Local anaesthetics

• History

Coca leaves = Chewed → psychotropic effects
south american indians.
psychic energetic power.
↓
numbing effect (tongue, mouth).
↓
Natural cocain = 1860 → local anaesthesia in surgery

synthetic procain → 1905

• Mechanism of action:

block the initiation ? propagation } action potential.

→ block sodium channels.

Examples :
- procain
- cocaine
- Tetracaine (amethocaine)
- Cinchocaine
- Lidocain (lignocain)
- prilocain
- Bupivacaine
- Benzocaine

- Surface anaesthesia

- Nose
- Mouth
- bronchial tree (spray form)
- Cornea
- urinary tract
- **Not effective for skin**

eutectic mixture of local anaesthesia or EMLA has been developed for application to the skin. (mixture of lidocain and prilocaine)

Drugs:
- lidocain
- tetracaine (amethocaine)
- dibucaine
- bengocain

Adverse effect:

systemic toxicity = absorption from high
- concentrations used
- large areas are involved

CNS:
- restlessness
- shivering
- anxiety
- convulsions
- respiratory depression

CVS:
- bradycardia
- ↓ cardiac output
- Vasodilatation
- Cardiovascular collapse.

Infiltration anaesthesia:

- Direct injection into tissues to reach Nerve branches and terminals:
  used in minor surgery.
- Drugs used: most of local anaesthetic drugs
- Adverse effects:

Note: Epinephrine (Adrenaline) or felypressin often used in addition as vasoconstrictors (but, Not with fingers or toes) for fear of causing ischaemia and tissue damage
only suitable for small areas, otherwise risk of systemic toxicity.

C.V. system and CNS effects, owing to block of amine uptake. as mentioned before.

Intravenous regional anaesthesia:

drugs injected intravenously distal to a pressure cuff to arrest blood flow. remains effective until the circulation is restored.

indication = Used for limb surgery.

Drug used: lidocain and prilocain

Toxicity: Risk of systemic toxicity when cuff is released prematurely
- Risk is small if cuff remains inflated to at least 20 minutes.

Nerve block anaesthesia:

- Drug is injected close to nerve trunks.
  - e.g. brachial plexus
    intercoastal nerves
    dental nerves
- objective: to produce Loss of sensation peripherally.
- Drugs used = ~~Not~~ most drugs

Note: . Less dose needed than for infiltration anaesthesia
. accurate placement of the needle is important
- onset of anaesthesia may be slow.
- Duration may be increased by addition of vasoconstrictor e.g. adrenaline.

Spinal anaesthesia:

- Local anaesthesia injected into the subarachnoid space (containing CSF)
- act on spinal cord and spinal roots.
- Glucose sometimes added so that spread of LA can be limited by tilting patient
- Used for surgery to:
  - abdomen surgery
  - pelvic "
  - Leg "
- indication when general ~~surgery~~ anaesthesia cannot be used.
- Drug used, mainly lidocain.

Side effects:

- bradycardia } sympathetic block
- hypotension }
- respiratory depression – phrenic N. ↓
  – Rc. ↓
- post-operative urine retention (block autonomic outflow).

Epidural anaesthesia:

- L A injected into epidural space blocking spinal cord

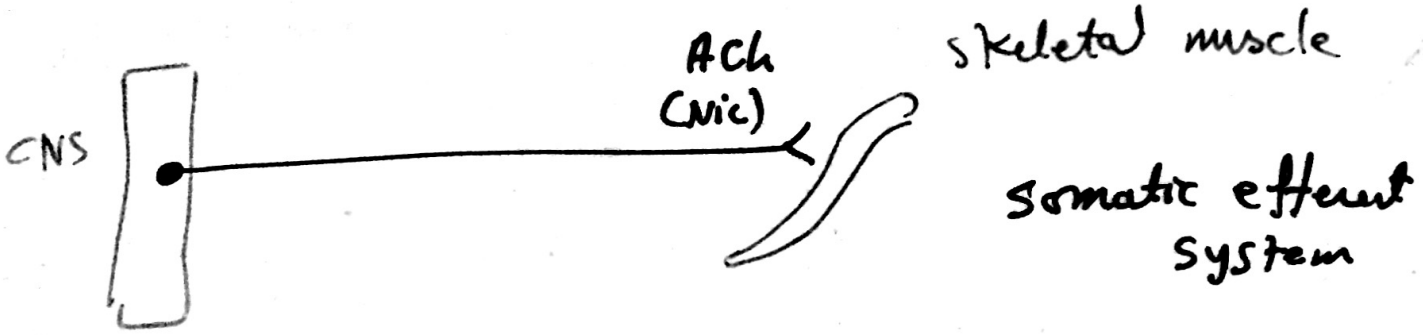
- indication :- . Spinal anaesthesia
  . painless childbirth.

- Drug used : - mainly lidocain
  - bupivacaine

side effects : . bradycardia
. hypotension
. R.C. ↓
. urinary retention.

- Note : opiate is also administered in combination
  - more effective analgesia (synergism)

Skeletal Muscle Relaxants



Neuromuscular blockers.

Classifications:

1- acting presynaptically = inhibit acetylcholine synthesis or release

2- acting post synaptically.

Clinical uses: only as an adjunct to anaesthesia when artificial ventilation is available.

Mechanism of action: works by interfering with the postsynaptic action of acetylcholine they fall into two categories:-

1- Non-depolarising drugs: (majority)
- blocking acetylcholine receptors
- blocking ion channels.

2- Depolarizing agents

Agonist

- Suxamethonium.

. used clinically as muscle relaxant

. Mechanism of action = Nicotine recept agonist
Depolarization block.

- site of action = Neuromuscular junction.

antagonists

- Pancuronium
- Atracurium
- Vecuronium

clinical use: widely used as muscle relaxants in anaesthesia.

Type of action: Nicotin receptor antagonists
Transmission block.

site of action Neuromuscular Junction.

Neuromuscular blocking drugs

- Substances that block choline uptake:
  - hemicholinium } Neither used clinically
  - triethylcholine }
- Substances that block acetylcholin release:
  - aminoglycosides
  - botulinum toxin.
- Drugs used to cause paralysis during anaesthesia are:
  - Non-depolarizing Neuromuscular blockers
    - tubocurarine
    - pancuronium
    - atracurium
    - vecuronium

competitive antagonists at nicotic acetylcholine receptors differ mainly in duration of action.

- depolarizing Neuromuscular-blocking drugs
  - suxamethonium

characteristics of both depolarizing & non-depolarizing drugs:

- Non-depolarising block is reversible by anticholinesterase drugs
- depolarizing block produces incial fasciculations and often post operative pain of muscles.
- Suxamethonium is hydrolysed by plasma cholinesterase and is normally very short acting but it may cause lasting pal paralysis in a small group congenitally cholinesterase-deficient individuals

Main- side effects

- tubocurarine: . ganglion block
  . histamine release
  . hypotension
  . bronchoconstriction } ? histamine release

- Suxamethonium: - bradycardia
  - cardiac dysrhythmias due to K^+ release (burned or injured patients)
  - increase intraocular pressure
  - Malignant hyperthermia (rare).

Antileprosy drugs

- For tuberculoid leprosy =

  dapson and rifampicin

- For lepromatous Leprosy

  dapson + rifampicin + clofazimine

- Dapsone - sulfonamide-like, may inhibit folate synthesis
  - given orally
  - unwanted effects are frequent
    few are serious
  - Resistance is increasing.

- Clofazimines = dye
  - orally
  - action delayed for 6-7 weeks
  - $t_{1/2}$ = 9 weeks.
  - side effects = red skin
    red urine

- Rifampicin : antituberculous drug
  - RNA-synthesis inhibiting antibiotic.

Leishmanias ذبابة الرمل

- Cutaneous form – simple – self limited
- mucocutaneous
- visceral

Main drugs

- pentavalent antimony compounds
- sodium stibogluconate
- Meglumine antimoniate
- Meltefosine
- pentamidine isethionate

- amphotericin
- Metronidazole