

March 2009
QUESTION 24

Explain the factors which influence the transfer of drugs across the placenta to the foetus

The placenta is an important link between the maternal and fetal circulations

Transport mechanism

passive diffusion

dependent on the lipid solubility

lower ionisation increases lipid solubility

maternal pH and the relationship to pKa and degree of ionisation

molecule size

<600 Daltons molecules are readily diffused down concentration gradients

protein bound drugs are less likely to diffuse

Local anaesthetics are an example of a drug which will readily cross the placenta

low molecular weight, lipid soluble and non ionised

furthermore may exhibit ion trapping due to the decreased pH in fetal circulation

active transport mechanisms

many act to limit transfer into the placenta by active efflux (ABC transporters)

some act to facilitate influx (folate transporters)

other

pinocytosis

transport immunoglobulins such as IgG

bulk transport/solvent drag

facilitated diffusion (glucose)

Physicochemical factors

Fick's law of diffusion characteristics

thickness, solubility, area, pressure difference

blood flow

fetal maternal concentration gradient

Drug factors

dose, bolus or infusion

plasma concentration

absorption

distribution

metabolism (hepatic and placental)

excretion

drug-drug interactions