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QUESTION 22

Outline the factors affecting drug transport across the placenta

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 molcules are readily diffused down concentration gradients
  - protien bound drugs are less likely to diffuse
  - Local anasethetics 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

- Ficks 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