Paralyzing Danger:
Safety Strategies for Neuromuscular Blocking Agents

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I have no conflict of interest to declare.

Which of the following drugs are neuromuscular blocking agents (NMBs)?

1. Cyclobenzaprine
2. Succinylcholine
3. Hydralazine
4. Clozepine
5. Carbamazepine

NMB Prototype: Curare

-Natural curare comes from a woody vine found in South America (Chondodendron tomentosum)
-First used by indigenous South American people as poison for arrow or dart tips
-Animals became paralyzed and died
-Not effective when orally ingested, so meat could be eaten safely

-Described in 1516 by Pietro Martire d 'Anghere in his book "De Orbo Novo"
-Spanish soldiers and explorers in Central and South America died when hit by poisoned arrows blown at them by natives
-Described by Sir Walter Raleigh in 1596
-Brought to Europe in 1745 by French explorers (Charles Marie de la Condamine) on scientific expedition to Ecuador
-Extensively studied and experimented with over the next 200 years

Booij , Leo . The history of neuromuscular blocking agents. Current Anaesthesia and Critical Care (2000) 11, 27-33.

How NMBs Work

- Acts at neuromuscular junction (motor endplate)
- Competitive antagonist of acetylcholine (ACh)
- Classified as
  - polarizing (succinylcholine)
  - nondepolarizing (everything else in clinical use today)

Historical Impact on Medicine

- Before NMBs were available, deep levels of anesthesia were required for intra-peritoneal surgeries
  - Caused cardiovascular and respiratory depression
  - High incidence of morbidity and mortality
- NMBs allowed development of "balanced anesthesia"
  - Lower, safer doses of anesthetic agents possible
- NMB as important to advancing the practice of anesthesia as ether, nitrous oxide, endotrachal intubation, and local anesthetics

Booij , Leo . The history of neuromuscular blocking agents. Current Anaesthesia and Critical Care (2000) 11, 27-33.

Clinical Use Today

- Produce skeletal muscle relaxation (including the diaphragm)
  - During surgery of intubated patient
  - During tracheal intubation
  - To facilitate mechanical ventilation of critically ill patients in ICU and decrease O2 requirement
- More rarely: to treat muscle spasms due to tetanus, epilepsy, drug overdose, black widow spider bite

Important FACTS!

- NMBs cause muscle paralysis ONLY!
- CNS is not affected
  - Consciousness and full awareness remain intact
  - Patient still senses pain

Therefore, it is essential to:

- **Intubate (artificial ventilation)**
- **Administer anesthesia**
- **Administer pain medication**

Meet the NMBs!

Ultra-Short-acting
- *Duration 4-6 minutes*
  - succinylcholine *

Short-acting
- *Duration 15-30 minutes*
  - mivacurium

Intermediate-acting
- *Duration 20-60 minutes*
  - vecuronium **
  - rocuronium
  - cisatracurium
  - atracurium

Long-acting
- *Duration 60-100 minutes*
  - pancuronium *

What's in a name?
*Similar to acetylcholine
**Similar to curare

Get To Know the NMBs!

...for the safety of our patients!

Generic Name	Brand Name	Confused Names
succinylcholine	Quelicin, Anectine	
vecuronium	Norcuran	Narcan (naloxone), vancomycin
rocuronium	Zemuron	
atracurium	Tracrium	Ativan
cisatracurium	Nimbex	
pancuronium	Pavulon	Peptavlon
mivacurium	Mivacron	

http://www.ismp.org/Tools/Confused-Drug-Names.aspx

Reports of Inadvertent Administration

- Pancuronium was misplaced among heparin flush stock…a nurse inadvertently administered 5ml to a non-intubated patient (recovered after 10 hours on ventilator). *2000*
- Verbal order for "Narcan" was misinterpreted by nurse to be 'Norcuron", obtained from cabinet and administered to patient, who experienced respiratory and cardiac arrest, was resuscitated, placed on ventilator and sent to ICU. *1998*
- ED physician mistakenly entered orders for midazolam and vecuronium for a trauma patient he was intubating into an oncology patient's record. Another ED nurse relieving for break administered to the patient, not realizing the patient must be intubated. She left the room and the patient arrested, could not be resuscitated. *2005*

Koczmara C, Jelincic V. Neuromuscular blocking agents: enhancing safety by reducing the Risk of accidental administration. ISMP Canada, 18 (1) Spring 2007. http://www.ismp.org/newsletters/acutecare/articles/20090226.asp accessed 8/7/2015.

Inadvertent Administration

- Atracurium was administered subcutaneously instead of hepatitis B vaccine to seven infants. Within 30 minutes all experienced respiratory distress. Five recovered, one sustained permanent injury, one died. Anesthesiologist had stored a vial in the refrigerator for convenience and it was similar in appearance to the vaccine vial. *2002*
- ED physician ordered NMB to sedate a combative patient. Nurse administered the drug too soon, before intubation. Patient arrested and suffered permanent anoxic injury.
- ED nurse prepared saline flush syringes each day. Left-over unlabeled vecuronium syringes from a trauma patient were inadvertently mixed in with the saline syringes. One was used to flush the line of a 3 year old child, who became flaccid and developed respiratory arrest. She was quickly intubated and ventilated and recovered. *2005*

Paralyzed by mistakes – preventing errors with neuromuscular blocking agents. ISMP Medication Safety Alert, Sept. 22, 2005. http://www.ismp.org/newsletters/acutecare/articles/20050922.asp accessed 7/11/2015

Predominant Medication Error Event Types Associated with NMB (n=120)

Event Type	Number	% of Total Reports (n=154)
Wrong drug	57	37%
Wrong dose / overdose	25	16.2%
Prescription / refill delayed	7	4.5%
Wrong technique	6	3.9%
Extra dose	6	3.9%
Other	19	12.3%

NMB: Reducing associated wrong-drug errors. PA Patient Safety Advisory 2009 Dec;6(4):109-14. http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2009/Dec6(4)/Pages/109.aspx Accessed 8/4/2015.

Contributing Factors

- Unsafe storage or products
- Look-alike labeling and packaging
- Look-alike drug names
- Unlabeled syringes
- Inadequate knowledge of drug action
- Failure to ensure ventilator support
- Ordering errors

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NMB: Reducing associated wrong-drug errors. PA Patient Safety Advisory 2009 Dec;6(4):109-14.
http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2009/Dec6(4)/Pages/109.aspx

Inattentional Blindness

A type of confirmation bias

- Failure to notice a fully visible but unexpected object because attention was engaged on another task, event, or object.
- The person performing the task fails to see what should have been plainly visible, and later, they cannot explain the lapse
- Vials and labels look similar to what we expect to see, so we tend to see what we expect

Inattentional blindness: What captures your attention? ISMP Medication Safety Alert, Feb. 26, 2009. https://www.ismp.org/newsletters/acutecare/articles/20090226.asp

Koczmara C, Jelincic V. Neuromuscular blocking agents: enhancing safety by reducing the risk of accidental administration. ISMP Canada, 18 (1) Spring 2007. www.ismp.org/newsletters/acutecare/articles/20090226.asp

Error Prevention Strategies

- Limit access
  - Allow floorstock only in OR, ED, critical care units where patients can be properly ventilated and monitored
- Segregate storage
  - Pharmacy should maintain a distinct sealed box with warnings affixed, in med area or refrigerator
- Warning labels
  - Affix fluorescent red labels on each vial, syringe, bag, and storage box

Error Prevention Strategies

- Safeguard storage in the pharmacy
  - Sequester NMB stored in the pharmacy
  - Affix warning labels to vials
- Standardize prescribing
  - Establish order sets and alerts to avoid misinterpretation
  - Include requirement or cross-checks for ventilator support and discontinuation after extubation
  - Do not allow "Resume previous meds" orders
  - Refer to as "paralyzing agents", not "muscle relaxants"
  - Do not allow "prn" orders

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Error Prevention Strategies

- Redundancies
  - Consider requiring independent double check before dispensing and administering
  - Double check against original order
- Require bedside attendance during initial administration
  - Licensed practitioner with experience in intubation and airway management

Error Prevention Strategies

- Prompt removal of discontinued products
  - Discard or sequester vials, IV bags, and syringes with NMB for immediate pharmacy pickup after discontinuation/ extubation
- Increase awareness
  - Educate staff about risks
  - Provide list of generic and brand names for all NMBs available at facility

In what areas do the errors involving NMBs most usually originate (in order of most-least)?

1. OR
2. ICU
3. ED
4. Pharmacy
5. Pediatrics

Predominant Care Areas Involved in Medication Errors Involving NMB (n=120)

Unit	Total	% of Total Reports
ED	21	13.6%
OR	19	12.3%
Pediatric ICU	15	9.7%
Anesthesia	15	9.7%
→ Pharmacy	10	6.5%
Med/Surg ICU	9	5.8%
Medical ICU	9	5.8%
Neonatal ICU	8	5.2%
Cardiac ICU	8	5.2%
Surgical ICU	6	3.9%

NMB: Reducing associated wrong-drug errors. PA Patient Safety Advisory 2009 Dec;6(4):109-14.
http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2009/Dec6(4)/Pages/109.aspx

In which of the following scenarios might "inattentional blindness" have played a role?

Pharmacy Errors

1. Cisatracurium infusion prepared for a ventilated infant. Delivered by accident to adult unit with 3 bags of antibiotics. Nurse verified the 1st 3 bags of antibiotics, but was interrupted and did not check the 4th (cisatracurium). Label similar in color and so the bag was hung. Patient experienced respiratory arrest and required ventilation for several hours.
2. Pancuronium was misplaced among heparin flush stock…a nurse inadvertently administered 5ml to a non-intubated patient (recovered after 10 hours on ventilator).
3. Anesthesiologist ordered trial supply of mivacurium infusion from a drug rep. Product was delivered to pharmacy, was stocked next to metronidazole. Infusion was in foil wrapper like metronidazole. Tech labeled several bags as metronidazole, pharmacist did not catch, nurse did not catch, 4 patients received mivacurium. All arrested; two recovered, one suffered permanent harm, one died.

Paralyzed by mistakes: preventing errors with neuromuscular blocking agents. ISMP Medication Safety Alert. 2005;10(19).

Oregon hospital admits mistake led to patient death *

Sisters woman, 65, given paralyzing agent in ER

By Tara Bannow / The Bulletin / @tarabannow
Published **Dec 5, 2014** at 12:01AM / Updated Dec 5, 2014 at 06:31AM

An Oregon hospital' s flat-out admission that a medication error resulted in a 65-year-old woman's death this week serves as a reminder of hospitals' efforts to increase transparency and communication when such incidents occur.

The patient died Wednesday, two days after going to the hospital emergency room. She had been accidentally given a paralyzing agent, which caused her to go into cardiac arrest. Hospital officials have been forthcoming with the family about the mistake, asserting it's long been the health system's policy to do so.

The patient went to the emergency room Monday with anxiety and concerns about the medications she was taking after recent brain surgery at a different hospital. Staff members determined she needed an intravenous anti-seizure medication called fosphenytoin. Instead, she was given the wrong medication, a paralyzing agent called rocuronium, which caused her to stop breathing and go into cardiac arrest, leading to irreversible brain damage. The patient was on life support until Wednesday morning.

Three staff members involved in the patient's care are on administrative leave, and are receiving counseling through the hospital's caregiver assistance program. The Chief Clinical Officer declined to say what their jobs are but said they're "devastated by this."

* Edited to remove identifiers.

What Happened?

- Pharmacy received order for fosphenytoin for seizures
- Pharmacy prepared the IV solution, but accidentally added rocuronium instead of fosphenytoin
- The bag was dispensed labeled as fosphenytoin
- After the bag was hung, a code red was announced. The door to the patient room was closed to protect from fire.
- When the nurse re-entered, the patient was found in respiratory and cardiac arrest.

Tragic error with neuromuscular blocker should prompt risk assessment by all hospitals. ISMP Medication Safety Alert, Dec 14, 2014.
www.ismp.org/newsletters/acutecare/showarticle.aspx?id=97

Reflection:

How could this tragedy have been prevented?
Which of the strategies discussed might have made a difference?

ISMP Recommendations

- Limit neuromuscular blockers in formulary
- Segregate or eliminate storage from active pharmacy stock when possible
  - Highly visible storage container
  - Bright warning labels
- Regularly review storage areas to assess potential for mix-ups
- Thoroughly examine the entire pharmacy IV admixture process
  - Review ISMP IV Sterile Compounding Guidelines (www.ismp.org/sc?id=461)
  - Consider implementing IV workflow technologies

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Consider implementing IV workflow technologies!!!

Future State (Why Not NOW?)

- IV workflow technologies utilize barcode scanning of products during IV admixture
- Double checks the accuracy of the ingredients of each compounded product (if utilized correctly)
- A number of systems are available on the market
- Potential to eliminate errors due to inattentional blindness

IV workflow systems "that utilize barcode scanning support can assure proper drug selection, but only if the systems are fully integrated with the pharmacy and hospital information systems. Without full integration between the IV workflow technology and the order entry system, errors can still be introduced into the process. Although some hospitals have chosen to limit use of these systems [IV workflow technology] *for focused areas like admixture of chemotherapy or high-alert drugs, there's no telling when someone might accidentally introduce a high-alert drug when preparing other drug classes that wouldn't ordinarily be scanned. Therefore, to be maximally effective, the system must be utilized for all compounded admixtures."*

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What was the first department in the hospital to adopt barcode scanning?

1. The pharmacy
2. The operating room
3. Nursing – BCMA (bar code medication administration)
4. The gift shop

http://jerryfahrni.com/2015/01/a-missed-opportunity-for-safety-why-scanning-a-limited-formulary-in-the-i-v-room-is-a-mistake/ (Paraphrased from blog comment by Ray Vrabel)

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Post-Test Questions

1. Which of the following drug groups are all neuromuscular blocking agents (NMBs)?
    a. succinylcholine, rocuronium, Narcan
    b. Peptavlon, mivacurium, acetylcholine
    c. rocuronium, Nimbex, succinylcholine
    d. atracurium, vecuronium, cyclobenzaprine

2. List five error prevention strategies recommended by ISMP to reduce the risk of error with NMBs.
    a. _____
    b. _____
    c. _____
    d. _____
    e. _____

3. Which of the following technologies has the potential to eliminate wrong-ingredient errors in pharmacy sterile compounding if used properly?
    a. BCMA (bar code medication administration)
    b. Remote pharmacist verification of compounded sterile products utilizing cameras in the laminar airflow workstation (hood)
    c. IV workflow technology utilizing barcode scan verification only when chemotherapy and high alert drugs are compounded
    d. IV workflow technology utilizing barcode scan verification of all ingredients used in all sterile compounding