1. Proposed Algorithm

Pre-Medication
• None

Induction Agent
• Etomidate 0.3 mg/kg IV
• Ketamine 1-2 mg/kg IV
• Midazolam 0.3 mg/kg IV (not preferred)

Paralytic
• Rocuronium 1-2 mg/kg IV
• Succinylcholine 1.5-2 mg/kg IV. No defasiculating doses.
• Vecuronium 0.1mg/kg IV (not preferred)
• Continued paralysis: Vecuronium 0.15-0.2 mg/kg bolus, initiate at 0.05 mg/kg/h or 0.1 mg/kg q1h PRN

Analgesia
• Morphine 0.1 mg/kg IV, initiate continuous infusion at 10-30 mcg/kg/hr
• Fentanyl 1-5 mcg/kg IV, initiate continuous infusion at 0.5-2 mcg/kg/hr

Sedation
• Midazolam IV boluses 0.05-0.2 mg/kg, infusion as needed

2. Clinical Evidence/Reasoning:

Pre-Medication: Atropine

This algorithm does not currently recommend the empiric administration of atropine as an antisialalagogue in the process of RSI due to the long onset of action (30-60 minutes).

This algorithm does not currently recommend the empiric administration of atropine for prophylaxis against bradycardia associated with succinylcholine administration and/or the process of the intubation itself. A retrospective review done by Fastle et al in 2004 looked at 143 pediatric patients ages 3 months to 19 years (median 12 months) who received laryngoscopy or
tracheal intubation in the pediatric emergency department. Sixty-eight of these patients received pre-medication with atropine, while the rest did not. The comparison between the atropine and control group found no difference in number of laryngoscopic or tracheal intubation attempts or bradycardic events. However, the atropine group had a higher incidence of hypoxic events (28% vs. 16%, p=0.046). Of note, succinylcholine was used in 16 of 143 patients and there were no findings of bradycardia.

Pre-Medication: Lidocaine
At this time, the use of lidocaine as a pre-medication to blunt increase in intracranial pressure (ICP) is not recommended due to the lack of evidence supporting its use in rapid sequence intubation (RSI). There is only 1 human trial that evaluates the use of intravenous (IV) lidocaine on ICP during endotracheal intubation. This study done by Bedford et al evaluated the potential benefit of IV lidocaine at 1.5 mg/kg compared to placebo 2 minutes before endotracheal intubation in 20 patients undergoing elective neurosurgery for cerebral neoplasm. Patients in both groups experienced a transient increase in ICP, but the group pre-treated with IV lidocaine experienced a mean increase in ICP that was 12 mmHg less compared to the placebo group (P <0.05). Limitations of this study include the location of intubation (the operating room) and the other medications used for RSI (induction agent thiopentone, paralytic succinylcholine), which restricting the external validity of this trial for the current ED population. Subsequent reviews that showed an association between lidocaine and decreased ICP were limited to patients who were already intubated, not undergoing RSI. In addition, none of the aforementioned studies attempted to correlate the lowering of ICP with lidocaine and outcomes. A systemic review done by Robinson and Clancy did not find any publication that supported the proposal that in traumatic brain injury (TBI) treatment with lidocaine before RSI reduces ICP or improves neurological outcome.

Induction Agent: Etomidate
Etomidate is recommended at a dose of 0.3 mg/kg IV (may be capped at 20 mg based on physician preference or dose reduced to 0.15 mg/kg in hemodynamically unstable patients). Its fast onset of 10-15 seconds, short duration of 5-10 minutes, and its ability to enhance the effects of GABA without compromising respiratory or cardiovascular drive makes it an ideal induction agent.

At this time, a diagnosis of sepsis is not considered an absolute contraindication to the use of etomidate. There is no question that etomidate reversibly inhibits 11-beta hydroxylase and 17-alpha-hydroxylase resulting in decreased cortisol synthesis for up to 72 hours, the clinical significance of this inhibition is unclear. A multitude of studies have looked at 28-day mortality, length of hospital and ICU stay, vasopressor requirements with etomidate vs. placebo or other induction agents with mixed results. The biggest proponent of the negative effects of

\[^3\] Donegan MF, Bedford RF. Intravenously administered lidocaine prevents intracranial hypertension during endotracheal suctioning. Anesthesiology. 1980;52:516-518.
etomidate on mortality is the CORTICUS trial that found in a post-hoc analysis that patients who received etomidate before randomization had approximately a 13 and 10% increase in mortality in the hydrocortisone and placebo arms respectively. However, CORTICUS only compared the mortality rate of etomidate vs. non-etomidate. It did not compare etomidate vs. other induction agents. Studies that have looked at etomidate vs. other induction agents such as midazolam and ketamine have not found a statistically significant difference in mortality. These conclusions have remained consistent in the pediatric population. Two retrospective reviews of pediatric patients (<10 years old) found no evidence of clinically significant adrenal suppression and minimal evidence of hemodynamic instability. In one of the studies, 4 patients experienced a hypotensive episode defined as a decrease in blood pressure to below one standard deviation of mean normal for age that were attributed to known trauma or unknown causes. While sepsis is not considered an absolute contraindication to the use of etomidate in RSI, providers may want to consider other induction agents such as ketamine in patients with severe sepsis and/or septic shock.

Of note, etomidate may lower the threshold for focal seizures in vulnerable pediatric populations. In a retrospective review done by Guldner et al, 4 patients who receive etomidate for RSI developed seizures after admission. All of these patients had come to the ED with a chief compliant of seizures or had a history of seizure disorder. The clinical significance of these findings is still unclear.

Induction Agent: Ketamine

Ketamine is a recommended induction agent at a dose of 1-2 mg/kg IV. It provides rapid analgesia, sedation, and amnesia while having limited suppression of respiratory drive. Ketamine should be considered first line in patients experiencing shock or asthma/chronic obstructive pulmonary disorder (COPD) exacerbations due its ability to induce endogenous release of catecholamines, increasing heart rate, blood pressure, and bronchodilation. It may also be considered as an induction agent in status epilepticus patients due to its mechanism of action as an NMDA antagonist. Multiple case series and studies have provided evidence of ketamine’s role in the management of benzodiazepine refractory status epilepticus.

Concerns regarding ketamine induced intracranial pressure elevations have previously limited its use.\textsuperscript{22,23} Jabre et al completed a large randomized, controlled trial that compared induction dose of ketamine vs. etomidate in a undifferentiated critically ill patient population who underwent RSI in the pre-hospital or ED setting.\textsuperscript{14} Of the 469 patients analyzed in the study, 104 (22\%) had a final diagnosis of trauma. No differences were found in the mean maximum SOFA score, intubation difficulty, or 28-day mortality. Several literature reviews looking at ketamine boluses and infusions in patients with neurological pathophysiology (traumatic and non-traumatic) have found that ketamine has minimal effect on ICP when ventilation is appropriately managed.\textsuperscript{14,24,25,26}

**Induction Agent: Midazolam**

Midazolam is considered a poor induction agent in this algorithm due to its slow onset, variable effectiveness, and the availability of other more reliable agents. In order to achieve optimal intubating conditions in a timely manner, high doses of midazolam, at a minimum of 0.3 mg/kg, are required. It should be noted that Solonen et al found inconsistent induction of pediatric patients at doses of 0.6 mg/kg during anesthesia.\textsuperscript{27} The selection of an absolute dose over a weight base dose should be avoided. In the ED, Sagarin et al showed that 56\% of children received less than 0.1 mg/kg of midazolam as a sole induction agent before emergent endotracheal intubation (mean dose of 0.08 mg/kg, 95\% CI 0.06 to 0.10 mg/kg).\textsuperscript{28} The mean age of children who were underdosed was 13.6 years, compared to the mean age of children who were adequately dosed was 2.9 years (P = 0.0005), indicating the selection of an absolute dose over weight based.

**Paralytic: Rocuronium**

Rocuronium is a recommended paralytic at a dose of 1-2 mg/kg and has an onset of 45 seconds, duration of 30-40 minutes, and minimal contraindications/adverse effects.

Rocuronium has been found to provide optimal intubating conditions (equivalent to succinylcholine) when dosed appropriately at 1-2 mg/kg.\textsuperscript{29,30,31} In the 2008 Cochrane review meta-analysis, an a-priori subgroup analysis was established look at the outcome of excellent intubating conditions with various doses of rocuronium (0.6, 0.9 or 1.2 mg/kg).\textsuperscript{23} Thirty-seven randomized trials were analyzed, with a total of 1409 patients in the rocuronium and 1281 in the succinylcholine groups. In the primary outcome of excellent intubation conditions, there was a statistically significant risk ratio that favored succinylcholine vs. rocuronium (RR 0.86, 95\% CI 0.8-0.92). This continued to be true in the a-priori subgroup when looking at rocuronium doses of 0.6-0.7 mg/kg (RR 0.81, 95\% CI 0.73-0.9). However, there was no statistically significant difference for excellent or acceptable intubating conditions in the group that received 0.9-1 mg/kg or 1.2 mg/kg of rocuronium (RR 0.96. 95\% CI 0.89-1.02). Patanwala et al performed a

retrospective analysis on a prospectively collected RSI data set in patients who received succinylcholine (n=113) vs. rocuronium (n=214). Both groups had 100% intubation success with no need for surgical airway, there was no difference in first intubation success (roc 72.9% vs. such 72.6%, p=1.00), and median # of attempts required (roc vs. such 1, p=0.87). The median dose of rocuronium was 1.19 mg/kg (IQR 1-1.45 mg/kg) vs. succinylcholine 1.65 mg/kg (IQR 1.26-1.95 mg/kg).

Rocuronium’s dose dependent effect remains consistent in the pediatric population. A prospective, randomized controlled trial of 120 children (1-10 years old) showed that rocuronium at doses of 0.9 mg/kg had similar excellent intubating conditions to succinylcholine 1.5 mg/kg, while doses of 0.6 mg/kg of rocuronium were considered inadequate. Paralytic: Succinylcholine

Succinylcholine, a depolarizing neuromuscular blocker, at 1.5-2 mg/kg IV should be used when a shorter acting paralytic (<10 minutes) is preferred and no contraindications to succinylcholine exist (history of malignant hyperthermia, risk factors for acute hyperkalemia, extensive denervation of skeletal muscle or upper motor neuron injury). When prolonged paralysis is required, re-dosing of succinylcholine is generally discouraged due to the possibility of a phase 2-muscle blockade.

Paralytic: Defasciculating Doses of Paralytics

This algorithm does not recommend defasciculating doses of non-depolarizing paralytics before the use of succinylcholine to mediate increases in IOP and ICP. There is no definitive evidence that a defasciculating dose of non-depolarizing muscular blocker negates fasciulations or the possible rises in intraocular pressure (IOP) and ICP after the administration of succinylcholine. Risks include premature apnea and prolonged muscle blockade.

Paralytic: Vecuronium

Vecuronium, a non-depolarizing neuromuscular blocker, at 0.1 mg/kg is an additional paralytic that may be used for RSI in the cases of succinylcholine and rocuronium shortage. Vecuronium is not a preferred paralytic for RSI due to its long onset of action (90-120 seconds) and duration of 25-40 minutes. In order to obtain a true RSI onset of approximately 60 seconds a dose of 0.3 mg/kg is recommended, but the duration is prolonged at 2 hours. The vial must be reconstituted with sterile water for injection.

Paralytic: Continuous Paralysis with Vecuronium

Continuous infusion or intermittent vecuronium may be used safely for continued paralysis after RSI to facilitate mechanical ventilation in pediatric patients.\textsuperscript{36,37} Of note, a short term study comparing continuous infusion vs. intermittent vecuronium in 12 pediatric patients (mean age 35.5 months, range 3 weeks to 13.5 years) found that despite clinically being equivalent, the total amount of vecuronium used in each method was significantly lower in the continuous infusion at 0.79 +/- 0.44 mg/kg/12 hrs than for hourly boluses 1.34 +/- 0.4 mg/kg/12h, P<0.01).\textsuperscript{36}

**Analgesia + Sedation:**

It is recommended that analgesia with morphine or fentanyl boluses and continuous infusion be initiated first in order to minimize benzodiazepine requirements.

**Route of Administration: Intramuscular**

When the intravenous and the intraosseous route are not available, specific induction and paralytic agents may be administered via the intramuscular (IM) route at increased doses. These include:

- Ketamine: 4 mg/kg IM
- Succinylcholine: 4 mg/kg IM

Of note, the onset of action of these drugs IM is 2-3 minutes. The onset and duration may be prolonged in those who are hemodynamically unstable. Medications should be administered in the anterolateral thigh to facilitate the fastest onset possible.