- AntiConvulsants
  - Selectivity
    - Neuronal selectivity
      - Drugs act at >1 site
      - Inhibition of reuptake and receptor antagonism
    - CNS Selectivity
      - Drugs act in the periphery as well as in the brain
      - Therapeutic effects in brain and side effects in periph
  - Epilepsy
    - 2nd most common neurological disorder after stroke
    - 0.5-1 % of population
    - Seizure: Sudden abnormal discharge of impulses from a group of neurons
    - Symptoms determined by site (focus) and spread (localised/generalised) of discharge as well as amplitude
    - Classification
      - No LOC
        - Simple Seizures
      - Some LOC
        - Complex Seizures
    - Generalized
      - Discharge from focus with rapid spread to other brain areas
      - Absence (Petite mal)
        - 1 Hz discharge between thalamus and cortex
        - Brief, sudden LOC and return
      - Tonic/Clonic Grand Mal
        - Widespread polyphasic
        - Repetitive contractions and relaxations
        - Unconsciousness
      - Myoclonus
        - Brief, jerking movements
      - Status epilepticus
        - Repeated seizures
        - No recovery of consciousness
        - Potentially life threatening
  - Drug interactions
    - Induction of hepatic microsomal enzymes
      - Phenobarbitone
        Carbamazepine
        Phenytoin
      - Increase clearance of self and other drugs
    - Inhibition of hepatic microsomal enzymes
      - Valproate
      - Decreases clearance of phenytoin phenobarbitol, and others giving toxicity
    - Interactions with other Drugs
      - enzyme inhibitors such as cimetidine decrease clearance of phenytoin to give toxicity
  - Newer Agents
    - Vigabatrin
      - MOA
        - Inhibition of GABA-T enhancing brain GABA
      - Use
        - Add on therapy for refractory partial seizures
        - Monotherapy?
      - S/E
        - Sedation
        - Occular
        - Mental
        - Minimal drug interaactions
    - Lamotrigine
      - MOA
        - Na ch
        - Decrease Glutamate release
      - Use
        - Add on therapy for refractory partial seizures
        - Monotherapy
      - S/E
        - Sedation
        - Occular
        - GIT
        - Rash
        - Minimal drug interactions
  - Drugs
    - General
      - Action at focus to reduce discharge
      - reduction of propagation from focus
    - Specific
      - Prolong inactivation state of Na channels
        - gate open but inactivated
      - Reduce Ca channel entry
        - Reduce flow through T-type Ca
        - Reducing Pacemaker current underlying peaks in Absence seizures
      - Enhance GABAa mediated inhibition
        - Increase Cl- ch opening through GABAa-BZD receptor complex
        - Inhibition of GABA-Transaminase
        - Inhibition of GABA uptake
      - Reduce glutamate-NMDA mediated excitation
        - Reduction in release of glutamate
    - Classical anticonvulsants
      - Phenobarbitone
        - MOA
          - Na and Ca channels
          - Enhances GABAa
          - Decreases glutamate release
        - S/E
          - Highly sedative
          - Behavioral changes
          - Enzyme inducer
        - Use
          - No longer front line
          - General T/C > Partial
          - Enzyme inducer
      - Phenytoin
        - MOA
          - Prolongs inactivation state of Na channels reducing likelihood of repetitive discharge
        - Use
          - gen T/C, partial (status epilepticus)
        - S/E
          - Occular, ataxia (sedation)
          - Gingival hyperplasia
          - Hirsuitism
          - Dysmorphogenic (cleft palate)
        - Pharmacokinetics
          - Lower doses, normal 1st order kinetics (constant fraction cleared/unit time
          - higher doses eliminate saturation mechanisms; constant amount cleared/unit time
          - Small increase in dose gives large increase in conventration giving toxicity
      - Carbamezepine
        - MOA
          - Na channels
        - Use
          - Partial-complex
          - gen T/C
          - Mod stabiliser
        - S/E
          - Occular ataxia
          - GIT
          - Aplastic anaemia
          - Agranulocytosis
          - Enzyme inducer
      - Valproate
        - MOA
          - Na ch
          - CA
          - Enhance GABA
        - Use
          - gen T/C
          - Absence
          - Myoclonus
          - Mood stabiliser
        - S/E
          - GIT
          - Tremor
          - Hepatotoxicity
          - Enzyme inhibitor
          - Dysmorphogenic - Spina bifida
      - Ethosuxamide
        - MOA
          - L-type Ca channel (NOT L-type Ca ch blockers
        - Use
          - Absence seizures
        - s/E
          - GIT
      - BZD
        - MOA
          - Enhance GABAa
        - Use
          - Diazepam (status epilepticus)
          - Clonazepam (Absence, Myoclonus)
        - S/E
          - Sedation
          - Tolerance