Induction agents for rapid sequence intubation in adults outside the operating room

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INTRODUCTION — The first task of any clinician managing an acutely unstable patient is to secure the airway. In most circumstances, emergency clinicians use rapid sequence intubation (RSI) to accomplish this task. RSI incorporates a rapidly acting sedative (ie, induction) agent, in addition to a neuromuscular blocking (ie, paralytic) agent, to create optimal intubating conditions. Selection of the sedative agent and dose most appropriate for the clinical scenario is an important component of RSI.

The pharmacology and selection of induction agents for use in emergency RSI outside of the operating theater will be reviewed here. The techniques and other medications used in the performance of RSI, as well as other aspects of airway management, are discussed separately. (See "Rapid sequence intubation for adults outside the operating room" and "Rapid sequence intubation (RSI) outside the operating room in children: Approach" and "Neuromuscular blocking agents (NMBAs) for rapid sequence intubation in adults outside of the operating room" and "Pretreatment medications for rapid sequence intubation in adults outside the operating room".)

RAPID SEQUENCE INTUBATION — Rapid sequence intubation (RSI) is the standard of care in emergency airway management for intubations not anticipated to be difficult [1-4]. RSI is the virtually simultaneous administration of a sedative and a neuromuscular blocking agent to render a patient rapidly unconscious and flaccid in order to facilitate emergency endotracheal intubation and to minimize the risk of aspiration. Multiple studies confirm the high-success rate of RSI using the combination of a sedative and a paralytic drug [2-4]. (See "Rapid sequence intubation for adults outside the operating room" and "Neuromuscular blocking agents (NMBAs) for rapid sequence intubation in adults outside of the operating room" and "Rapid sequence intubation (RSI) outside the operating room in children: Approach".)

INDUCTION AGENTS

Overview — Induction agents (sedatives) are integral to the performance of rapid sequence intubation (RSI) [5]. They provide amnesia, blunt sympathetic responses, and can improve intubating conditions.

When a paralytic agent is used for intubation without sedation, the patient may be fully aware of his or her environment, including pain, but unable to respond [6-9]. In addition to its inhumanity, this circumstance allows for potentially adverse physiologic responses to airway manipulation, including tachycardia, hypertension, and elevated intracranial pressure (ICP) [10]. Sedative use prevents or minimizes these effects. Furthermore, clinicians can sometimes select an induction agent that both facilitates RSI and ameliorates the patient's underlying condition. As an example, ketamine can be used in severe asthma to reduce bronchospasm [11].

Use of sedatives may also improve the laryngoscopic view obtained during RSI [5,12,13]. During RSI, the clinician must perform laryngoscopy during the earliest phase of neuromuscular paralysis. Sedatives improve laryngoscopy in part by supplementing the yet incomplete relaxation provided by the paralytic. Even in the presence of a full neuromuscular blocking dose of a paralytic, the addition of a sedative improves intubating conditions during RSI [5].

Each of the major induction agents in common use is discussed below (table 1).

Etomidate

General use — Etomidate is an imidazole-derived, sedative-hypnotic agent that is frequently used for RSI. Etomidate acts directly on the gamma amino butyric acid (GABA) receptor complex, blocking neuroexcitation and producing anesthesia. For RSI, etomidate is given by intravenous push in a dose of 0.3 mg/kg, with a time to effect of 15 to 45 seconds and a duration of action of 3 to 12 minutes [14]. It is the most hemodynamically neutral of the sedative agents used for RSI, and does not stimulate histamine release [15-21].

Etomidate provides no analgesic effect, so it does not blunt the noxious stimulation of the upper airway during laryngoscopy and intubation. For patients in whom this is a concern (eg, patients with cardiovascular disease or elevated intracranial pressure), an opioid analgesic, such as fentanyl, is often given during the pretreatment phase of RSI [22]. (See "Pretreatment medications for rapid sequence intubation in adults outside the operating room".)

The hemodynamic stability associated with etomidate makes it a particularly useful medication for the intubation of hypotensive patients, as well as for patients with intracranial pathology, when hypotension must be avoided [15-19,21]. Etomidate causes a mild increase in airway resistance, but may be used in patients with bronchospasm [23].

Concerns with etomidate include adrenal suppression, myoclonus, and evidence of regional cerebral excitation (determined by electroencephalogram) after intubation [18,24,25]. Myoclonus has been misidentified as seizure activity, leading to incorrect recommendations that etomidate be avoided in patients with seizure disorders. Myoclonus during RSI is brief and minimal, because of the concomitant administration of a paralytic agent, and of no clinical significance. Etomidate decreases cerebral blood flow and cerebral metabolic oxygen demand, while preserving cerebral perfusion pressure [21]. Postintubation sedation with propofol or a benzodiazepine helps to prevent neuroexcitation.

Adrenocortical suppression — The major controversy surrounding etomidate stems from the reversible adrenocortical suppression associated with its use. The evidence surrounding this issue is reviewed separately. (See "General anesthesia: Intravenous induction agents", section on 'Etomidate'.)

Etomidate is a reversible inhibitor of 11-beta-hydroxylase, which converts 11-deoxycortisol to cortisol (figure 1). (See "Adrenal steroid biosynthesis".) A single dose of etomidate causes a transient but measurable decrease in the level of circulating cortisol that occurs in response to the administration of exogenous ACTH, although cortisol levels do not fall below the normal physiologic range. This effect does not persist beyond 12 to 24 hours.

We recognize the critical importance of maintaining adequate blood pressure early in the treatment of sepsis and, pending more definitive studies, we believe that etomidate is an acceptable induction agent for patients with severe sepsis. Etomidate has the advantages of hemodynamic stability, when compared with most other sedative or induction agents, and familiarity because of its widespread use for RSI outside the operating room. When intubating the critically ill patient with possible adrenal insufficiency, the clinician must weigh the theoretical risk of cortisol suppression against the hemodynamic instability that may be caused by alternative induction agents.

Etomidate should **NOT** be used as an infusion or in repeated bolus doses for maintenance of sedation after intubation. Emergency clinicians should inform the physicians assuming care for the patient in the intensive care unit or operating suite if etomidate has been used for induction. If ACTH stimulation testing is being considered, clinicians should be aware that the results may be affected by prior administration of etomidate. (See "Evaluation and management of suspected sepsis and septic shock in adults".)

Some authors recommend the use of empiric glucocorticoids for the first 24 hours after a dose of etomidate in patients with sepsis, but this approach lacks support from outcome studies [26,27]. We suggest that patients with sepsis who receive etomidate for RSI also receive a single dose of glucocorticoid (eg, hydrocortisone 100 mg IV) **only** if they manifest hypotension that is refractory to treatment with aggressive fluid resuscitation and a vasopressor. This approach is consistent with that used for patients who do not receive etomidate. A discussion of the role of glucocorticoids in septic shock is discussed separately. (See "Glucocorticoid therapy in septic shock".)

Benzodiazepines — Benzodiazepines cause sedation and amnesia through their effects on the gamma amino butyric acid (GABA) receptor complex. Midazolam is the most rapidly acting benzodiazepine commonly used for RSI [28,29]. The induction dose for midazolam is 0.1 to 0.3 mg/kg IV push, with a time to effect of approximately 30 to 60 seconds, and a duration of action of 15 to 30 minutes [28,29].

Like all benzodiazepines, midazolam does not provide analgesia but does possess anticonvulsant effects, making it an effective agent for RSI in patients with status epilepticus.

The routine induction dose of midazolam for RSI is 0.2 mg/kg. In this dose, midazolam causes moderate hypotension, with an average drop in mean arterial blood pressure in healthy patients of 10 to 25 percent [28,29]. This tendency to induce hypotension limits midazolam's usefulness in the setting of hypovolemia or shock. If midazolam must be used in such patients, we suggest a dose of 0.1 mg/kg, which will somewhat delay the speed of onset and decrease the depth of sedation achieved, but should not severely compromise intubating conditions. For patients in shock, we suggest etomidate or ketamine because of their superior hemodynamic profiles. (See 'Etomidate' above and 'Ketamine' below.)

Midazolam is frequently underdosed (common dose 0.05 mg/kg) when used for emergency department RSI [30]. Midazolam is often used for procedural sedation in much smaller doses than are required for RSI, which may contribute to underdosing [29].

Midazolam can be used as an infusion for long-term sedation. Doses of 0.05 to 0.4 mg/kg per hour IV have been shown to be safe and effective in critically ill neonates and children [31,32], including neonates undergoing extracorporeal membrane oxygenation [33]. Dosing in intubated adults should be titrated to an endpoint of adequate sedation, preferably using a sedation scale.

Lorazepam and diazepam are benzodiazepines used frequently for long-term sedation following intubation, but are not recommended for RSI. Both require propylene glycol as a diluent, and there are reports of propylene glycol toxicity associated with long-term infusions [34]. (See "Sedative-analgesic medications in critically ill adults: Properties, dosage regimens, and adverse effects", section on 'Benzodiazepines'.)

Ketamine

General use — Ketamine is a dissociative anesthetic agent, structurally similar to phencyclidine (PCP). It is unique among sedative agents in that it provides analgesia along with its amnestic and sedative effects. Ketamine is given intravenously in doses of 1 to 2 mg/kg, with a time to effect of 45 to 60 seconds, and a duration of action of 10 to 20 minutes.

Ketamine acts at many receptors causing a range of effects. It is thought to stimulate the N-methyl-D-aspartate receptor at the GABA receptor complex, causing neuroinhibition and anesthesia. It excites opioid receptors within the insular cortex, putamen, and thalamus, producing analgesia [35,36]. It stimulates catecholamine receptors and release of catecholamines leading to increases in heart rate, contractility, mean arterial pressure, and cerebral blood flow [35,37-39]. Ketamine decreases the production of vascular nitric oxide, diminishing its vasodilatory effect [40], and inhibits nicotinic acetylcholine receptors [41].

Ketamine preserves respiratory drive and has both a quick onset of action and analgesic properties. This makes it a good choice for "awake" intubation attempts, when laryngoscopy is performed on a patient who is moderately sedated and topically anesthetized but not paralyzed due to concerns about a difficult airway (see 'Conditions precluding use of a paralytic' below).

Ketamine causes sympathetic stimulation, and is among the most hemodynamically stable of all of the available sedative induction agents, making it an attractive choice for hypotensive patients requiring RSI [37,38]. However, according to limited observational evidence and clinical experience, patients who are depleted of catecholamines due to their underlying disease or otherwise at increased risk of shock have a blunted sympathetic response, and may even develop hypotension, following administration of ketamine for RSI [42].

Theoretically, ketamine causes bronchodilation by stimulating the release of catecholamines. Limited evidence from animal studies suggests the drug may also have direct bronchodilatory effects. Although definitive evidence is lacking, many clinicians use ketamine as an induction agent in severe asthmatics needing RSI. Use of ketamine infusions in subanesthetic doses during asthma exacerbations provides no additional benefit compared with standard therapy [39]. Case reports suggest larger doses may be needed [11].

Ketamine appears to have beneficial effects on stunned myocardium in vitro [38]. When used prior to myocardial oxygen deprivation, ketamine resulted in better recovery after reperfusion. Contractility may also improve with ketamine use [37]. Clinicians must weigh ketamine's potential cardiovascular benefits against its potential to induce cardiac ischemia in patients with significant coronary disease.

The reemergence phenomenon, in which patients experience disturbing dreams as they emerge from ketamine-induced anesthesia, limits use of the drug for procedural sedation or elective anesthesia in adult patients. Reemergence phenomena are of less concern when ketamine is used for RSI, after which the patient is generally sedated with benzodiazepines for a substantial period. One study found that while dreams occurred frequently following sedative doses of ketamine, they were generally pleasant, and the frequency of reemergence phenomena and delirium was markedly reduced by concomitant use of a benzodiazepine [43].

Elevated intracranial pressure — Controversy persists regarding the use of ketamine in patients with a head injury due to concerns about elevating intracranial pressure (ICP). Opponents emphasize that ketamine can cause a rise in ICP through sympathetic stimulation, potentially exacerbating the condition of such patients [44,45]. However, when ketamine is used with a GABA agonist, this rise in ICP may not occur [46,47]. Furthermore, by increasing cerebral perfusion, ketamine may benefit patients with a neurologic injury [35,46].

On balance, evidence suggesting ketamine elevates ICP is weak, and evidence that harm might ensue is weaker. We believe ketamine is an appropriate induction agent for RSI in patients with suspected ICP elevation and normal blood pressure or hypotension [48,49]. In patients with hypertension and suspected ICP elevation, ketamine should be avoided because of its tendency to further elevate blood pressure.

The best available evidence about this issue comes from a systematic review of 10 trials involving 953 critically ill patients, all managed with intubation and mechanical ventilation, which concluded that the use of intravenous ketamine did not adversely affect patient outcomes, including mortality and neurologic outcome [50]. Although most trials included in the review had methodological limitations, two randomized, double-blinded trials comparing the effects of prolonged ketamine and sufentanil infusions found no difference in the mean daily intracranial pressure and cerebral perfusion pressure of patients, all of whom had sustained traumatic brain injury.

Other studies suggest ketamine does not interfere with cerebral metabolism; it does not increase cerebral oxygen consumption and does not reduce regional glucose metabolism [35,51,52]. Ketamine can also offset any decrease in mean arterial pressure caused by fentanyl, a drug commonly used as part of RSI in patients with a head injury [53].

Propofol — Propofol is a highly lipid-soluble, alkylphenol derivative that acts at the GABA receptor causing sedation and amnesia. Sedation occurs through direct suppression of brain activity, while amnesia appears to result from interference with long-term memory creation [54,55]. Induction doses of 1.5 to 3 mg/kg IV can be used, with a time to effect of approximately 15 to 45 seconds, and a duration of action of 5 to 10 minutes. Propofol does not provide analgesia. In addition to its use for RSI, propofol is used for long-term sedation in critically ill patients, sedation for brief procedures, and induction of anesthesia, all of which are discussed separately. (See "Sedative-analgesic medications in critically ill adults: Properties, dosage regimens, and adverse effects", section on 'Propofol' and "Procedural sedation in adults outside the operating room", section on 'Propofol' and "General anesthesia: Intravenous induction agents", section on 'Propofol'.)

The pharmacokinetic properties of propofol do not appear to differ among races or between genders [56,57], but children appear to have a slightly longer time to peak serum concentration [58].

Propofol reduces airway resistance and can be a useful induction agent for patients with bronchospasm undergoing RSI [23,59,60]. Its neuroinhibitory effects make propofol a good induction agent for patients with intracranial pathology, provided they are hemodynamically stable. Propofol suppresses sympathetic activity, causing myocardial depression and peripheral vasodilation [61-64]. A decrease in mean arterial pressure (MAP) caused by propofol can reduce cerebral perfusion pressure, thereby exacerbating a neurologic injury [65]. The usual decrease in MAP is approximately 10 mmHg [66].

Propofol does not prolong the QT interval, unlike some other anesthetic agents [67,68]. Serum triglycerides and serum lipase rise during propofol infusions [69]. Although the manufacturer lists egg or soybean allergies as contraindications to the use of propofol, significant allergic reactions to the newer preparation of the drug appear to be rare. (See "Perioperative anaphylaxis: Clinical manifestations, etiology, and management", section on 'Hypnotic induction agents'.)

Ketamine and propofol combination (ketofol) — The combination of ketamine and propofol ("ketofol") was developed for procedural sedation and is used by some clinicians for induction during RSI. The purported benefit of this combination is to obtain the benefits of each drug (eg, analgesic effects of ketamine), while minimizing the potential harms (eg, hypotensive effects of propofol). In addition, as both medications are potent bronchodilators, the combination may be ideal for patients with bronchospasm. Ketofol is discussed in greater detail separately. (See "Procedural sedation in adults outside the operating room", section on 'Ketamine and propofol (ketofol)'.)

Few, small studies address the efficacy of ketofol for RSI [70-74]. While sedation is reported to be adequate, ketofol does appear to cause a small decline in mean arterial pressure (approximately 2 to 6 mmHg in most studies) when used for RSI, although such declines are comparable to or less than those caused by propofol alone. As dosing varies among studies, it is difficult to determine the best approach to dosing. Further study is needed before ketofol can be recommended for widespread use with RSI.

Barbiturates — Barbiturates are no longer readily available nor widely used as induction agents for intubation. For those with access to these medications, a brief overview of their use is provided here. The ultrashort-acting barbiturates interact with the barbiturate component of the GABA receptor complex, causing profound amnesia and sedation. Thiopental sodium was the barbiturate most commonly used for RSI. The induction dose is 3 to 5 mg/kg IV, with a time to effect of less than 30 seconds, and a duration of action of 5 to 10 minutes [75]. Methohexital is another barbiturate used for induction; its induction dose is 1 to 3 mg/kg IV, with a time to effect of less than 30 seconds, and a duration of action of approximately 5 to 10 minutes. Barbiturates do not provide analgesia.

Thiopental suppresses neuronal activity, making it a useful induction agent in hemodynamically stable patients with conditions that can elevate intracranial pressure (ICP), including seizures, intracranial bleeding, or trauma. However, thiopental is a venodilator with negative cardiac inotropic effects, and can induce profound hypotension in the doses used for induction of anesthesia. Clinicians must exercise great care when using it in hemodynamically unstable patients or patients prone to hypotension, such as the elderly. For emergency RSI, a dose of 3 mg/kg is used; a reduced dose of 2 or 1 mg/kg is used in the setting of hemodynamic compromise [76]. Reductions in ICP associated with thiopental may be caused in part by a decrease in mean arterial pressure, which decreases cerebral perfusion.

Thiopental causes histamine release and can induce or exacerbate bronchospasm [77]. Therefore, thiopental should not be used in patients with reactive airway disease. Thiopental and methohexital suppress white blood cell recruitment, activation, and activity, both in vitro [78,79] and in vivo [80-82]. This effect has been attributed to a number of causes, including suppression of nuclear transcription factor [83], an increase in apoptosis [78], and a decrease in phagocytosis [79]. These immunosuppressive effects make barbiturates poor induction agents in the setting of sepsis.

CHOICE OF INDUCTION AGENT — Certain induction agents may offer advantages over others in specific clinical scenarios.

Head injury or stroke — In the patient with potentially elevated intracranial pressure (ICP) from head injury or stroke or other conditions, adequate cerebral perfusion pressure must be maintained to prevent secondary brain injury. This means avoiding significant elevations in ICP and maintaining adequate mean arterial pressure [76]. For these reasons, we suggest etomidate or ketamine be used for induction of these patients [20]. If signs of cerebral herniation are present prior to intubation, we suggest using etomidate and avoiding ketamine [49]. (See 'Etomidate' above and 'Ketamine' above and "Management of acute severe traumatic brain injury" and "Initial assessment and management of acute stroke".)

If significant hypertension (mean arterial blood pressure >120 mmHg) is present at the time of induction, etomidate is preferable, as it will not further elevate the blood pressure. In normotensive or hypotensive patients, either agent can be used. In the severely hypotensive patient, ketamine is preferable because of its superior hemodynamic profile. Ketamine's analgesic effects minimize the adverse sympathetic stimulation caused by laryngoscopy; etomidate lacks such analgesic effects.

Midazolam and propofol have been used in head-injured patients, but before doing so the risk of hypotension-induced brain injury must be considered [5,20,65,81,84-86]. If these agents are used, the dose should be reduced to minimize the risk of hypotension. However, dose reduction raises the risk of hypertension and increased ICP during and following intubation because of suboptimal suppression of the reflex responses to laryngoscopy and intubation.

Status epilepticus — We suggest propofol or, alternatively, etomidate be used for RSI of patients in status epilepticus. Propofol is a potent anticonvulsant, but dosage must be carefully calculated to avoid dose-dependent hypotension. Etomidate can cause myoclonus, and has a slightly higher rate of EEG-documented seizure activity compared with other medications [87], but may be used for RSI in status epilepticus when the patient manifests hemodynamic compromise. Etomidate use for RSI requires initiation of appropriate anti-convulsant treatment as soon as is feasible following successful intubation. (See "Convulsive status epilepticus in adults: Treatment and prognosis" and "Nonconvulsive status epilepticus".)

Midazolam may be used for induction, but care must be taken to use doses appropriate for RSI [29,30]. We suggest ketamine not be used because of its stimulant effects.

Reactive airway disease — For hemodynamically stable patients with severe bronchospasm requiring intubation, we suggest ketamine or propofol be used for induction, because of their bronchodilatory properties [23,39]. Etomidate and midazolam are acceptable alternatives. In hypotensive patients, we prefer ketamine or etomidate. None of these agents causes histamine release. (See "Management of acute exacerbations of asthma in adults".)

Cardiovascular disease — We suggest etomidate for induction of the patient with significant cardiovascular disease requiring RSI [17,18,20,88]. The hemodynamic stability it provides and the absence of induced hypertension make it preferable to other sedatives. (See 'Etomidate' above.)

In patients with coronary artery disease or suspected aortic dissection, we suggest giving fentanyl (3 mcg/kg) as a pretreatment agent to mitigate the catecholamine release associated with laryngoscopy and intubation. Pretreatment is discussed separately. (See "Pretreatment medications for rapid sequence intubation in adults outside the operating room", section on 'Choice of pretreatment agents'.)

Shock — We suggest ketamine or etomidate for induction of the patient in shock requiring RSI. (See 'Etomidate' above and 'Ketamine' above and "Evaluation of and initial approach to the adult patient with undifferentiated hypotension and shock".)

Ketamine causes a sympathetic surge that may augment endogenous catecholamines but may also elevate intracranial pressure. Etomidate has been scrutinized because of its transient suppression of endogenous cortisol. Both agents cause a small drop in MAP in patients with severe hypotension, but less than other sedative agents. These issues are discussed in detail above. (See 'Elevated intracranial pressure' above and 'Adrenocortical suppression' above.)

CONDITIONS PRECLUDING USE OF A PARALYTIC — Conditions may exist that preclude the use of a paralytic for intubation (ie, precludes rapid sequence intubation [RSI]). The clinician may then decide to use an appropriate sedative or combination of sedatives and topical anesthesia to facilitate laryngoscopy and assess the airway, while allowing the patient to maintain his respiratory drive. This approach, referred to as a "sedated look" or "awake look," is used when the clinician suspects the airway will be difficult to intubate, and allows the practitioner to verify that laryngeal structures are visible, before committing to paralysis.

The sedated look approach is distinct from the older practice of "intubation with sedation alone" or "non-paralytic RSI," in which the patient receives a full induction dose of a sedative agent, but no neuromuscular blocking agent. The older practice is to be avoided, as it creates a vulnerable, compromised patient in whom intubating conditions are far from ideal [89,90]. In general, if the clinician anticipates a difficult intubation which may preclude successful RSI, an "awake look" or "sedated look" is advised. If the clinician does not anticipate a difficult airway, RSI with a full induction dose of a sedative agent, accompanied by a full dose of a paralytic agent, is advised.

Multiple medications have been studied, primarily in the operating room, to determine which agents are appropriate for "sedated looks" [1,91-98]. In general, the use of topical anesthesia (eg, nebulized 4 percent lidocaine) along with moderate sedation allows for a look into the airway, while enabling the patient to maintain respiratory drive and protective airway reflexes.

Ketamine is gaining popularity in this circumstance because it allows the patient to maintain respiratory drive while providing analgesia, amnesia, and sedation [36,46,92,99]. Ketamine's analgesic properties allow it to be used as the sole agent in the bloody traumatized airway, when topical anesthesia is unlikely to work effectively. More research is needed to determine which sedatives are best for "sedated looks" in the emergency setting.

SUMMARY AND RECOMMENDATIONS — Rapid sequence intubation (RSI) is the standard of care in emergency airway management for intubations not anticipated to be difficult. RSI involves combining a sedative and a paralytic agent to render a patient rapidly unconscious and flaccid in order to facilitate emergency tracheal intubation and to minimize the risk of aspiration. (See "Rapid sequence intubation for adults outside the operating room" and "Rapid sequence intubation (RSI) outside the operating room in children: Approach".)

Different clinical scenarios lend themselves to the use of certain sedatives when RSI is needed (table 1). We suggest the following induction agents be used in the specific clinical circumstances described below (**Grade 2C**):

- In the patient with a head injury or potentially **elevated intracranial pressure** (ICP), adequate cerebral perfusion pressure must be maintained to prevent secondary brain injury. We suggest etomidate or ketamine for induction of these patients during RSI. For hypotensive patients, etomidate or ketamine may be used. Ketamine should be avoided in patients with hypertension (MABP >120 mmHg) or if signs of cerebral herniation are present. (See 'Head injury or stroke' above and 'Etomidate' above and 'Ketamine' above.)
- For RSI of patients in **status epilepticus**, we suggest propofol or, alternatively, etomidate be used for induction. Etomidate may be used when the patient manifests hemodynamic compromise. We suggest ketamine **NOT** be used because of its stimulant effects. Midazolam is an acceptable alternative, but care must be taken to administer an appropriate induction dose (0.1 to 0.3 mg/kg). (See 'Status epilepticus' above.)
- For the **hemodynamically stable** patient with **severe bronchospasm** requiring intubation, we suggest induction with ketamine or propofol. Etomidate or midazolam is an acceptable alternative. In **hemodynamically unstable** patients with severe bronchospasm, we suggest ketamine or etomidate. (See 'Reactive airway disease' above.)
- For induction of the patient with **cardiovascular compromise** requiring RSI, we suggest etomidate because of the hemodynamic stability it provides. (See 'Cardiovascular disease' above and 'Etomidate' above.)
- For induction of the patient in **shock** requiring RSI, we suggest ketamine or etomidate. If etomidate is used in a patient with sepsis and hypotension refractory to treatment with fluid resuscitation and a vasopressor, we suggest that a single dose of glucocorticoid (eg, hydrocortisone 100 mg IV) be given. (See 'Shock' above and 'Etomidate' above and 'Ketamine' above.)
- For induction of most patients with conditions precluding the use of paralytics in whom an "awake look" is necessary for intubation, we suggest ketamine. Ketamine may not be appropriate when these patients have cardiovascular disease or hypertension. (See 'Conditions precluding use of a paralytic' above and 'Ketamine' above.)

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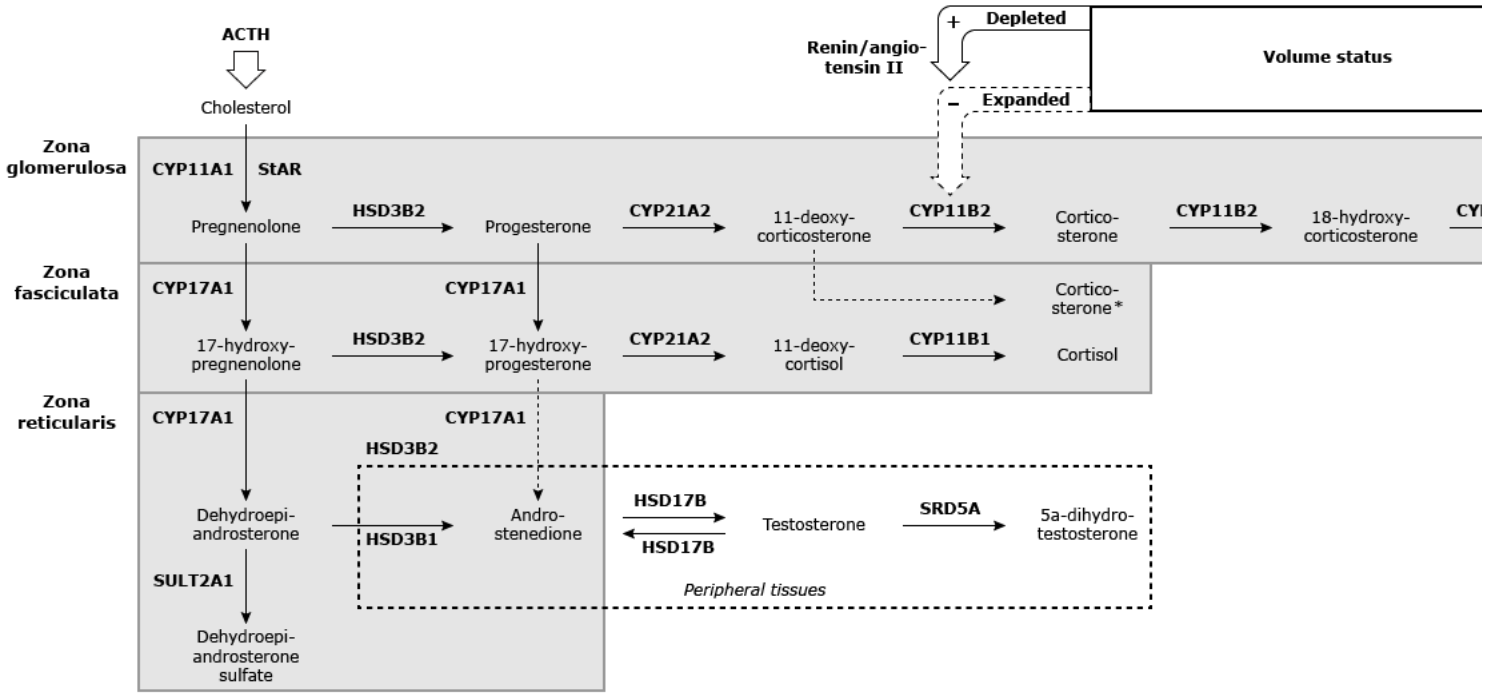
GRAPHICS

Rapid sequence intubation induction agents for adults

Drug name	Class	Benefits	Contraindications	Notes	Dose
Etomidate	Imidazole derivative	Excellent sedation with little hypotension	Known to suppress adrenal cortisol production	Use cautiously if patient has sepsis; initial dose of glucocorticoid may be needed	0.3 mg/kg
Ketamine	Phencyclidine derivative, dissociative anesthetic	Stimulates catecholamine release Bronchodilation	Use in patients with elevated ICP or elevated blood pressure is controversial	May be an excellent induction agent for patients with bronchospasm, septic shock, **AND** hemodynamic compromise	1 to 2 mg/kg
Midazolam	Benzodiazepines	Potent dose-related amnesic properties	Dose-related myocardial depression can result in hypotension	Frequently underdosed	0.2 to 0.3 mg/kg
Propofol	Alkylphenol derivative	Bronchodilation	No absolute contraindications Dose-related hypotension		1.5 to 3 mg/kg
Thiopental sodium	Ultrashort-acting barbiturate	Cerebroprotective and anti-convulsive properties	Potent venodilator and myocardial depressant; can cause hypotension Relatively contraindicated in reactive airway disease due to histamine release Acute intermittent and variegate porphyrias	May not be commercially available. Rarely used.	3 to 5 mg/kg

Graphic 64272 Version 10.0

Normal adrenal steroidogenesis



ACTH: corticotropin.
* The CYP11B1 enzyme also converts 11-deoxycorticosterone to corticosterone in the zona fasciculata, but this is ordinarily a minor pathway compared with cortisol formation, except in 17-hydroxylase d becomes the dominant glucocorticoid.

Graphic 71558 Version 5.0

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