Chapter 18

Skeletal Muscle Relaxants
(Neuromuscular Blocking Agents)
Uses of Neuromuscular Blocking Agents

- Facilitate intubation
- Surgery
- Enhance ventilator synchrony
- Reduce intracranial pressure (ICP)
- Reduce $O_2$ consumption
- Terminate *status epilepticus* and *tetanus*
- Facilitate procedures and studies
- Keep patients immobile
Physiology of the Neuromuscular Junction

- **CNS**
  - Brain
  - Spinal cord

- **PNS**
  - Somatic motor nervous system (skeletal)
    - Voluntary control
  - Autonomic nervous system
    - Involuntary control
Physiology of the Neuromuscular Junction (cont’d)

- **Neuron**
  - Cell body
  - Axons
  - Dendrites

- **Neurotransmitter**
  - Acetylcholine
  - Acetylcholinesterase (AChE)
Physiology of the Neuromuscular Junction (cont’d)

- **Depolarization**
  - Action potential occurs

- **Repolarization**
  - Membrane potential returns to baseline
Physiology of the Neuromuscular Junction (cont’d)

- Two ways to block muscle contraction
  - Competitive inhibition
    - Nondepolarizing agents
  - Prolonged occupation and persistent binding
    - Depolarizing agents
Nondepolarizing Agents

- Block acetylcholine receptors without activating them
- Mode of action
  - Affect postsynaptic cholinergic receptors
  - Compete against endogenous acetylcholine
  - Effect is dose related
  - Acetylcholinesterase inhibitors (neostigmine) can reverse blockade
Nondepolarizing Agents (cont’d)

- Pharmacokinetics of nondepolarizing agents
  - Chemically resemble acetylcholine
  - Onset of paralysis and duration of action vary widely and are dose dependent
  - Duration can be increased by
    - Advanced age
    - Hepatic or renal failure
Nondepolarizing Agents (cont’d)

- **Metabolism**
  - When normal conduction returns, 75% of receptors may still be occupied by blocker
    - Additional boluses may appear more potent
  - *d*-Tubocurarine and doxacurium
    - Minimally metabolized
  - Pancuronium
    - Hepatic metabolism
Nondepolarizing Agents (cont’d)

- Metabolism (cont’d)
  - Atracurium and cisatracurium
    - Spontaneous degradation by pH and temperature
  - Vecuronium
    - Hepatic metabolism
  - Mivacurium
    - Shortest acting (10 to 20 minutes)
    - Eliminated by plasma cholinesterase
Nondepolarizing Agents (cont’d)

- Adverse effects and hazards
  - Cardiovascular effects
    - Vagolytic effect
  - Histamine release
    - Cause histamine release from mast cells
  - Inadequate ventilation
    - Paralysis of diaphragm and intercostals
Nondepolarizing Agents (cont’d)

- Reversal of nondepolarizing blockade
  - Produced by cholinesterase inhibitors
  - Inhibits cholinesterase that breaks down acetylcholine
  - Allows more acetylcholine at junction to displace blocker
- Agents
  - Neostigmine
  - Edrophonium
  - Pyridostigmine
Depolarizing Agents

.mode of action
- Depolarizes muscle membrane like acetylcholine
  - Resistant to AchE for longer period
  - Causes fasciculations
- Phase I block
  - Prolonged depolarization/flaccid paralysis
- Phase II block
  - Resembles nondepolarizing block
  - Limits use in repeat doses
Depolarizing Agents (cont’d)

- **Metabolism**
  - Rapid hydrolysis by plasma cholinesterase

- **Reversal**
  - No agents available for reversal of succinylcholine
Depolarizing Agents (cont’d)

- Adverse effects and hazards
  - Sympathomimetic response
  - Vagal response with repeat boluses
  - Muscle pain/soreness
  - Hyperkalemia
  - Increased intracranial, intraoptic, and intragastric pressure
  - Malignant hyperthermia
Neuromuscular Blocking Agents and Mechanical Ventilation

- Used to improve ventilation and oxygenation and to reduce pressure
- Beneficial in:
  - Status asthmaticus
  - Inverse ratio ventilation and high-frequency oscillatory ventilation (HFOV)
  - Status epilepticus
  - Neuromuscular toxins
  - Tetanus
  - Acute respiratory distress syndrome (ARDS)
Neuromuscular Blocking Agents and Mechanical Ventilation (cont’d)

- Precautions and risks
  - Proper eye care
  - Suctioning
  - Proper sedation and analgesia
  - Aspiration/nosocomial pneumonia
  - Risk of prolonged skeletal muscle weakness
  - Decubitus ulcers
  - Deep venous thrombosis (DVT)
Neuromuscular Blocking Agents and Mechanical Ventilation (cont’d)

- Use of sedation and analgesia
  - Absolutely essential!
  - Monitor for tachycardia, hypertension, diaphoresis, and lacrimation
  - Analgesics
    - Fentanyl
    - Morphine
  - Amnestic sedatives
    - Propofol
    - Lorazepam
    - Midazolam
Neuromuscular Blocking Agents and Mechanical Ventilation (cont’d)

- Interactions with neuromuscular blocking agents
  - Inhaled anesthetics potentiate blockade
  - Aminoglycosides also produce NMB
  - Agents antagonizing NMB
    - Phenytoin
    - Azathioprine
    - Theophylline
  - Potentiate blockade
    - Acidosis
    - Hypokalemia
    - Hyponatremia
    - Hypocalcemia
    - Hypomagnesemia
Neuromuscular Blocking Agents and Mechanical Ventilation (cont’d)

- **Choice of agents**
  - Situation dependent
  - **Factors**
    - Duration of procedure
    - Need for quick intubation
    - Adverse effects
    - Route of elimination
    - Drug interactions
    - Cost
Monitoring of Neuromuscular Blockade

- Paralysis may mask clinical signs/symptoms

- Methods
  - Visual
  - Tactile
  - Electronic
Monitoring of Neuromuscular Blockade (cont’d)

- Loss of muscle activity
  - Eyelids
  - Face
  - Neck
  - Extremities
  - Abdomen
  - Intercostals
  - Diaphragm

- Return of muscle activity
  - Occurs in reverse order
Monitoring of Neuromuscular Blockade (cont’d)

- Twitch monitoring
- Train-of-four evaluation
  - 2 Hz over 2 seconds
    - 0 twitches = 100% blockade
    - 1 twitch = 95% blockade
    - 2 twitches = 90% blockade
    - 3 twitches = 80% blockade
    - 4 twitches = <75% blockade
The Future of Neuromuscular Blocking Agents and Reversal

- **Gantacurium**
  - Nondepolarizing
  - Rapid onset
  - Short-acting
  - Organ-independent inactivation
  - Less histamine release

- **Sugammadex**
  - Inactivates and removes NMBA
  - Reverses rocuronium and vecuronium
  - Less effective on pancuronium, succinylcholine, and benzylisoquinoliniums