SI Pharmacology

her Brand, MD

ntroduction

Sedatives

Paralytics

Adjunctive medication

Why RSI?

- Indictions?
- Who should do RSI?
- What are the dangers?
- What are the alternatives?

SI - Process

Rapid Sequence Induction”

- Induction
- Paralytic
- Intubation
- Ongoing sedation

SI - Contraindications

- Uncorrectable hypoxia
- Difficult airway on exam
- Profound instability

SI - Considerations

- Awareness
- Hemodynamics
- Ease of intubation
- Physiologic effects
- Adverse reactions

SI Pharmacology

nduction & Sedation

Paralytics

nduction/Sedation

- Render unconsiousness
- Reduce response to laryngoscopy
- Reduce metabolic demand

gents

- Etomidate
- Propofol
- Benzodizepines
- Opiates
- Ketamine
- Barbiturates

tomidate

- Unique anesthetic
- Rapid acting
- Hemodynamically stable

tomidate

- mg/cc
- 0 and 40 cc vials
- Abbojet (?availability)
- n USA 1 year half life
- Pregnancy Risk “C”

tomidate

Commonly used

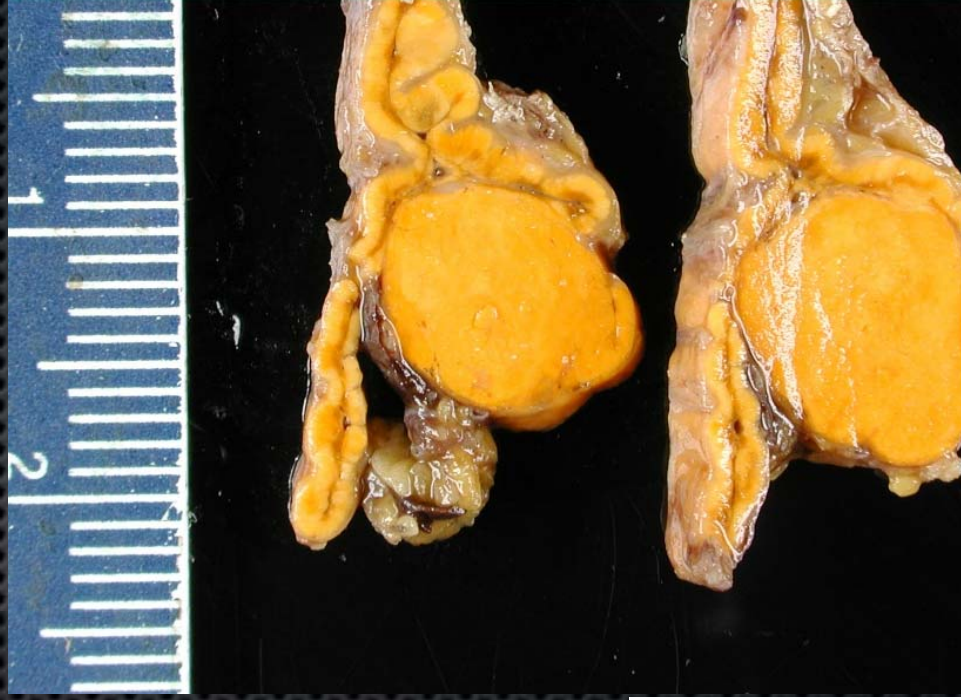
Predictable & seemingly safe

Falling into disfavor

Good: Hemodynamic stability

Bad: Adrenal supression

tomidate



drenal supression:

- Sepsis
- Trauma
- ? any significant stressor

Single-Dose Etomidate for Rapid Sequence Intubation May Impact Outcome After Severe Injury

Keir J. Warner, BS, Joseph Cuschieri, MD, Gregory J. Jurkovich, MD, and Eileen M. Bulger, MD

round: Etomidate is an induction agent used for the rapid-sequence on (RSI) of trauma patients because of its favorable hemodynamic and rapid onset. However, recent studies have shown etomidate to e circulating cortisol concentrations, potentially influencing inflam. We hypothesized that etomidate may alter the occurrence of acute tory distress syndrome (ARDS) in injury victims.
ds: We analyzed data collected prospectively from a clinical trial of spital hypertonic saline administration. Post hoc, patients were grouped ing to whether they did or did not receive etomidate for prehospital management. The incidence of ARDS was compared between the two by Fisher's exact test. Logistic regression was used to adjust for the of other known risk factors for ARDS.
s: Over a 2-year period, 94 study patients underwent RSI, of which 35 d etomidate (37%). There were no significant differences in demo, physiology, anatomic injury scores, or use of hypertonic saline ation between the groups. After adjusting for physiology, injury y, and transfusion, etomidate use remained associated with ARDS 3.9, 95% CI 1.24–12.0).
sions: Single-dose etomidate for RSI in severely injured trauma s is associated with increased ARDS and multiple organ dysfunction me, in part, because of an effect of etomidate on the inflammatory se.
ords: Etomidate, Acute respiratory distress syndrome, Intubation, . Multiple organ dysfunction syndrome.

uma. 2009;67:45–50.

their intensive care unit (ICU) stay.[3] The clinical signifi of these findings is uncertain.

Elevated circulating cortisol concentrations traumatic injury.[4] The effect of altering this response m evident as an increase in the risk for inflammation- complications, such as the acute respiratory distress drome (ARDS). The biological effects of cortisol are n ous and include maintenance of vascular tone and endo integrity, phospholipase A2 suppression, and leukocy optosis. Cortisol has been shown to decrease L-selecti CD 11b expression on neutrophils and monocytes, t ceptors that are involved in rolling and margination in tissues.[5] The inhibition of cortisol synthesis by etom may allow for an increase in their expression, thereb creasing neutrophil margination potentially contribut the development of ARDS and multiple organ dysfu syndrome (MODS).[6,7] We therefore sought to dete whether a single dose of etomidate, used for emergen bation in severely injured patients, was associated wi development of posttraumatic ARDS.

PATIENTS AND METHODS

Study Design

Warner, et. al. 2009

End point => ARDS

- 40% in etomidate vs. 20% in others
  - p=.02 OR=3.86 [1.24-12]
- Longer stay p=.02
- Fewer Days on Vent p=.04

tomidate

What to expect

- Very rapid take down
- last 3-5 min
- Be ready with second sedative
- n/v common if used without paralytic

Appropriate role??

gents

Etomidate

Propofol

Benzodizepines

Opiates

Ketamine

Barbiturates

ropofol

- Not a common EMS drug
- Frequently used in OR's, ICU's & ER's
- Can cause hypotension
  - Particularly in volume depletion
- Excellent sedative and induction agent

ropofol

Milk of Anesthesia

Mechanism of Action Unclear

hypnotic”

Michael Jackson

Role in EMS

ropofol

deal uses

- Seizures
- Adgitated delerium
- Eclampsia
- Isolated TBI and Head Bleeds

gents

Etomidate

Propofol

Benzodizepines

Opiates

Ketamine

Barbiturates

enzodiazepines

Diazepam (Valium)

Lorazepam (ativan)

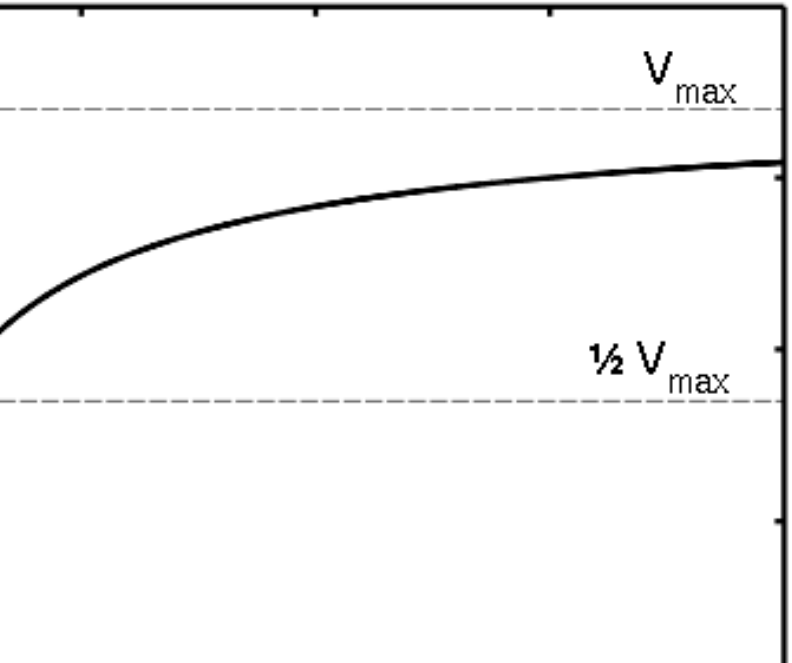
Midazolam (Versed)

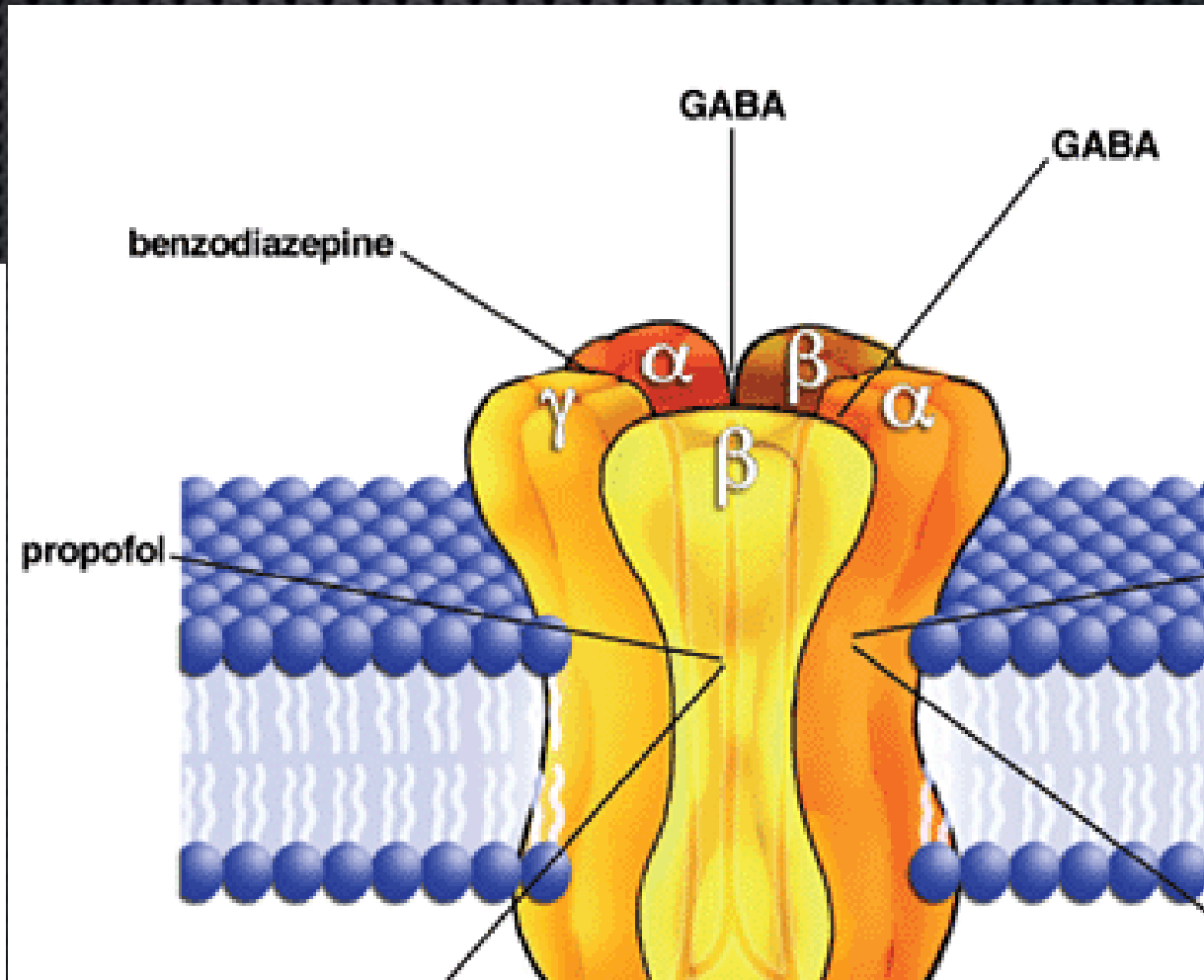
...and others

enzodiazepines

Receptor mediated

GABA receptor





lidazolam

Uses:

- Anti-convulsant
- Sedation and hypnosis
- Anxiolysis
- Antegrade amnesia
- Muscle Relaxation

lidazolam

Most suited for critcially ill

V, IM, IN, etc

apid predictable onset

(not fast enough for Induction)

Sedation (45 min - 1 hr)

lidazolam

- Water soluble
- One compartment model
- Highly protein bound
- $t_{1/2}$ = 3-6 hrs
- Metabolized by liver

lidazolam

Provides safe sedation

Doses for sedation:

- 0.1 - 0.2 mg/kg

Very freqently underdosed

NOT a god induction agent

ONLY provides sedation/amnesia

- No analgesia

lidazolam / Fentanyl

requently combined

ery dangerous in hypovolemic pts

Causes Hypotension

VERY DANGEROUS IN HEAD INJURED PATIENTS!!!!!!

THERE ARE BETTER OPTIONS

The Equation:

- cbf = map - icp

gents

Etomidate

Propofol

Benzodizepines

Opiates

Ketamine

Barbiturates

piates

- Morphine
- Opium
- Hydromorphone
- Fentanyl
- Sufentanyl

piates

- ery important class
- ain medication
- nesthetic
- ntitussives, antidepressants

piates

Discovered” in 1552

Popularized in 1804

Heroin in 1900

Crimialized in 1914

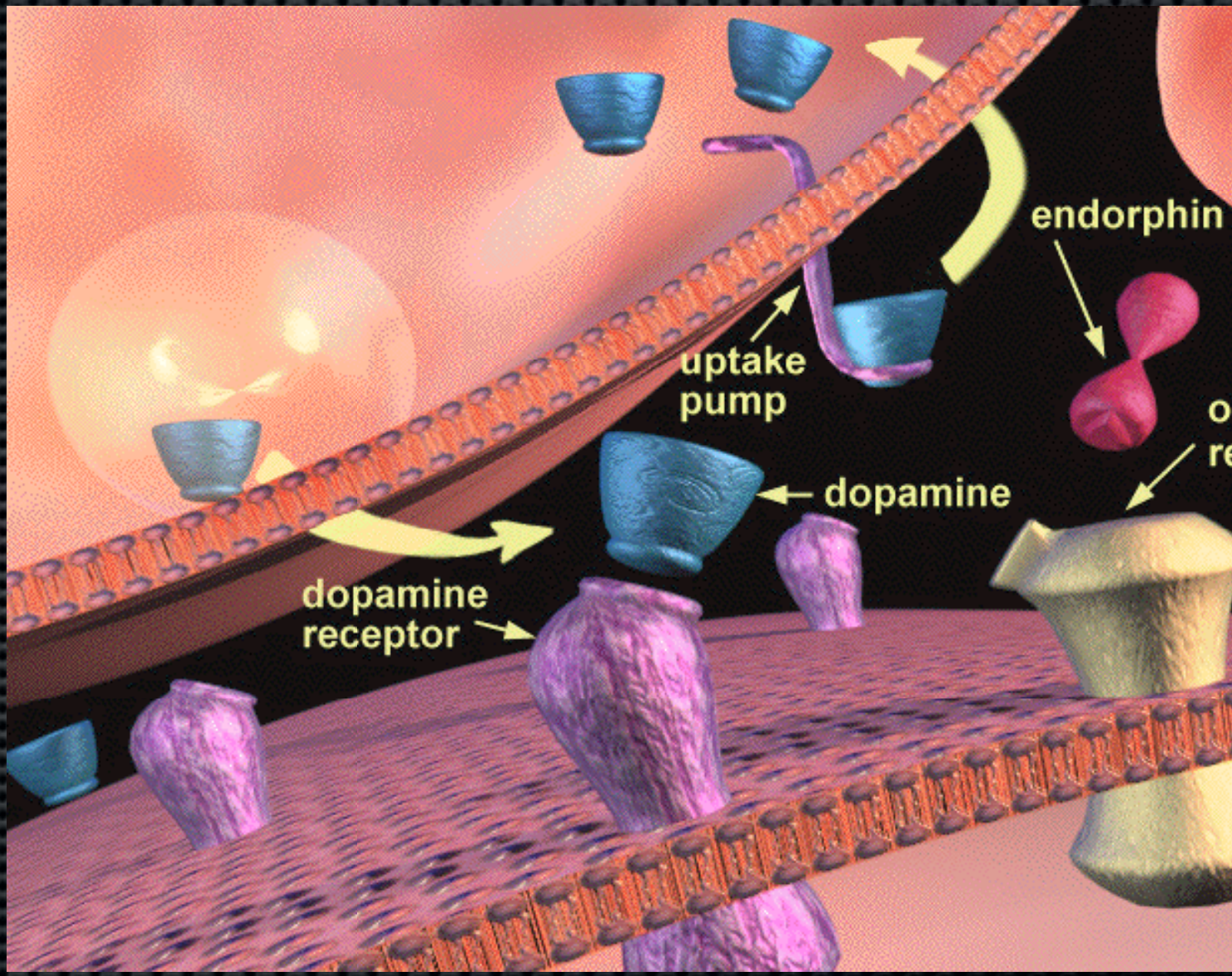
c. 1910

piates

Recpetor

nediated

rugs”



piates

elta - recpetors

- peripheral neurons
- analgesia
- antidepressant
- dependancy

piates

appa - recpetors

- brain
- spinal cord
- sedaiton
- miosis
- dysphoria

piates

u - Receptors

- brain
- spinal cord
- peripheral neruons
- intestinal tract
- analgesia
- dependance
- euphoria

piates

Nociceptin - Receptor

- Brain
- spinal cord
- anxiety
- depression
- appetite
- tolerance

entanyl

Sublimaze

Very Lipophilic

First pass effect in lungs

entanyl

Blood pressure may decline

Hemodynamically stable Agent

Dangerous in combination w/ Benzodiazepines

- TBI, Volume depleted, etoh
- THE EQUATION

entanyl

Pain 0.5 - 1.5 mcg/kg

Can cause apena in some people

Sedation 5-7 mcg/kg

Anesthesia 10-40 mcg/kg

ummary

- Can be used for sedation
- Not rapid enough For RSI
- Large role in pain
- Caution w/ other sedative
  - Except ketamine

gents

Etomidate

Propofol

Benzodizepines

Opiates

Ketamine

Barbiturates

etamine

Class: Phencyclidine

Conger: Ketamine

Developed in Mid 60’s

Used in Vietnam

Popular in 70’s

Sometimes sold as Ecstasy

“Special K”

etamine

MDA Receptor Antagonist (dissociates brain form
inal cord)Hallucinogenic Dissociative
esthesiaBinds to μ receptors (higher
ses)hyperdynamic effects

etamine

How does it work?

- Separates the mid-brain from the cortex
- Disorganizes the brain
- Lower brain controls vital functions and is stimulated by Ketamine => excitation
- Occupies opiate receptor

etamine

Pharmacokinetics:

- IV/PO/IM
- Lipid soluble (two compartments)
- Hepatic Metabolism
- 3 hour half life (20-40min duration of action)
- Two compartment model
- Hepatic clearance

etamine

nduction:

- 2-4 mg/kg IV (quickly)
- 4 mg/kg IM

Sedation

- 2mg/kg IV (slowly) or IM

etamine

Dosing: Pain adjunct

0.1 mg/kg IV increments to effect

etamine

Physiologic effects

- Increased CBF out of proportion to CNS metabolic needs
- Sympathetic tone
- Respiratory drive is reduced but ventilation persists (descriptions of apnea at higher does)
- Betsy's case

etamine

Physiologic Effects

- Smooth muscle relaxant => bronchodilitation
- ⇓ peak pressures
- ⇑ HR, MAP, Contractility ∴ MVO2 (1st dose)
- Subsequent doses do not further ⇑ sympathetic tone

etamine

dvantages

- No hypotension
- Continues to ventilate (usually)
- Can combine benzo’s or opiates (dose sparing)
- Anesthesia, Sedation and/or analgesia
- IM/IV/PO/PR

etamine

Emergence Reaction

- Vivid dreams (stronger w/ PCP)
- More common in adults
- Benzo's reduce frequency and severity

Hypersalivation / Laryngospasm

Resp sedation in higher doses (rapidly given)

etamine - cautions

- Caution with Cardiac disease
- Caution with Psychiatrically Ill
- Pregnancy
- Early in pregnancy can increase uterine pressures and cause contractions
- Does not have FDA pregnancy classification
- Laryngospasm

etamine - ideal uses

- nduction for trauma or sepsis
- Post intubation Sedation
- Smoother transition from induction to sedation
- Head Injury – particularly multi-trauma
- Procedural sedation
- Acute bronchospasm
- Pain out of control
- Agitated delirium (maybe)

gents

Etomidate

Propofol

Benzodizepines

Opiates

Ketamine

Barbiturates

arbiturates

Pentobarbitol

Thiopental

Methohexitol

arbiturates

Lipid soluble

Open chloride channels

Can produce “flat eeg”

- (propofol, etomidate)

arbiturates

Prone to cause hypotension

Limited or No EMS role

SI Pharmacology

nduction & Sedation

Paralytics

euromuscular Blockers

Succinyl Choline

Rocuronium

Vecuronium

Atracurium

urarie

- The poison arrow
- South american hunters
- Sir Walter Raleigh
- ery important to science
- rtificial ventilation

euromuscular Blockers

Blocks the neuromuscular junction

at the muscle cell itself

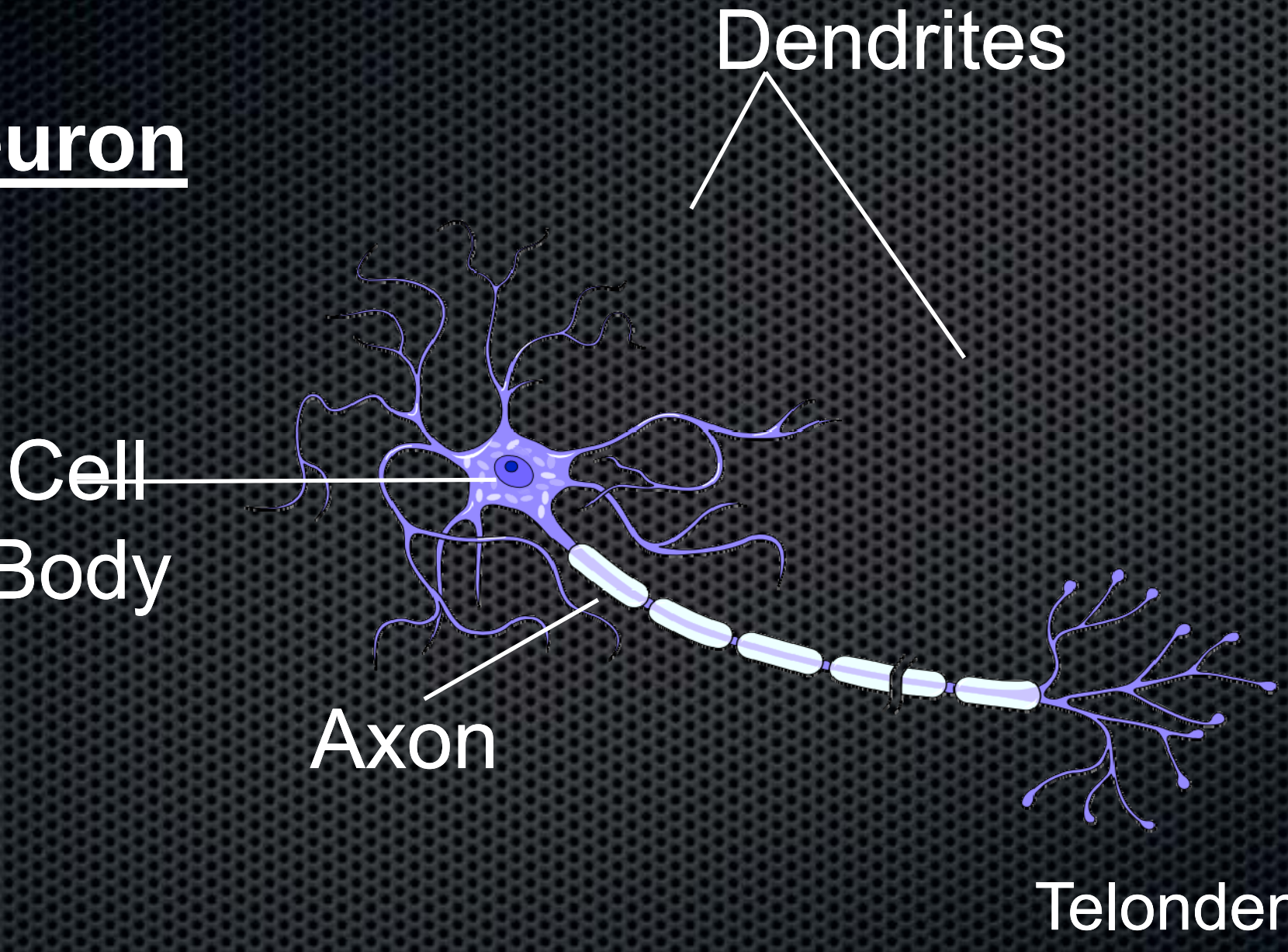
Acetycholine is the transmitter

Acetylcholinesterase breaks down Ach

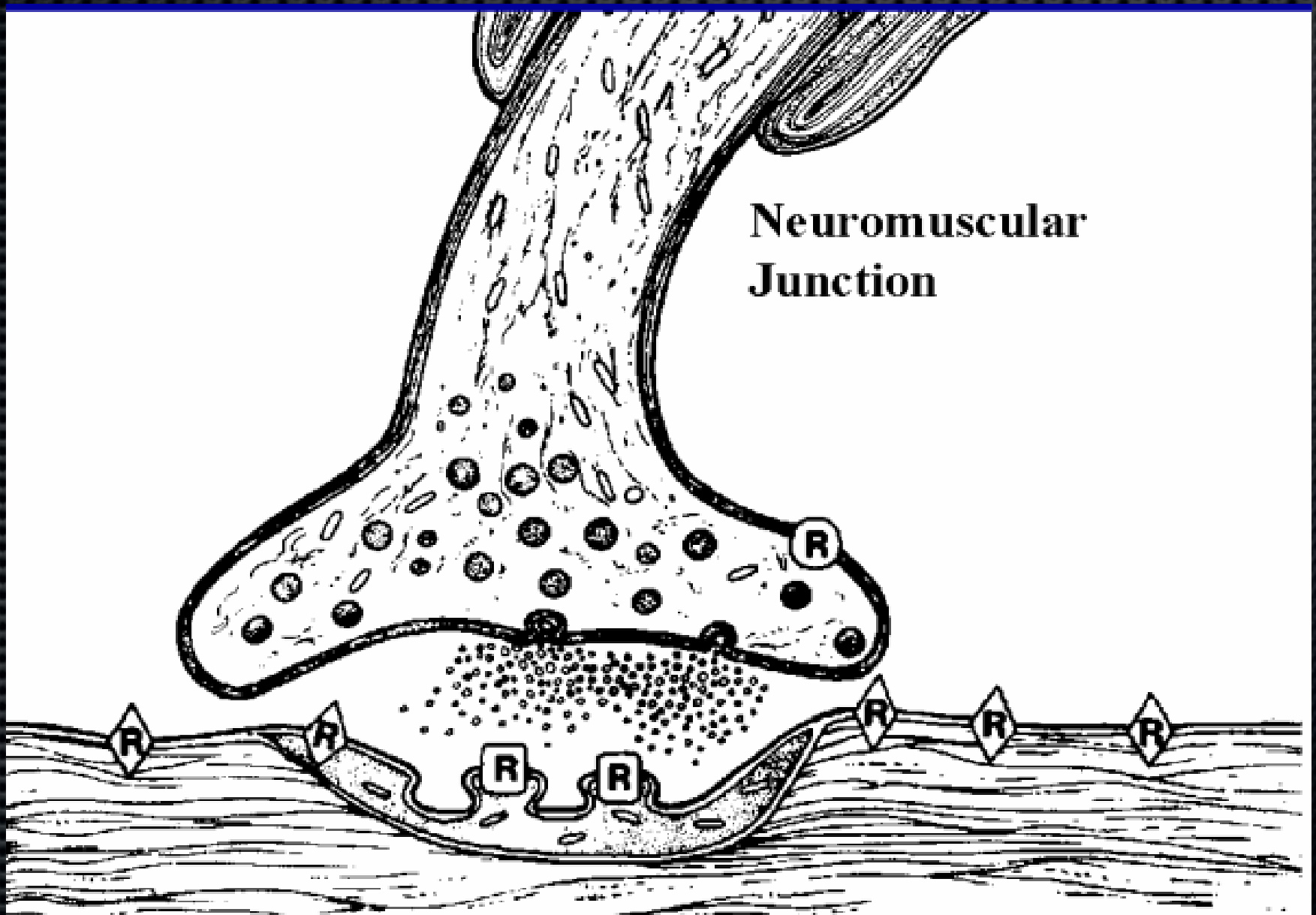
- Neostigmine & Organophosphates

euromuscular Blockers

uron



euromuscular Junction



uccinylcholine

Sux for short

<u>Depolarizing agent</u>

- Causes stimulation at the ACh receptor
- 2 phase action
  - Stimulation
  - Relaxation
- Very fast onset

uccinylcholine

Dose: 1 - 1.5 mg/ kg

Onset 30 seconds

Push quickly, precede with anesthetic

uccinylcholine

ADVERSE REACTIONS

yperkalemia (K

- neuromuscular disease
- Paralysed
- subacute burns
- Rhabdomyolosys
- Acute Kidney Injury

uccinylcholine

dvantages:

- Fast onset
- Short duration of action

Disadvantages:

- Risk of hyperkalemia and death

on-Depolarizing Agents

Rocuronium

Vecuronium

Atracurium

ocuronium

astest of the ndpa's

5 second onset

.5 -1.5 mg/kg (higher for RSI)

ntubating conditions in 60 sec

sux is faster

ocuronium

Pharmacokinetics

- Two Compartment Model
- Hepatic metabolism
- Biliary and renal clearance
- 20-40 min duration 1st dose
- 20 min (0.5mg/kg) subesquent dose

ocuronium

Cautions:

- Pregnacy Category C
- Liver and renal disease

ecuronium

-4 min onset

epatic/renal/hoffman

0 min with typical dose

tracurium

Similar to Vecuronium

Hoffman

Questions? Comments?