from the mother. The glucose transporter systems that are found in both the apical and basal surfaces of the human trophoblast appear to be the type named GLUT1; in other words, they are sodium-independent facilitated transporters that are not regulated by insulin. The Michaelis constant (K_m) for glucose transport at both surfaces is relatively high (approximately 30 mM), and the maximal transport rate (V_{max}) is very substantial. The result of this is that glucose delivery across the brush-border membrane of the placenta will be in a direction and rate that are dependent solely on the chemical driving force from mother to baby (maternal–fetal plasma glucose concentration). It seems likely that this fundamental property is the basis for the macrosomia ('large-for-dates') found in the babies of mothers with elevated plasma glucose concentration, as typically found in diabetes mellitus. Transport of glucose, which is stereospecific, may be inhibited by glucose analogs that share the chemical structure of D-glucose at carbon 1; for example, both 3-0-methylglucose and 2-deoxyglucose are transported, whereas α-methylglucoside (with a methyl group on carbon 1) is not. The transport of other monosaccharides has been studied rather little; in the human, fructose is transported much more slowly than glucose itself (in contrast to other nonprimate species). The question of regulation of carbohydrate delivery across the placenta is not fully resolved since some glucose transporters may be regulated by phosphorylation, and the gradient for transplacental glucose delivery will also depend upon factors regulating glucose utilization and production by the placenta itself; little is known of the physiological regulation of either of these processes. (*See* **Carbohydrates**: Digestion, Absorption, and Metabolism; **Glucose**: Maintenance of Blood Glucose Level.)

In contrast to glucose transport, amino acid transport can be powered. The overall gradient of amino acid between maternal plasma and fetal plasma varies

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