Chapter 18
Neuromuscular Blocking Agents
Study Guide and Application Exercise

1. Read chapter

2. Review objectives (p. 305)

3. Review key terms and definitions (p. 305)

Add:
Cholinesterase inhibitor
Vagal stimulation and effects
Vagolytic effects

4. For the respiratory care profession, the primary indications for NMBA include: perform rapid sequence intubation, maintain patient-ventilator synchrony, reduce intracranial pressure and seizures. (p. 300)

5. Stimulation of acetylcholine (Ach) facilitates nerve conduction to the skeletal muscles and muscle movement. (T/F)

6. Activation of acetylcholine leads to muscle _______ (contraction, paralysis)

7. Acetylcholine (Ach) is metabolized by an enzyme called _______. When this enzyme is blocked, the level of acetylcholine _______ (increases, decreases).

**Non-Depolarizing NMBA (p. 308-310)**

8. Non-depolarizing neuromuscular blocking agents (NMBAs) do not cause depolarization of the Ach receptors. This class of NMBAs compete with the natural occurring acetylcholine for the receptor sites. Once the receptor sites are occupied by these NMBAs, the natural occurring acetylcholine cannot exert its normal functions (depolarization → muscle contration).

9. Since acetylcholine (Ach) is metabolized by the enzyme cholinesterase, blocking cholinesterase can increase the overall level of acetylcholine - depolarization → muscle contraction.

10. Acetylcholinesterase = cholinesterase = AChE
11. Review Table 18-1 (p.307) and note the clinical duration and mode of elimination for nondepolarizing NMBAs.

<table>
<thead>
<tr>
<th>Factors affecting degree of neuromuscular blockage</th>
<th>Dose</th>
<th>Age</th>
<th>Organ function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption</td>
<td>Poorly lipophilic</td>
<td>Poor diffusion across blood-brain barrier</td>
<td></td>
</tr>
<tr>
<td>Route of administration</td>
<td>IV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of action</td>
<td>Short (mivacurium)</td>
<td>Intermediate (atracurium*, cisatracurium*, vecuronium, rocuronium) *(ideal for patients with hepatic or renal failure)</td>
<td>Long (tubocurarine, pancuronium, pipecuronium, doxacurium)</td>
</tr>
<tr>
<td>Vagal effects</td>
<td>Vagolytic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mast cells</td>
<td>Histamine release</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilation</td>
<td>Significantly decreased</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical use</td>
<td>Must add sedative (and analgesic, if pain is present)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use cautions</td>
<td>Histamine release, cardiovascular effects</td>
<td></td>
<td></td>
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</tbody>
</table>

12. Explain how does the “clinical duration of action” an important factor for certain patients (i.e., surgery, mechanical ventilation, seizure).

13. Explain how does the “mode of elimination” affect the effects and duration of nondepolarizing NMBAs.

14. Explain how does the “mode of elimination” affect the selection of an ideal NMBA.

15. Some nondepolarizing NMBAs may produce ______ (vagoactive, vagolytic) effects. List these effects. (p.309)

16. Nondepolarizing NMBAs can be reversed. (T/F)

17. Review Table 18-5. These reversal agents are essentially cholinesterase agents. (T/F)
18. Review Table 18-5. Atropine or glycopyrrole is sometimes used in conjunction with the “reversal” agents. This is because the reversal agents may often cause _______ (adrenergic; cholinergic) effects.

19 Why is pyridostigmine (Mestinon) an ideal drug to manage myasthenia gravis?

Note: Patients with myasthenia gravis have a reduced number of working ACh receptors. The available ACh also undergo rapid degradation. This combination renders these patients unable to use the respiratory (and other) muscles effectively.

Edrophonium (Tensilon) is a cholinesterase inhibitor (used to increase the level of ACh and to reverse the effects of non-depolarizing blocking agents). It has quick onset and short duration. Tensilon is used to test presence of Myasthenia gravis.

Myasthenia gravis is treated with pyridostigmine (Mestinon) because of its long duration of action and availability in oral form.

Patients who overdose on anticholinesterase (cholinesterase inhibitor) may develop cholinergic crisis because the neuromuscular junctions are overstimulated due to excessive ACh. They may exhibit the same signs and symptoms of acute Myasthenia gravis (called Myasthenia crisis). If the patient responds to Tensilon, the condition is likely _______ (cholinergic crisis, Myasthenia crisis).

Flaccid paralysis resulting from cholinergic crisis can be distinguished from myasthenia gravis by the use of the drug edrophonium (Tensilon). Tensilon worsens the paralysis caused by cholinergic crisis (caused by using too much tensilon to reverse the effects of non-depolarizing agent). Tensilon strengthens the muscle in the case of myasthenia gravis.

**Depolarizing NMBA (p.310-312)**

20. Normal muscle movement (contraction) requires a continuing sequence of depolarization/repolarization of the Ach receptors at the postsynaptic muscle membrane.

21. Depolarizing NMBA induces muscular blockage by initiating a sustained (prolonged) depolarization of the Ach receptors at the postsynaptic muscle membrane. When sustained depolarization occurs, repolarization is delayed (or stop), resulting in muscle paralysis.

22. Succinylycholine (Anectine) is the one and only depolarizing NMBA available in the USA for clinical use.
23. List the adverse effects of succinylcholine (Anectine).

24. Malignant hyperthermia.

Malignant hyperthermia (MH) is a life-threatening clinical syndrome of hypermetabolism involving the skeletal muscle. It is triggered in susceptible individuals primarily by the volatile inhalational anesthetic agents and the muscle relaxant succinylcholine. MH is not an allergy but an inherited disorder that is found both in humans and in swine.

In persons susceptible to MH, the ryanodine receptor in skeletal muscle is abnormal,[2] and this abnormality interferes with regulation of calcium in the muscle. An abnormal ryanodine receptor that controls calcium release causes a buildup of calcium in skeletal muscle, resulting in a massive metabolic reaction.

This hypermetabolism causes increased carbon dioxide production, metabolic and respiratory acidosis, accelerated oxygen consumption, heat production, activation of the sympathetic nervous system, hyperkalemia, disseminated intravascular coagulation (DIC), and multiple organ dysfunction and failure. Early clinical signs of MH include an increase in end-tidal carbon dioxide (even with increasing minute ventilation), tachycardia, muscle rigidity, tachypnea, and hyperkalemia. Later signs include fever, myoglobinuria, and multiple organ failure.

25. Treatment for malignant hyperthermia.

Malignant hyperthermia can be treated with dantrolene (Ryanodex). It has a shelf life of 3 years and costs about $200 per vial. But the overall cost per life saved is over $200,000.

26. The duration of succinylcholine (Anectine) is _______ (short, intermediate, long, ultra-long) and it is _______ (reversible, irreversible).

27. Succinylcholine (Anectine) is often used in rapid sequence intubation. (see last page for algorithm)

Rapid sequence intubation: Rhabdomyolysis is a condition where skeletal muscle is broken down, releasing muscle enzymes and electrolytes from inside the muscle cells. Risks of rhabdomyolysis include muscle breakdown and kidney failure because the cellular component myoglobin is toxic to the kidneys. Rhabdomyolysis is relatively uncommon, but it most often occurs as the result of extensive muscle damage as, for example, in crush injury or electrical shock.

28. Succinylcholine (Anectine) must be used with sedative. (T/F)
29. Succinylcholine (Anectine) should be used with analgesic if indicated. (T/F)

30. What is a “Train of Four” device and how does it work?

31. “Train of Four” delivers 4 electric impulses at 2 Hz in 0.5 sec intervals. (2 seconds total for each test)

32. For management of patient-ventilator dyssynchrony, the ideal titration end-point for TOF should be ______ (0, 1 or 2, 2 or 3, 4) twitches every 2 seconds.

https://www.youtube.com/watch?v=CNWRDP-bv2E

https://www.youtube.com/watch?v=Fa9OoHBQoLs

33. Review “Clinical Scenario” (p.317). With pH = 7.20, PaCO2 = 50 mm Hg, the patient has ______ (respiratory acidosis, metabolic acidosis, combined acidosis).
Figure 6-13: Rapid sequence intubation practice guideline.

**Indications:**
- Inability to maintain patent airway
- GCS: ≤8 (nonpurposeful)
- \( \text{paO}_2/\text{FIO}_2 \) ratio <250
- Respiratory rate <10, >30
- Hemodynamic instability

**Equipment:**
- Cardiac monitor
- IV access
- ACLS drugs
- Pulse oximetry
- \( \text{O}_2 \)
- Cricoid tray

**Succinylcholine**

**Contraindications:**
- Hyperkalemia
- Penetrating eye injuries
- SCI (quad, para)
- CVA
- Burns
- Crush injury
- Rhabdomyolysis
- Hx malignant hyperthermia

**Onset:** 20–50 sec
**Duration:** 4–6 min

**Etomidate**
- No contraindication
- Onset: 60 sec
- Duration: 3–5 min

**Sedation/Paralytics:**
- Vecuronium 0.1 mg/kg IV
- Valium 5–10 mg IV
- Fentanyl 200 mcg IV

**Initial Ventilator Settings**
- \( \text{FiO}_2 \): 100%
- \( V_t \): 5 to 7 mL/kg
- Mode: SIMV
- Rate: 12
- PEEP: 5
- PS: 0

**Cricoid pressure with in-line stabilization**