Neuromuscular Blocking Agents

- **Mechanism of Action**
  - Prevent acetylcholine stimulation at the motor endplate by
    combining with and occupying these specific receptors
  - This prevents muscle contraction and induces temporary muscle
    paralysis
- **Two classes of neuromuscular blocking agents**
  - Non-depolarizing agents (aka curariform) competitively engage
    the receptor site in the muscle cell, blocking the action of
    acetylcholine
  - Depolarizing agents initially instigate muscle contraction, then
    sustain depolarization time (receptors cannot respond)
    - Further stimulation to the muscle is prevented until the
      depolarizing effect is terminated

**Neuromuscular Blocking Agents**

- **Indications**
  - As an adjunct to anesthesia to induce skeletal muscle
    relaxation during surgery
  - During endotracheal intubation
  - Aide in the prevention of laryngospasm
  - Facilitate prolonged mechanical ventilation among patients
    who otherwise would be difficult to ventilate
- **Contraindications**
  - Hypersensitivity to the drugs
  - More specific contraindications will be listed with each drug

**Neuromuscular Blocking Agents**

- **Precautions**
  - Respiratory depression and apnea may follow the use of these
    drugs
    - Intubation with assisted ventilations should be immediately available
  - These agents have no effect on pain threshold or consciousness
    - Use only with adequate anesthesia
  - Use with caution in patients with MG and in patients with
    cardiovascular, renal, hepatic, pulmonary or endocrine dysfunction
  - Use with extreme caution in patients in which histamine release is
    a known hazard
    - Have antidotes readily available (neostigmine, edrophonium,
      pyridostigmine)
  - Use with caution in patients in which histamine release is a
    known hazard
- **Adverse Reactions**
  - Most frequent: Sustained pharmacologic action of the drug
    - Cardiovascular: Bradycardia, tachycardia, blood pressure
      changes, arrhythmias, cardiac arrest
    - Pulmonary: respiratory depression, apnea, bronchoconstriction
      (with histamine release)
    - GI: Excessive salivation
- **Overdosage**
  - Sustained apnea, cardiovascular collapse, prolonged muscle
    weakness, release of histamine
  - Treatment consists of ventilatory support and the administration
    of a cholinergic muscle stimulant
Neuromuscular Blocking Agents

• Non-depolarizing Agents
  – Atracurium Besylate (Tracrium)
    • May be used to facilitate endotracheal intubation and mechanical ventilation
    • Onset of action ≤ 3-5
    • Duration 20-40 min
    • Adverse reactions
      – histamine release
      – hypotension, tachycardia, circulatory collapse
      – erythema, edema
      – bronchospasm
    • Contraindications
      – patients with MG, electrolyte disorders, asthma

• Non-depolarizing Agents
  – Metocurine Iodide (Metubine)
    • Onset of action ≤ 2 min
    • Duration 25-90 min
    • Adverse reactions
      – histamine release
      – hypotension, tachycardia, circulatory collapse
      – erythema, edema
      – bronchospasm
    • Contraindications
      – patients sensitive to iodide

• Non-depolarizing Agents
  – Pancuronium Bromide (Pavulon)
    • May be used to facilitate endotracheal intubation and mechanical ventilation
    • Onset of action <1 min
    • Duration >60 min
    • Adverse reactions
      – salivation, skin rashes, tachycardia
    • Contraindications
      – patients sensitive to bromide

• Non-depolarizing Agents
  – Vecuronium Bromide (Norcuron)
    • May be used to facilitate endotracheal intubation and mechanical ventilation
    • Does not cause histamine release and rarely causes cardiovascular side effects
    • Onset of action ≤ 2.5-3 min
    • Duration 25-40 min
    • Adverse reactions
      – skeletal muscle weakness
      – respiratory insufficiency, apnea
    • Contraindications
      – patients sensitive to bromide

• Depolarizing Agents
  – Succinylcholine Chloride (Anectine)
    • used as an adjunct to general anesthesia during surgery and during endotracheal intubation and to reduce the severity of convulsions during electroshock therapy. Not generally used to facilitate mechanical ventilation due to short duration of action.
    • Onset of action 1 min
    • Duration 4-6 min
    • Recovery 8-10 min

• Depolarizing Agents
  – Succinylcholine Chloride (Anectine)
    • Adverse reactions
      – histamine symptoms
      – bradycardia, tachycardia, blood pressure changes, cardiac arrest, arrhythmias
      – respiratory depression, apnea
    • Contraindications
      – use with caution in patients with renal, liver, cardiovascular, or pulmonary dysfunction
      – relative contraindications include patients with severe burns, tetanus, spinal cord injuries, multiple trauma
Diuretic Agents

• Have the ability to facilitate urinary output of water and sodium by enhancing the normal function of the kidneys
  – Achieved through one of three primary mechanisms
    - Increasing glomerular filtration rate
    - Decreasing sodium reabsorption by the renal tubules
    - Excretion of sodium by the kidney
• Classification of diuretic agents is based on their primary mechanism of action

Diuretic Agents

• Carbonic Anhydrase Inhibitors
  – Generic name - Acetazolamide
  – Brand names - Diamox
  – Actions
    - Inhibit the action of carbonic anhydrase, blocking the reabsorption of Na⁺ and HCO₃⁻ from the proximal tubule
    - Prevent H⁺ formation and secretion in the renal tubule, which then causes excretion of Na⁺, K⁺, HCO₃⁻ and H₂O.
  – Indications
    - Edema due to CHF
    - Drug-induced edema
    - Treatment of hyperkalemic periodic paralysis
    - Acute mountain sickness after exposure to high altitude

Diuretic Agents

• Thiazide Diuretics
  – Generic names - Chlorothiazide; Hydrochlorothiazide
  – Brand names - Driurel; HCTZ
  – Action
    - Increases the excretion of Na⁺ and Cl⁻ with a corresponding loss of H₂O by blocking Na⁺ and Cl⁻ reabsorption by the distal renal tubules
  – Indications
    - Used in conjunction with other diuretics in pts with edema associated with CHF, pts with hepatic cirrhosis and pts with edema due to renal impairment
    - Hypertension; this drug may be used alone or with other hypotensive agents to enhance their effectiveness.

Diuretic Agents

• Loop Diuretics
  – Generic name - Furosemide
  – Brand names – Lasix
  – Action
    - Blocks the reabsorption of Na⁺ and Cl⁻ in the ascending loop of Henle and in the proximal and distal tubules
    - Promotes the excretion of K⁺, Mg²⁺, Ca²⁺ and to a lesser extent, HCO₃⁻
  – Indications
    - Edema associated with CHF, hepatic cirrhosis, renal disease
    - Used as an adjuvant in acute pulmonary edema
    - Hypertension (oral route only)

Diuretic Agents

• Osmotic Diuretics
  – Generic name - Mannitol
  – Brand names - Osmitrol
  – Action
    - Blocks the reabsorption of Na⁺ and H₂O in the proximal tubules, and the descending loop of Henle, increasing the excretion of H₂O, Na⁺ and Cl⁻
  – Indications
    - Treatment or prevention of acute renal failure
    - To decrease intracranial pressure and cerebral edema
    - To decrease intraocular pressure
    - As a diagnostic tool to measure the glomerular filtration rate
Diuretic Agents

- K⁺ Sparing Diuretics
  - Generic name – Amiloride, triamterene
  - Brand names - Midamor, Dyrenium; Dyazide (triamterene and hydrochlorothiazide)
  - Actions
    - block Na⁺ reabsorption in the distal tubule
    - K⁺ is normally exchanged for Na⁺ in the distal tubule and then secreted into the urine; by preventing the K⁺/Na⁺ exchange, K⁺ is spared from secretion
  - Indications
    - essential hypertension
    - hypokalemia
    - management of edema and Na⁺ retention in the CHF patient
    - cirrhosis of the liver, when accompanied by edema or ascites

Anticonvulsant Agents

- Actions
  - Inhibit seizure activity at the motor cortex level
  - Promote the efflux of Na⁺ from neurons, thereby stabilizing the threshold against hyperexcitability
- Generic name Phenytoin Sodium
- Brand names Dilantin
  - Preferred over phenobarbital in the adult, however due to phenytoin’s adverse reactions, phenobarbital is the drug of choice in children and infants
  - Phenytoin and phenobarbital are occasionally used together when a single drug is ineffective in controlling seizures

Anticonvulsant Agents

- Indications
  - Control of grand mal and psychomotor seizures
  - Prevention and treatment of seizures occurring during or after neurosurgery
  - Control of status epilepticus of the grand mal type
  - Unlabeled use: antiarrhythmic agent useful in digitalis-induced arrhythmias