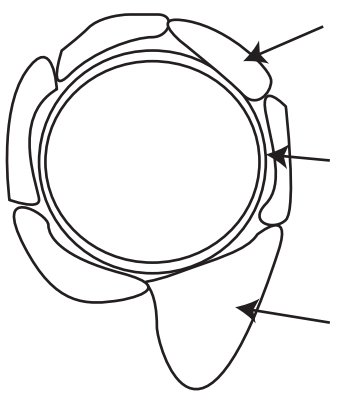
Sept 2009
QUESTION 08

Describe the blood brain barrier. (50% of marks) What characteristics does a drug need to effectively penetrate into the central nervous system? (50% of marks)

Anatomy



astrocytes
surround the BBB and provide structural support

endothelial cells
tight junctions - form the main barrier in the BBB
basement membrane

pericyte
regulate and maintain BBB
influence transport across the BBB
inhibit the effects of microglia on the endothelial cells

Blood brain barrier
- Exists at all the
  - tissue capillary membranes
  - choroid plexus
  - brain parenchyma
    - except - area postrema, some areas of the hypothalamus, pineal gland
    - this is important for sensors located in these areas (CTZ etc)
- Creates the ultrafiltrate of CSF
  - dependent on cerebral perfusion pressure
  - stops large molecules, especially protiens diffusing, non lipid soluble organic molecules
  - highly permiable to H_2O, CO_2, O_2 and lipid soluble molcules
  - semipermiable to ions such as Na and Cl
  - other transport is via active transport mechanisms (eg hormone transporters - leptin)

Drug characteristics
- Dependent on Ficks Law - variables
  - concentration gradient, surface area, thickness and permiability coefficient
  - Concentration gradient
    - Low potency will indicate more molecules, increased likelihood of BBB penetrance
  - Permiability
    - Lipid solubility is the most important factor
    - Polarity BBB is impermiable to polar drugs,
      - the classic example is the quaternary compounds such as glycopyrolate
    - Molecule size
    - Protien binding increases size and decreases permiability
    - Intergrity of BBB may be comprimised in pathology such as meningitis
      - this is important for the BBB penetration of antibiotics
- Drugs similar to natural ligands may be actively transported across the BBB